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Rising Star Plenary Session

0-001

Peribiliary glands are key in regeneration of the biliary epithelium after severe ischemic bile duct injury during liver transplantation

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Peribiliary glands (PBG) are a source of stem/progenitor cells organized in a cellular network encircling large bile ducts. Severe ischemic bile duct injury during liver transplantation, with loss of luminal biliary epithelium, has been proposed to activate PBG, resulting in cell proliferation and differentiation to restore biliary epithelial integrity. However, formal evidence for this concept in human donor livers is lacking. We, therefore, developed a novel *ex vivo* model using precision-cut slices of extrahepatic human bile ducts obtained from discarded donor livers, providing an intact anatomical organization of cell structures, to study spatiotemporal differentiation and migration of PBG cells after severe biliary injury. Post-ischemic bile duct slices were incubated in oxygenated culture medium for up to a week. At baseline, severe tissue injury was evident with loss of luminal epithelial lining and mural stroma necrosis. In contrast, PBG remained relatively well preserved and different reactions of PBG were noted, including PBG dilatation, cell proliferation and maturation. Proliferation of PBG cells increased after 24 h of oxygenated incubation, reaching a peak after 72 h. Proliferation of PBG cells was paralleled by a reduction in PBG apoptosis and differentiation from a primitive and pluripotent (Nanog+/Sox9+) to a mature (CFTR+/secretin receptor+) and activated phenotype (increased expression of HIF-1α, Glut-1, and VEGF). Migration of proliferating PBG cells in our *ex vivo* model was unorganized, but resulted in generation of epithelial monolayers at stromal surfaces.

Conclusion: Human PBG contain biliary progenitor cells and are able to respond to bile duct epithelial loss with proliferation, differentiation, and maturation to restore epithelial integrity. The *ex vivo* spatiotemporal behaviour of human PBG cells provides evidence for a pivotal role of PBG in biliary regeneration after severe ischemic injury during liver transplantation.

0-002

Transplantation of discarded livers following viability testing with normothermic machine perfusion: the VITTAL (Viability Testing and Transplantation of mArginal Livers) trial outcomes

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Background: Assessment of livers prior to transplantation is mostly subjective and in 2017/18 in the UK, 599 livers from potential solid organ donors were not used for transplantation. Utilisation varies widely between centres. The aim of the VITTAL trial was to objectively assess donor liver viability and achieve successful transplantation of discarded livers using normothermic machine perfusion (NMP).
Method: This prospective, non-randomised, single-arm adaptive phase II trial included livers discarded by all UK centres, that met one or more specific high-risk criteria. These included donor risk index >2.0, biopsy-proven macrosteatosis >30%, transaminases ³1000IU/mL, or warm ischaemic time >30mins in livers donated after circulatory death (DCD). The viability criteria were based on the clearance of perfusate lactate to levels ≤2.5mmol/L, bile production, glucose metabolism, pH and physiological flow rates - within 4 hours of commencing NMP. Livers deemed viable were transplanted to adult first-graft recipients without portal vein thrombosis or cardiovascular comorbidities. The co-primary endpoints were liver salvage rate and recipient 90-day survival.

Results: Thirty-one discarded livers met inclusion criteria and were a suitable match for potential consented recipients. Seventeen donors after brainstem death and 14 donors following circulatory death were enrolled and perfused. Of these, 22 (71%) livers were transplanted after a median total preservation time of 18 hours, with 100% patient and graft 90-day survival. Seven (32%) patients developed early allograft dysfunction, and six (27%) patients suffered from Clavien-Dindo complications grade ³3, including four (18%) who required dialysis. During the median follow up of 297 days, 4 (18%) patients developed biliary strictures requiring subsequent re-transplantation. Matched-control comparisons at 180 days showed no differences between patient or graft survival, complication rates or hospital stay.
Conclusion: Viability testing with NMP is feasible, and the criteria safely enabled the salvage of 71% of perfused discarded livers, with 100% early graft survival.

0-003

Prospective study of stereotactic body radiation therapy as bridging therapy for hepatocellular carcinoma patients on waiting list for liver transplantation

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Background: No prospective data on stereotactic body radiation therapy (SBRT) as bridging therapy for hepatocellular carcinoma (HCC) patients on deceased donor liver transplant (DDLT) waitlist.
Objective: To investigate safety and effectiveness of SBRT as bridging treatment for HCC patients on DDLT waitlist.
Method: This was a prospective study from a university center. All HCC candidates on DDLT waitlist were prospectively enrolled for SBRT under standard protocol since 2016. Outcomes of SBRT patients were compared to a retrospective HCC cohort who was listed from 2010 to 2015. Primary safety endpoint was SBRT-related complications and efficacy endpoint was dropout rate.
Results: From 2010 to Aug 2018, there were 156 patients listed for DDLT. Thirty-one patients underwent SBRT, 37 patients had transarterial chemoembolization (TACE) alone, fifty had ablative therapy (radiofrequency ablation or high intensity focused ultrasound +/- TACE) and 38 had no bridging treatment.
Table 1 showed the baseline characteristics for all patients. SBRT patients received a median of 50Gys/ 5 fractions. None developed radiation induced liver disease (RILD) and one patient required hospitalization within 30 days after SBRT.
Overall dropout rate was 66/156 (42.3%). Dropout rate for SBRT patients was 8/31 (25.8%) and was significantly lower than patients who received other treatments [35/87 (40.2%)] and no bridging treatment [23/38 (60.5%), p=0.012].
Table 2 showed the perioperative and pathological outcomes of all DDLT patients. Pathological complete response was found in 12/20 (60%) SBRT patients. Survival from the time of listing was better in SBRT group and survival from the time of transplant was comparable to other HCC patients. (Figure1a&b)
Conclusion: This is the first and only prospective study on SBRT as bridging therapy for waitlist patients. SBRT was safe and was more effective to reduce dropout and had 60% of pathological complete response.

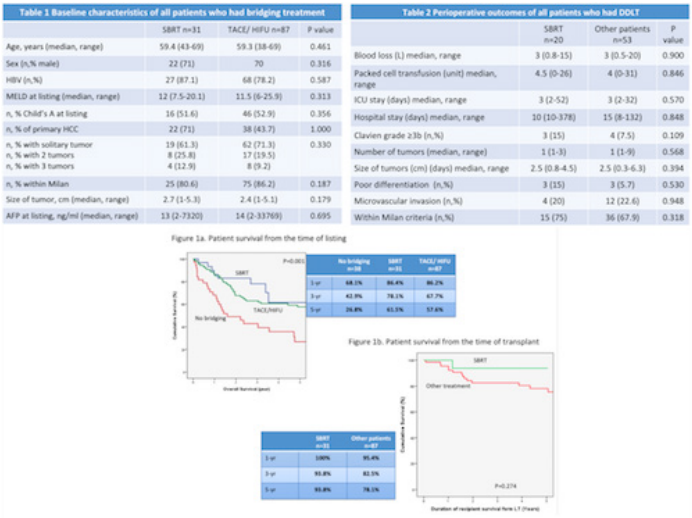

Table 1 Baseline characteristics of all patients who had bridging treatment

	SBRT n=31	TACE/ HIFU n=87	P value
Age, years (median, range)	59.4 (43-69)	59.3 (38-69)	0.461
Sex (n,% male)	22 (71)	70	0.316
HBV (n,%)	27 (87.1)	68 (78.2)	0.587
MELD at listing (median, range)	12 (7.5-20.1)	11.5 (6-25.9)	0.313
n, % Child's A at listing	16 (51.6)	46 (52.9)	0.356
n, % of primary HCC	22 (71)	38 (43.7)	1.000
n, % with solitary tumor n, % with 2 tumors n, % with 3 tumors	19 (61.3) 8 (25.8) 4 (12.9)	62 (71.3) 17 (19.5) 8 (9.2)	0.330
n, % within Milan	25 (80.6)	75 (86.2)	0.187
Size of tumor, cm (median, range)	2.7 (1-5.3)	2.4 (1-5.1)	0.179
AFP at listing, ng/ml (median, range)	13 (2-7320)	14 (2-33769)	0.695

Table 2 Perioperative outcomes of all patients who had DDLT

	SBRT n=20	Other patients n=53	P value
Blood loss (L) median, range	3 (0.8-15)	3 (0.5-20)	0.900
Packed cell transfusion (unit) median, range	4.5 (0-26)	4 (0-31)	0.846
ICU stay (days) median, range	3 (2-52)	3 (2-32)	0.570
Hospital stay (days) median, range	10 (10-378)	15 (8-132)	0.848
Clavien grade ≥3b (n,%)	3 (15)	4 (7.5)	0.109
Number of tumors (median, range)	1 (1-3)	1 (1-9)	0.568
Size of tumors (cm) (days) median, range	2.5 (0.8-4.5)	2.5 (0.3-6.3)	0.394
Poor differentiation (n,%)	3 (15)	3 (5.7)	0.530
Microvascular invasion (n,%)	4 (20)	12 (22.6)	0.948
Within Milan criteria (n,%)	15 (75)	36 (67.9)	0.318

[Table 1& 2 and Figure 1]

0-004

Impact of intraoperative portal flow on graft outcomes after deceased donor liver transplantation

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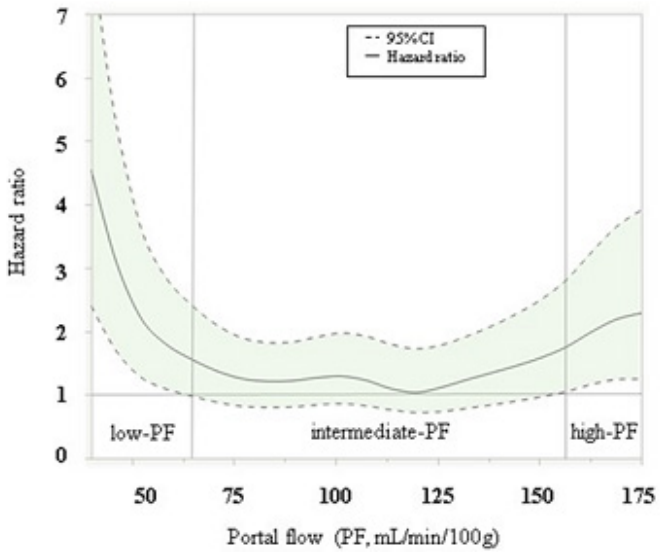
Background: Although the impact of intraoperative portal flow (PF) on graft outcomes after living donor liver transplantation is known well, its impact on whole liver graft after deceased donor liver transplantation (DDLT) remains unclear. The aim of the present study was to investigate the impact of PF on graft and recipient outcomes after DDLT.
Methods: A total of 1,001 patients who underwent DDLT at our institution between January 2007 and June 2017 were analyzed retrospectively. The patients were divided into three groups according to hazard ratio for one-year graft loss at each PF value; the low-PF group (PF < 65 mL/min/100g, n = 210), the intermediate-PF group (PF ≥ 65 mL/min/100g and < 155 mL/min/100g, n = 632) and the high-PF group (PF ≥ 155 mL/min/100g, n = 159). The graft and recipient survival, early graft function, and postoperative complications were compared between the three groups.
Results: Graft and patient survival rates in the low-PF group and the high-PF group were significantly poorer than in the intermediate-PF group. The frequency of primary non-function and early allograft dysfunction in the low-PF group were higher than the other groups (P = 0.013 and P < 0.0001, respectively). With regard to postoperative complications, the incidence rates of hepatic artery thrombosis and biliary complications in the high-PF group were significantly higher than in the-intermediate PF group (P = 0.028 and P = 0.017, respectively). Intraoperative hepatic artery flow in the high-PF group was significantly lower than the intermediate-PF group (P = 0.025).
Conclusions: Not only low PF but also high PF have negative impacts on the outcomes after DDLT. Our results highlight the importance of adequate PF in successful DDLT.



[Hazard ratio for one-year graft loss at each PF value]

0-005

Bile as a non-invasive source of cholangiocyte organoids for developing patient-specific disease models

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Introduction: Bile duct related diseases are the leading cause for pediatric liver transplantation (LT) and adult re-transplantation of a liver graft. Studying biliary diseases has been hampered by the inability to culture cholangiocytes long-term. It was shown that Extra-hepatic Cholangiocyte Organoids (ECOs), derived from extra-hepatic bile duct (EHBD) tissue can be long-term expanded *in vitro* and used for bile duct engineering. However, current applications of ECOs are limited because invasive bile duct biopsies are required to obtain ECOs from individual patients. The aim of this study is to investigate a less invasive source and test whether ECOs can be obtained from human bile samples.
Methods: Bile-derived Cholangiocyte organoids (BCOs) were cultured, according to standard protocol and collected from gallbladder bile obtained from donor liver grafts during LT and from bile obtained by endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic cholangiography drain (PTCD) in patients. Cultures were initiated from 1 ml of bile. ECOs (n=3) and BCOs (n=5) were compared for gene expression (qRT-PCR), protein level (immunohistochemistry, immunofluorescence or Western blotting) and functional level by testing cholangiocyte-specific transporter channels (Ussing chamber and transport assay).
Results: BCOs could be effectively (89% efficiency) expanded from all sources of bile from patients with a variety of diseases (primary sclerosing cholangitis, cholangiocarcinoma, bile stones and biliary stenosis after LT). BCOs expressed similar cholangiocyte markers on gene and protein level as tissue-derived ECOs and both lacked stem cell- and hepatocyte markers. Furthermore, these cells expressed and responded similarly to stimulation and inhibition of different cholangiocyte ion-channels. Interestingly, cholangiocyte-organoids from a cystic-fibroses patient lacked CFTR channel activity, showing that cholangiocyte organoids can be used for modeling biliary diseases.
Conclusion: Our study showed that bile provides a novel less-invasive source of patient-specific cholangiocyte-organoids. This creates new opportunities to develop patient-specific disease models and study autologous bile duct regeneration.

Concurrent Oral Abstract Session: Acute Liver Failure

0-006

Living donor liver transplant for ACLF with multi organ dysfunction have similar and acceptable outcomes

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Background: Acute on chronic liver failure (ACLF) patients have a significant risk of developing multi organ dysfunction (MODS). Liver transplant (LT) for severely ill ACLF with MODS (ACLF3) remains controversial. We aimed to report the results of LT in patients with ACLF3 and compared it with Non ACLF with LT and ACLF3 without LT.
Material and method: We retrospectively enrolled 288 LDLT patients from Feb 2017 to June 2018. Among them non ACLF patient with LT (NACLFT,n=211) and ACLF with LT (ACLFT, n=77). We also enrolled 62 ACLF patient who did not undergo transplant for several reasons (ACLF0, n=62) at the same period of time. 9 of 77 from ACLFT were ACLF grade 3 (ACLF3T) and 32 of 62 from ACLF0 group had ACLF grade 3 (ACLF30) as calculated by Chronic liver failure (CLIF)- sequential organ failure assessment (SOFA) score.
Results: First, we found similar outcomes between NACLF and ACLFT. We next analyzed several factors between ACLFT vs ACLF0. CLIF- C ACLF score was higher in ACLF0 group (54.33 ± 7.74 Vs 61.28 ± 7.49, P< 0.05). 1-month survival was significantly better in ACLFT group (Log rank, P< 0.0001). We next compared outcomes among ACLF3T vs ACLF30. These severely ill patients at LT, avg MELD at 36.33 ± 3.12, avg CLIF-C ACLF at 54.33 ± 7.74 were transplanted following stabilization in a mean of 11 days after admission. CLIF-C ACLF scoring was higher in ACLF3 without Ltx (54.33 ± 7.74 vs 61.28 ± 7.49, P< 0.03). 1 month survival was significantly superior in ACLF3T group (Log rank, P< 0.0001). 3 months survival and complication rate were also comparable with NACLFT group (Log rank; P=0.85). However, ACLF3T had longer hospital stay and longer follow up period compared to that of NACLFT.
Conclusion: LT strongly influences survival with acceptable outcomes in ACLF3 patient.

0-007

Multidisciplinary approach consisting of neurology-oriented intensive care, aggressive artificial liver support, and liver transplantation for pediatric acute live failure

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Background: Acute liver failure (ALF) is a life-threatening disease. Although liver transplantation (LT) is the only known curative treatment, effective artificial liver support is necessary as bridge to liver regeneration or LT in countries where donated organ is scarce. The purpose of this study was to assess our multidisciplinary approach consisting of early application of neurology-oriented intensive care, aggressive artificial liver support, and LT for ALF in the view of neurological sequelae.
Method: We conducted a retrospective cohort study for children with ALF who subsequently underwent LT between November 2005 and December 2016. Pediatric Cerebral Performance Category was assessed at December 2016 for survivors.
Results: There were 61 children with ALF who underwent LT. Age varied from one month to 12 years, with a median of 10 months. The median body weight was 8.5 kg (range, 2.7-32). The etiology of ALF was unknown in 49 children (80%). Continuous veno-venous hemodiafiltration and plasma exchange were applied to all children. The median duration after admission to LT was five days (range, 1-24). Living donor LT was performed in 59 children (92%). The graft survival rate was 77% (47/61) and the overall survival rate was 85% (52/61) in a median follow-up period of 4.2 years. 25% (13/52) of the survivors had neurological sequelae due to ALF or underlying disease, such as mitochondrial depletion.
Conclusion: Our multidisciplinary approach for pediatric ALF achieved favorable outcomes in mortality, however, 25% of the survivors sustained neurological sequelae. Further investigation is needed to evaluate the factors associated with neurological sequelae.

0-008

Impact of acetaminophen on acute liver failure of unknown cause

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Background: Acute liver failure (ALF) is a serious condition but no specific etiology is found in 25% of cases. These ALF of unknown cause (ALF-UC) have a poor prognosis and higher death rate post transplantation. The aim of this study was to evaluate if in patients who develop ALF-UC, acetaminophen use below toxicity threshold impacts on the prognosis.
Method: This study is an ancillary program from HASIPRO: a multicenter prospective French cohort study aimed to investigate prognostic factors and new etiology related to ALF-UC. ALF-UC is defined by INR up to 1.5 without any identified cause at diagnosis. To be enrolled, patients should have not taken more than 3g/day of acetaminophen and acetaminophen would not be the cause of ALF according to physicians' discretion.
Results: From june 2013 to december 2016: 27 patients (median age: 42[22-80]years; 51,85% women) took acetaminophen and 43 (45y[18-82]; 74,42%] with no acetaminophen use were included. In the acetaminophen group, patients used a median dose of 3[0,85-8]g/day. At baseline there is no significant difference between both group except a higher median AST level (2442UI/L[21-18 330] vs. 610UI/L[46-12 788];P=0.007), ALT level (2150UI/L[30-10 349] vs. 732UI/L[71-8506];P=0.005) and lower phosphatemia level (P=0.039) in acetaminophen group. Median MELD score was 27[11-40], no statistically different between both groups.
Survival rate without transplantation at 3 month wasn't different between both groups (P=0.15). In the acetaminophen group, 10 patients were transplanted and 20 in the other group (P=0.43). Death rate was 11.1% and 16.3% (P=0.73), respectively. Median time to transplantation was 4.5[1-33] days versus 3[1-48] days(P=0.47).
Conclusion: Despite a clinical-biological profile compatible with an ALF induced by acetaminophen with higher AST level and lower phosphatemia, acetaminophen alone could not explain patient's phenotype and does not impact the prognosis.
GST and NRf2 gene mutations predisposing to acetaminophen toxicity are currently on going.

0-009

A central role for macrophages pyroptosis in hepatitis B virus-related acute-on-chronic liver failure

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Background: Acute-on-chronic liver failure (ACLF) in HBV related cirrhosis is an increasingly recognized syndrome characterized by high short-term mortality and no efficacious medical treatment. Recent findings suggest that an overexuberant systemic inflammation plays a primary role in ACLF progression. However, due to lack of animal model, what underlies this transition from HBV related cirrhosis to ACLF and systemic inflammation is largely unknown.
Methods: We collected peripheral blood mononuclear cells from patients with ACLF and controls from October 2013 through October 2018 (120 patients with ACLF, 30 patients with cirrhosis with no evidence of acute decompensation and 30 healthy individuals). Relative resected diseased liver sample (cirrhosis, ACLF and donor liver) were also used for analysis.
Results: We found that accumulation of functional CD68(+) macrophages and neutrophils but not the CD4+ or CD8+ T cells in resected liver tissues and increased circulating chemokines such as IL-1β in serum from ACLF patients, which was significantly increased and associated with more severely impaired hepatic function, a higher prevalence of multiple organ failure (as indicated by higher CLIF-SOFA scores). GSDMD and its pyroptosis-inducing fragment GSDMD-N were upregulated in liver tissues of ACLF. GSDMD-N was associated with the secretion of pro-inflammatory cytokines (IL-1β, IL-6, TNF-α, MCP-1 and GM-CSF) and CLIF-SOFA scores. Immunoblotting of caspase-11 activation and GSDMD-N in macrophage of ACLF livers, but not in chronic cirrhosis and healthy human livers. Macrophages from Gsdmd(-/-) or caspase-11(-/-) mice exhibit defective pyroptosis and interleukin-1β secretion induced by cytoplasmic lipopolysaccharide. In ex vivo model, human ACLF liver was perfused by normothermic machine perfusion and whole blood, macrophage depletion reduces pro-inflammatory cytokines (IL-1β, IL-6, TNF-α, MCP-1 and GM-CSF) release, liver neutrophils accumulation and bacterial load in the perfused liver.

Conclusions: These results reveal the key role of macrophage pyroptosis induced by the caspase-11-GSDMD pathway in the pathogenesis of ACLF.

0-010

Development of a simple predictor model for transplant-free survival of childhood acute liver failure

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Background: Until the introduction of HAV universal immunization program in 2005, HAV was the main cause of pediatric acute liver failure (PALF) in Argentina.
Aims: To develop a predictor model assessing 3-months transplant-free survival in children with PALF after the elimination of HAV.
Methods: We retrospectively included 135 patients with PALF listed for liver transplantation (LT) between 2007-2016. Patients with autoimmune hepatitis (AIH), Wilson's disease (WD) or inborn error of metabolism (IEM) were classified as PALF chronic liver disease (PALF-CLD). The other patients were classified as PALF. A predictive model for transplant-free survival was developed to identify independently associated variables. Calibration and discrimination of the model were evaluated with the Hosmer-Lemeshow goodness-of-fit test and AUC. Internal validation of coefficient estimation was performed by using bootstrapping.
Results: Patients median age was 3.7 years [IQR 1.2-11.1]. Overall, most common etiologies were indeterminate (50%), AIH (23%), WD (6%) and IEM (6%). Transplant-free survival was 35%, 50% of the patients underwent LT and 15% died on the waiting list. The Kaplan-Meier survival curve showed that the 3-months transplant-free survival rate was significantly higher among patients with PALF-CLD compared to PALF (55% vs 32%, p=0.002). The model identified three risk factors associated with transplant-free survival: INR >3.5 (OR, 3.1, 95%CI, 1.34-7.2]), Bilirrubin >17mg% (OR, 4.4 95%CI, 1.9-10.3]), PALF-CLD (OR, 3.8 95%CI, 1.6-8.9). The prediction rule identified 4 risk groups according to the number of risk factors: patients with 0, 1, 2, or 3 risk factors presented a 3-months transplant-free survival rate of 84%, 58%, 25% and 11%, respectively.
Conclusion: Although limited by the lack of external validation and a small sample size, this simple risk staging system including type of PALF, INR and bilirubin, might be helpful to stratify patients with different transplant-free survival rates and may contribute to establish the optimal timing for LT.

0-011

Living donor liver transplantation for acute liver failure: experience from a large volume center

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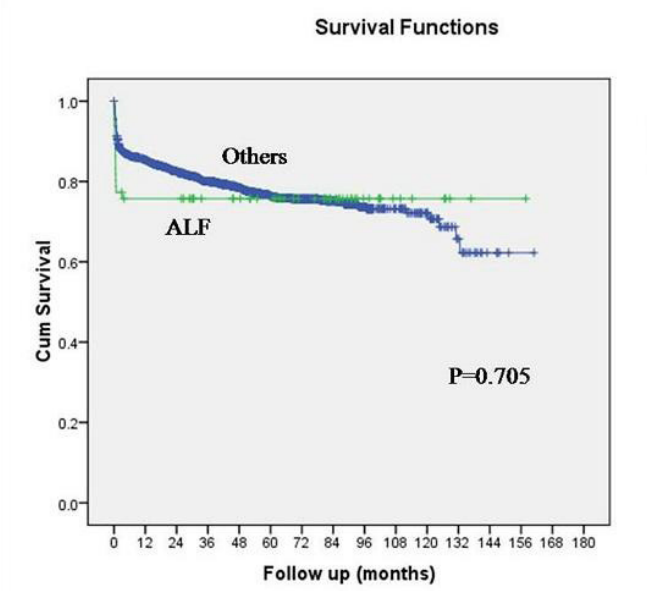
Background: Living donor liver transplantation (LDLT) for acute liver failure (ALF) is a challenging but only option in countries where deceased donation rates are low. It is not known if the metabolic need is more important than portal hypertension in determining the minimum liver graft volume in ALF setting. We present our experience of LDLT in ALF.
Methods: A retrospective analysis of database was performed. Patient selection for LDLT was based on King´s college hospital criteria. The survivors and non-survivors were compared to know factors predicting mortality.
Results: Seventy adults underwent LDLT (17 males and 53 females) for ALF. The study group aged 33.9±11.5 years; etiology of ALF was cryptogenic in 21, viral in 18 (acute hepatitis E in 9 followed by hepatitis A and B), drug induced liver injury in 18, other etiologies in 13. Admission to surgery interval was 2(1-3) days. The median (IQR) ICU stay was 5(5-7.5) days and hospital stay was 16(13-22) days. A total of 15 patients died in first month and none died thereafter during a follow up of median 63 (IQR 3-93) months. GRWR (available in 50 survivors and 14 non-survivors) was the only statistically significant factor between survivors (1.09±0.22) and non-survivors (0.87±0.15), p=0.002. A GRWR ≤0.9 predicted post transplant mortality with a sensitivity of 78.5%, specificity of 84%, negative predictive value 93.3% and positive predictive value of 57.8%. Post transplant survival was similar to transplant recipients for other non-ALF indications as shown in figure 1.



[Survival of ALF patients (n=70) a compared to other cirrhosis (n=2197) after adult LDLT]

Conclusion: A GRWR of >0.9 should be aimed in prospective LDLT recipients for ALF.

O-012

CCAAT-enhancer-binding protein homologous protein deficiency attenuated acute liver injury by promoting macrophage M2 polarization via ATG5-mediated autophagy activation

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Background and aims: Critical role of CCAAT-Enhancer-Binding Protein Homologous Protein (CHOP) have been found in mediating acute liver injury. The aim of this study is to determine the underlying mechanism of CHOP signaling in regulating innate immune activation and liver injury in a toxin-induced liver injury model.
Method: Wild-type (WT) and CHOP KO mice were subjected to a murine thioacetamide (TAA) induced acute liver injury model. Liver injury and intrahepatic inflammation were compared between groups. Bone-marrow derived macrophages (BMDMs) were isolated from WT and KO mice, and the macrophage M1/M2 phenotype was determined in vitro. Autophagy and its regulatory signaling pathways were analyzed as well.
Results: CHOP KO significantly decreased liver injury, as evidenced by lower sALT levels and better preserved liver architectures. CHOP KO mice demonstrated significantly increased intrahepatic inflammation. BMDMs from CHOP KO mice secreted much higher levels of TNF-a and IL-6, but lower levels of IL-10. CHOP KO also promoted macrophage M2 polarization as shown by increased Arg1 gene induction and CD206 staining. Interestingly, CHOP KO BMDMs showed enhanced autophagy activation as shown by LC3B staining and transmission electron microscope detection. Signaling pathway analysis revealed that ATG5 activation was enhanced in CHOP KO BMDMs. Furthermore, ATG5 knockdown by siRNA increased pro-inflammatory activation and inhibited M2 polarization in CHOP KO BMDMs. Finally, in vivo ATG5 knockdown in macrophages increased intrahepatic inflammation and liver injury in CHOP KO mice.
Conclusion: Our results indicated that CHOP deficiency promoted macrophage M2 polarization and protected livers against TAA-induced liver injury. ATG5-mediated autophagy was critical for regulating macrophage M2 activation by CHOP KO. Strategies targeting CHOP or autophagy signaling in macrophages may provide therapeutic effects against liver acute injury in patients.

O-013

Short-term outcome of living donor liver transplantation for acute liver failure: a Japanese single-center experience

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Background: The survival rate of acute liver failure (ALF) has considerably improved with the advent of liver transplantation (LT). However, its short-term outcomes are inferior to other indications. Moreover, artificial liver support followed by living donor liver transplantation (LDLT), the mainstay of treatment for ALF in Japan, remains controversial in western countries. We aimed to identify prognostic factors after LDLT for ALF.
Method: We conducted a retrospective cohort analysis of 36 consecutive adult patients undergoing LDLT for ALF between December 1998 and November 2018. Indications for steroid pulse treatment and artificial liver support (plasma exchange and high-flow continuous hemodiafiltration) before LDLT were determined on case-by-case basis per multidisciplinary discussion between the hepatologists and transplant surgeons. The patients were divided into two groups according to 6-month mortality (survival group:

survived ≥6 months after LDLT, fatal group: died within 6 months), and logistic regression/log-rank analyses were performed to investigate prognostic factors.
Results: Six patients (16.7%) died within 6 months after LDLT (fatal group). There were no statistical differences between the two groups regarding recipient age and etiology and type (acute vs. subacute depending on the onset of encephalopathy) of ALF. Pretransplant infections were more common in the fatal group ($P < 0.05$). The need for mechanical ventilation before LDLT, steroid-pulse treatment and the model for end-stage liver disease score were also comparable between groups. The median graft-to-recipient body weight ratio of the survival group was numerically greater than the fatal group (0.88 vs. 0.78, $P = 0.20$). The overall 5- and 10-year survival rates were 67.7% and 63.2%, respectively.
Conclusions: Pretransplant infections and small graft size are poor prognostic factors after LDLT for ALF. Meticulous management to minimize infection and judicious donor-recipient matching are paramount.

O-014

Low volume plasma exchange (LVPE) in the management of acute liver failure (ALF): a case series

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Introduction: Larsen et al showed high volume plasma exchange (HVPE) to be effective in the management of ALF. We hypothesized that low volume plasma exchange (30-50ml/kg/section) may be equally efficacious in ALF with less cost and less complications.
Methods: Retrospective analysis of prospective data base of patients undergoing LVPE. Patients with acute liver failure as per AASLD definition were included in the analysis. Patients with ALF and met King's college criteria were evaluated for liver transplantation. Patients who had a suitable live donor underwent liver transplantation (**Group-1**), those on deceased donor waiting list or who were too sick for transplant underwent low volume plasma exchange (LVPE) along with standard medical therapy (SMT) (**Group-2**) or standard medical therapy alone (**Group-3**).
Results: Between August 2017 and September 2018, we had 42 cases of ALF meeting AASLD definition. Of these 29 met King's college criteria for liver transplantation. [Age 9months to 58 years, M:F 14:15, Etiology- Zinc Phosphide-10, AIH-7, HAV-4, Drug-3, HBV-2, Wilson -1, Ischemic-1, Indeterminate-1]
Group-1 10/29 patients underwent live donor liver transplantation. 3month and 6-month survival in patients who underwent liver transplantation was 100%.
Group-2 10/29 underwent LVPE + SMT. 5/10 patients made a complete recovery and was taken off the waiting list and 1 patient was bridged to liver transplant. 2 patients died in hospital and 2 were discharged at request and lost follow up.
Group-3 9/29 underwent SMT alone for various personal reasons. 5/9 patients made a complete recovery.
Conclusion: In hospital mortality was 0% in liver transplant group (Group-1), 20% in the LVPE + SMT group (Group-2) and 44.44% in the SMT alone arm (Group-3). LVPE along with SMT may improve transplant free survival in patients with ALF. Further large randomized control trials are needed to evaluate the efficacy of LVPE in ALF management.

Concurrent Oral Abstract Session: Donor Selection Criteria / Patient Selection / Organ Allocation

O-015

Liver transplant candidates derive a survival benefit from accepting a macrosteatotic liver

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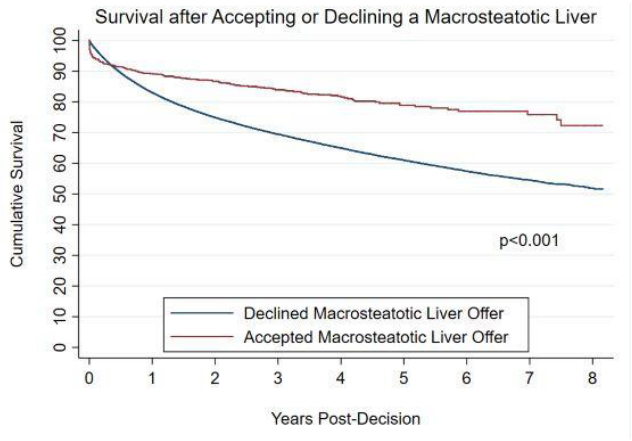

[After the first month post-decision, accepting a macrosteatotic liver graft is associated with a substantial long-term survival benefit.]

Introduction: Accepting a liver with macrosteatosis might increase the risk of adverse post-transplant outcomes, however candidates who decline must then wait for an uncertain future offer. We sought to characterize the survival benefit of accepting a macrosteatotic liver compared to declining and waiting for another offer.
Methods: We used SRTR (US national registry) data from 2010-2016 to identify candidates who were offered livers with at least moderate macrosteatosis (≥ 30% on liver biopsy) that were eventually accepted by someone. We followed candidates from the date of decision (accept or decline) until death or end of the study period, irrespective of subsequent transplantation. We used adjusted Cox regression to quantify the survival benefit of accepting a macrosteatotic liver compared to declining and waiting for another offer, and used interaction terms to determine whether this survival benefit varied by candidate age, MELD, and BMI.
Results: We identified 1,132 candidates who accepted and 31,050 who declined a macrosteatotic liver. Overall 1-year survival for those who accepted vs. declined was 89.0% vs 83.0%, and 5-year survival was 78.7% vs. 61.0% (p< 0.001) (Figure). After declining, only 44.6% of candidates were subsequently transplanted within 6 years, whereas 24.3% of candidates died, 25.8% were removed for worsening condition, and 5.3% were still waiting. Following a brief perioperative risk within the first month of acceptance (adjusted HR: $_{1.79}2.40_{3.21}$, p< 0.001), accepting a macrosteatotic liver was associated with a 65% reduced risk of mortality (adjusted HR: $_{0.29}0.35_{0.42}$, p< 0.001). This long-term survival benefit did not vary for candidates with BMI ≥ 30, MELD score ≥ 35, or age ≥ 60 years (p>0.1 for interaction terms).
Conclusion: Accepting a macrosteatotic liver was associated with substantial survival benefit, even across higher risk subgroups.

O-016

Does donor allograft microsteatosis matter? Comparison of outcomes in liver transplantation with a propensity matched cohort

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Background: Microsteatosis has previously been suggested not to negatively impact graft survival. The present study represents the largest series on donor livers with significant microsteatosis and investigates the impact of microsteatosis on peri-operative factors such as post reperfusion syndrome (PRS), early allograft dysfunction and post-operative renal dysfunction.
Methods: Clinical outcomes of all patients undergoing LT with donor livers with isolated Microsteatosis (≥30%)(N = 248) between 2000-2017 were compared to a propensity score matched cohort of patients undergoing LT with donor livers with No Steatosis(N = 248).
Results: Patients in the Microsteatosis group had a higher rate of PRS (33.1% vs. 24.2%; p=0.03), EAD (38.2% vs. 22.2%; < 0.001) and CRRT requirement following LT (10.9% vs. 3.6%; p=0.002) than the No Steatosis group. No difference in patient (p=0.33) or graft survival(p=0.18) was observed between the 2 groups. An analysis was performed to examine variables predicting graft loss in the Microsteatosis group. On multivariate Cox proportional hazard regression with backward stepwise selection, re-transplantation (HR 1.59; p< 0.001), increasing calculated MELD score (HR 1.13;p=0.01),

increasing donor age (HR1.10; p< 0.001), DCD donor (HR 1.46;p=0.003) and CIT (HR 1.05;p=0.001) were all associated with inferior graft survival
Conclusion: Recipients of donor livers with significant microsteatosis are at an increased risk of PRS, EAD, and post-operative renal dysfunction requiring CRRT. Once patients are able to overcome the initial peri-operative implications of using these donor livers, long term patient and graft survival is similar to recipients receiving grafts with no steatosis. Re-transplantation using donor livers with microsteatosis is associated with an increased risk of graft loss and should be avoided. These data suggest that the dogmatic thinking that "microsteatosis does" not matter may be only partially correct.

0-017

The impact of share 35 on LDLT utilization in the United States: analysis of UNOS data

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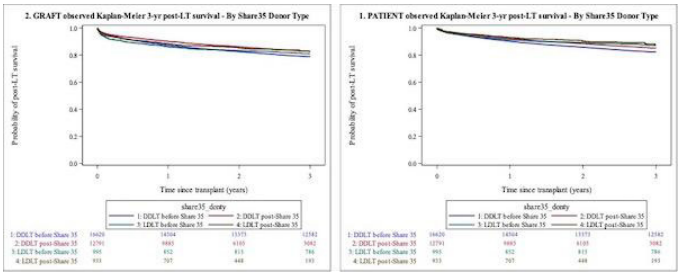
Introduction: In 2013, Share 35 was implemented in the United States (US) to improve timely liver allocation to high MELD patients awaiting liver transplantation (LT). Living donor liver transplantation (LDLT) utilization in the US is highest in high MELD regions, however the median MELD at transplant for LDLT is 15. The purpose of this study was to investigate the impact of Share 35 on LDLT utilization. We hypothesized that LDLT would increase after Share 35 to offset the shift in allocation of deceased donor livers to higher MELD patients.
Methods: United Network for Organ Sharing (UNOS) data from 2008-2018 was analyzed; 2008-2013 classified as the pre-Share 35 era, and 2013-2018 classified as post-Share 35. Among the two eras, we compared demographic data using Wilcoxon rank sum and chi-squared tests; graft and patient survival were estimated using Kaplan-Meier methods.
Results: 52,225 eligible liver transplants occurred during the study period, with 25,701 pre-Share 35 (24,701 deceased donors, 995 LDLT) and 26,524 post-Share 35 (24,706 deceased donors, 1215 LDLT). The percent of LDLT of total liver transplant volume increased significantly (4.6% post vs. 3.9% pre, p< 0.001). Post-Share 35, there was a significant improvement in graft survival among DDLT recipients at one and three years after transplant (90.1% vs. 87.2% and 82.7% vs. 78.7%, respectively, p-values< 0.001) and in patient survival at one and three years after transplant (92.2 vs. 90.1% and 85.1% vs. 82.2%, p-values < 0.001). There was no significant difference for LDLT recipients pre versus post-Share 35 (Figure 1).
Conclusion: LDLT volume increased significantly following the implementation of Share 35. DDLT outcomes post-Share 35 improved and there was no change in LDLT outcomes, suggesting that Share 35 is not compromising survival.



[Figure 1]

0-018

Donor quality (DQ) score and prediction of graft failure after LT: how far can an organ travel with excellent outcomes

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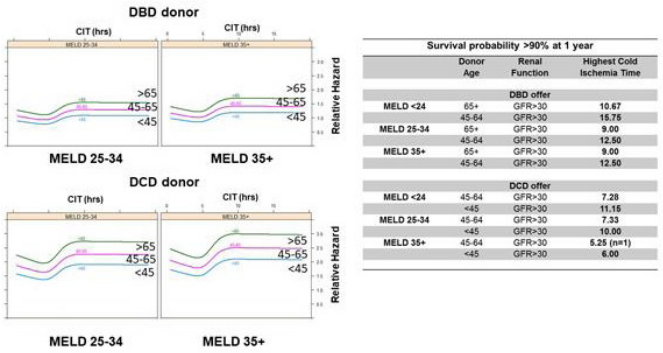
Background: Current donor risk models were developed in pre-MELD era and had less sick recipients. Further, the new liver distribution policy (Dec 2018) emphasizes distance from donor hospital. We sought to
(1) create/validate a novel model for donor quality (DQ score)
(2) assess the farthest a donor organ can travel with acceptable results.
Methods: We examined all non-HCV patients (2002-2015). We assessed the impact of donor factors on graft failure within 1 year. Continuous predictors were transformed using restricted cubic splines functions and modeled as non-linear predictors. The final parsimonious model included donor age and donor kidney function (surrogates of organ quality), DCD, and CIT. The model was validated for calibration and discrimination ability using bootstrapping.
Results: The model had excellent calibration (optimism corrected slope 0.96, ideal model slope =1) in identifying predicted versus observed outcomes. **Figure 1** shows hazard of death after considering CIT, type of donor and MELD score. E.g. for a DBD offer for MELD 35+, a CIT of 10 hours is associated with HR 1.7 for an older donor (>65 years) but 1.2 for younger donor (< 45 years). **Table 1** shows representative examples of how far an organ can travel based on DQ score stratified by MELD score. To achieve 90% survival,

a 65-year DBD donor with GFR>30 may travel 10.67 hours (MELD < 24) or 9.0 hours (MELD 35+). A 45-year DCD donor with GFR>30 may travel 7.3 hours (MELD < 24) or 5.2 hours (MELD 35+).
Conclusion: The DQ score predicts graft failure after LT and may help augment clinical decision making regarding how far an organ can travel with excellent outcomes. This tool may help clinicians accept organs in the setting of the recently approved liver distribution policy in US.



Survival probability >90% at 1 year

	Donor Age	Renal Function	Highest Cold Ischemia Time
		DBD offer	
MELD <24	65+	GFR>30	10.67
	45-64	GFR>30	15.75
MELD 25-34	65+	GFR>30	9.00
	45-64	GFR>30	12.50
MELD 35+	65+	GFR>30	9.00
	45-64	GFR>30	12.50
		DCD offer	
MELD <24	45-64	GFR>30	7.28
	<45	GFR>30	11.15
MELD 25-34	45-64	GFR>30	7.33
	<45	GFR>30	10.00
MELD 35+	45-64	GFR>30	5.25 (n=1)
	<45	GFR>30	6.00

[Figure: Relation between Donor age, CIT, MELD; Table: Maximum Cold Ischemia Time for >90% survival]

0-019

Liver transplantation using pre-conditioned hypoxic donor livers is a safe way to increase the donor pool - a case controlled study.

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Introduction: Liver grafts from hypoxic donors (ligature asphyxiation, out of hospital cardiac arrest - downtimes > 30minutes) are high risk not often utilised for liver transplantation. However, hypoxic donor livers are considered pre-conditioned particularly if liver enzymes are improving pre-retrieval. The aim of the study was to compare outcomes of liver transplantation from hypoxic and non-hypoxic donors.
Methods: Retrospective study of adult liver transplants (LT) from hypoxic donors - (Group A) between 2014 and 2018. Parameters evaluated were short- term outcomes, survival, donor AST at presentation and pre-retrieval, recipient peak AST and AST at Day 7. Outcomes were compared with a matched cohort of non-hypoxic DBD donors (Group B).
Results: A total of 782 LT were identified of which Group A (hypoxic donors) consisted of 140 patients (73.2% DBD) with a mean age of 44.8 years. Initial donor AST was 456±509 (mean±SD), (range: 103-3994). The pre-retrieval AST 203±199 (range: 34-1557) (Wilcoxon Signed Ranks: $p< 0.0001$), with an average decrease of 47.63%. Initial donor AST did not correlate with AST on day 1 or day 7 (Spearman: $p=0.935$ and 0.761 respectively). We matched 140 non-hypoxic DBD donors with mean age 53.2±15.7 years (Group B). AST values did not differ between the 2 groups (day 1 or day 7) post liver transplantation (Mann-Whitney: $p=0.555$ and $p=0.866$) (day 1: median ± SEM: 866±2988 vs 788±1295, day 7: 61±66 vs 58±123, respectively). Decrease of AST between day 1 and day 7 in group A and group B was not significant (92.3%±13.6 vs 91.5%±15.6 respectively). Both study groups had no primary non- function. Kaplan Meier analysis revealed no difference in graft or patient survival between 2 groups (Log Rank (Mantel-Cox) $p=0.07$ & $p=0.065$, respectively).
Conclusions: Hypoxic donors with downward trending pre-retrieval AST can be considered for LT with comparable outcomes to non hypoxic DBD donors.

0-020

Development of a model based on case-mix analysis to predict 6-month patient survival and identify futility after liver transplantation: a multicenter Italian study

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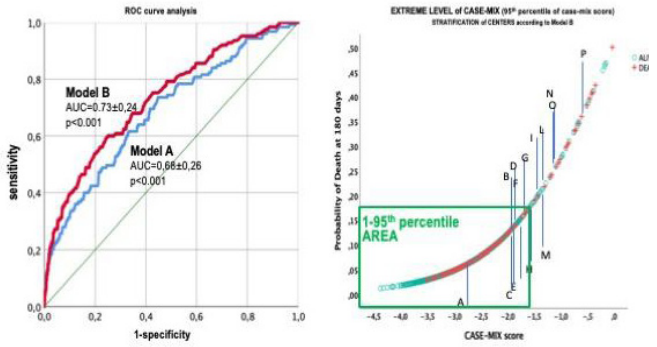
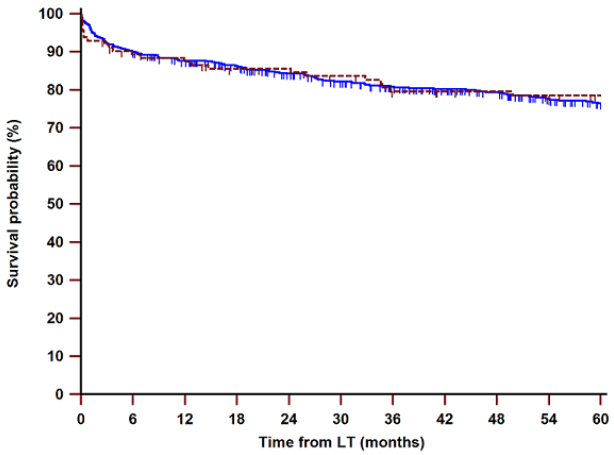
Short-term patient survival (PS) after liver transplantation (LT) is predicted by MELD. The study aimed to identify, besides MELD, factors predicting 6- and 12-month PS after LT, in order to develop case-mix models. Primary endpoint was 6-month PS; secondary end-points were 6-month graft survival and 12 month PS. LT was considered futile if associated with 5 years PS < 50% and/or 6 months PS < 60%.

From 2016 to 2017, fourteen Italian LT Centers collected recipient and donor characteristics of 1680 consecutive adult LT recipients with a median follow-up of 15 months. Furthermore, intraoperative parameters were included.
At univariate analysis, factors significantly associated with PS after LT were: MELD (p< 0.001); PV Thrombosis (PVT) Yerdel 3-4 (p=0.002); dialysis (DIA) (p< 0.001) and mechanical Ventilation (MV) 72h before LT (p< 0.001); recipient age (p=0.067); packed red blood cells units (PRBCu, Class 6-10: p< 0.001; Class 16-20: p< 0.001; Class >20: p< 0.001) and packing (PA) at the end of surgery (p< 0.001). At the multivariate analysis, 2 predictive models for 6 and 12 months PS after LT (model A, for pre-LT and model B for both pre and post-LT) were identified.
In the model A, the predictive variables were MELD score (p< 0.001); PVT (p=0.013); DIA (p< 0.001); MV (p=0.016) and recipient age (p=0.034). In the Model B, MELD score (p=0.009); DIA (p< 0.001); MV (p=0.019); PRBCu (Class 6-10: p=0.013; Class 16-20: p=0.007; Class 20 and over: p=0.005); PACKING (p=0.006) and recipient age (p=0.043) were identified as predictive factors for 6 months PS after LT. Accordingly, in the final model B based on the case-mix analysis, for each patient (or Center) a risk-score was calculated.
The aforementioned recipient characteristics may be useful to prevent futile LT.
[ROC & risk curve]



[ROC & risk curve]

Background: Due to organ shortage, the use of steatosic donors is a forced option to decrease waiting list mortality. However, admitted steatosis grade and survival outcomes of liver transplantation (LT) with steatosic grafts remain controversial.
Methods: Data were retrieved from the prospectively maintained databases of two Italian liver transplant centers (Bergamo and Ancona), including LTs from January 2000 to September 2018.
At the time of procurement, each organ was evaluated with biopsy; the study group included grafts with steatosis ≥ 30% (IQR: 30-80%). The study considered all first, adult, non-urgent, ABO-identical liver transplants. Among 709 recipients included, 113 (15.9%) received a steatosic graft and 596 a non-steatosic graft . All data related to the recipient (LT-year, age, gender, liver disease etiology, presence of HCC, lab-MELD) and to the donor (gender, cause of death, Na peak, BMI, anti-HBc positivity, cold ischemia time) were collected.
Results: After a median follow-up of 71.4 (IQR: 0.1-223.3) months, overall patient survival (OS) was 1- 3- and 5-year was 87.7%, 80.6% and 76.8%. The analysis in the two groups showed a OS in the steatosic group of 87.4%, 79.6% and 78.5% vs 87.7%, 80.8% and 76.5% in the non-steatosic group, respectively at 1-3 and 5 years (log-rank p-value:0.65). Early (within 30 days) re-LTx rate in the steatosic group was 0.7 % instead of 4.1% in the control group. Subgroup analysis revealed similar 5-year survival outcomes when steatosic grafts were allocated in higher (≥25) MELD recipients. Results were stratified on the gravity of steatosis (from 30% to 80%). After multivariate analysis, there was no independent prognostic factor for graft loss.
Conclusions: Use of steatosic grafts, even when the grade is very high (80%), is not associated with a worse outcome.



[OS steatosic grafts vs non- steatosic grafts]

0-021

Liver transplantation with fatty graft: how far can we push the steatosis limit?

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0-022

Justification of choosing liver resection or liver transplantation for hepatocellular carcinoma within Milan and UCSF criteria with normal, medium, high and very high AFP

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Introduction: Liver transplantation (LT) is the best treatment option for hepatocellular carcinoma (HCC). This study aimed to compare the long-term outcome of liver resection (LR) and LT with different levels of AFP.
Methods: Prospectively collected data of patients suffering from HCC who had undergone either primary LR or LT at our hospital from 1995 to 2017 were reviewed. Tumors which were within Milan or UCSF criteria were included. They were stratified according to level of AFP, normal (< 10ng/mL), medium (≥ 10 to < 400 ng/mL), high (≥ 400 to < 1000 ng/mL) and very high (≥ 1000 ng/mL). The Kaplan-Meier method was used for survival analysis and the log-rank test was used for survival comparison.
Results: During the study period, there were 911 patients underwent LR and 196 patients underwent LT. LR patients had better liver function, better Child grading, creatinine, platelet, INR and liver function test (p< 0.001). Patient underwent LR had fewer complications and shorter hospital stay (8 vs 16 days). There was no difference in hospital mortality. 3% (p=0.029) patients in LR had margin involvement. Patients in LT who had normal and medium level of AFP had better 5-year disease-free and overall survival (LR >72.3% vs LT 86.8%, p< 0.001). However, for high to very high AFP level, there was no difference in overall survival. Multivariate analysis suggested the size and number of tumor, and the grouping of AFP levels were the independent predictors of the overall survival. An equation was further formulated to predict the overall survival after different surgical treatments.
Conclusion: LT offered better survival than LR for patients who suffered from HCC with normal and medium AFP. However, for those with high and very high AFP, the overall survival is going to be poor anyway, offering LT might not be beneficial.

0-023

Prospective validation of our new selection criteria considering pre-transplant body compositions in living donor liver transplantation

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Background: We reported that preoperative sarcopenia was an independent risk factor in living donor liver transplantation (LDLT). In the present study, we established new selection criteria for LDLT considering pre-transplant body compositions and prospectively validated the usefulness of the criteria.
Methods: 1) Establishment: We evaluated pre-transplant skeletal muscle mass, muscle quality, and visceral adiposity using skeletal muscle mass index (SMI), intramuscular adipose tissue content (IMAC), and visceral-to-subcutaneous adipose tissue area ratio (VSR) for 277 consecutive patients who underwent adult LDLT between January 2008 and July 2016. We investigated the impact of these three parameters on survival after LDLT. Based on the findings of this study, we have implemented new selection criteria for LDLT since October 2016.
2) Validation: We examined overall survival of 45 consecutive patients who underwent adult LDLT between October 2016 and November 2018.
Results: 1) Establishment: Overall survival rates of patients with low SMI, high IMAC, and high VSR (abnormal factors) were significantly lower than those with high SMI, low IMAC, and low VSR, respectively. On multivariate analysis, low SMI, high IMAC, and high VSR were identified as independent risk factors for mortality after LDLT. One-year overall survival rate of patients with no, one, two, and three abnormal factors were 98%, 78%, 60%, and 41%, respectively. Based on these findings, we have established new selection criteria for LDLT: to exclude patients with three abnormal factors, and to perform perioperative nutrition and rehabilitation therapy especially for patients with one or two abnormal factors.
2) Validation: Among 45 patients, 23 patients had no abnormal factor, 17 patients had one abnormal factor, and 5 patients had two abnormal factors. One-year overall survival after LDLT under new criteria was 98%.
Conclusion: We have first established and implemented new selection criteria for LDLT considering pre-transplant body compositions and validated the usefulness of the criteria.

Concurrent Oral Abstract Session Basic Science / Translational Research

0-024

Design by nature: creating a clinical grade hydrogel from liver extracellular matrix to improve culture expansion and differentiation of human liver organoids

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Erasmus University Medical Center Rotterdam, Surgery, Rotterdam, Netherlands

Introduction: Human LGR5+liver organoids have great potential for personalized regenerative medicine or liver tissue engineering purposes. Culture of organoids is conventionally performed in non-clinical grade hydrogels derived from mouse tumor basement membrane extracts, such as Matrigel. These basement membrane extracts maintain 'stemness' of progenitors, thereby inhibiting differentiation towards functional hepatocytes. The aim of this study is to create a clinical grade hepatic micro-environment from human liver extracellular matrix (ECM), which is suitable for culture and differentiation of human liver organoids.
Methods: Human livers, discarded for transplantation, were decellularized via perfusion with a Triton X-100 solution. Decellularized ECM was milled to a fine powder and digested in a 10(W/W) % pepsin solution in 0.1M Acetic acid for 72 hours. After pH correction the viscous pre-gel solution formed a hydrogel at 37°C. This gel was characterized as composition and stiffness were determined. Human liver organoids were cultured in mouse or liver hydrogels and analyzed for proliferation and differentiation capacities (n=5).
Results: Human liver-derived hydrogel mainly consists of collagens and was significantly stiffer (300-400Pa) compared to Matrigel (100Pa). Liver organoids grew efficiently in the liver hydrogel and could be passaged multiple times. Metabolic assays showed similar cell proliferation in matrigel and human liver hydrogels. However, human liver hydrogels improved the differentiation of liver organoids towards hepatocytes. The gene expression for albumin after differentiation was 15-fold higher compared to matrigel conditions.
Conclusion: This study shows the feasibility of creating a hydrogel from human liver-ECM that support the proliferation and differentiation of human liver organoids. This human liver hydrogel could provide an important step forward in the clinical application of human liver organoids for tissue engineering and regenerative medicine.

0-025

A novel plasma inflammatory fingerprint predicting hepatocellular carcinoma recurrence after liver transplantation

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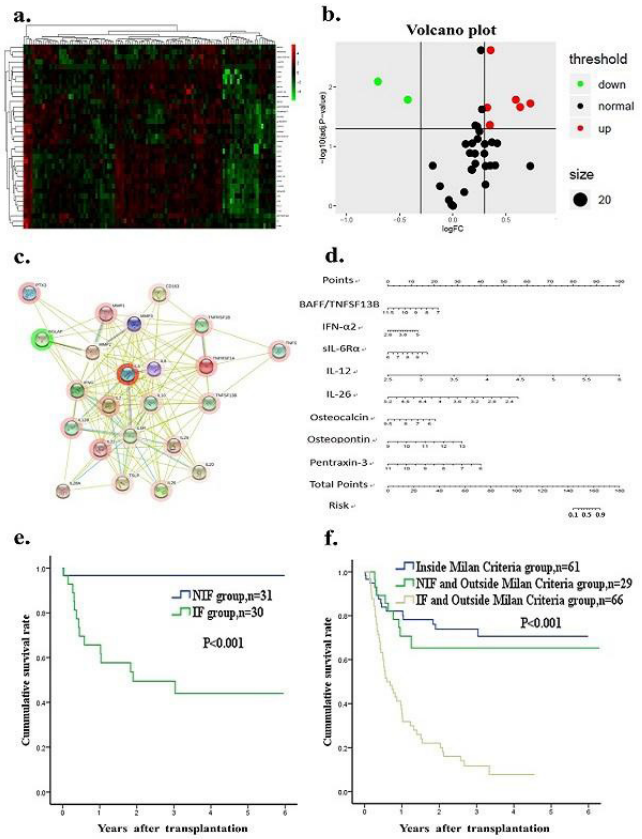
Background: Our study aims to build an effective fingerprint to evaluate the risk of hepatocellular carcinoma (HCC) recurrence after liver transplantation based on plasma inflammatory profiling.
Methods: This study enrolled 156 HCC patients undergoing liver transplantation. We detected 38 inflammation-related markers in the pre-operative plasma of those patients using Bio-Plex Pro™ Human Inflammation Assays and Elisa assay.
Results: All the 38 inflammation-related factors were analyzed and shown by heatmap and volcano plot (Figure a and b). Univariate analysis screened out 28 molecules as risk factors for post-transplant recurrence ($p< 0.01$), a Protein protein interaction (PPI) network was constructed to show the connections in between (Figure c). The differential molecules (AFP et al.) were thereby enrolled into multivariate analysis, which, in turn, identified 9 independent risk factors. And they were BAFFTNFSF, IFNα, sIL6Rα, IL12, IL26, Osteocalcin, Osteopontin, Pentraxin and AFP. Accordingly, a fingerprint was established as a nomogram (Figure d). According to this fingerprint/nomogram, we stratified the patients into the NIF group (Non-Inflammatory, n=60) and IF group (Inflammatory, n=96). The patients in the NIF group had lower post-transplant recurrence risk compared to the IF group ($p< 0.001$). In the patients fulfilling Milan criteria(n=61), the NIF subgroup had remarkably reduced recurrence risk compared to the IF group (5-yrs RFS rate: 96.8% vs 44.0%, $p< 0.001$, Figure e). In the patients exceeding Milan criteria(n=95), we also found reduced risk of recurrence in the NIF subgroup (n=29, $p< 0.001$). These identified 29 patients outside Milan criteria had acceptable post-transplant outcomes comparable to those inside Milan criteria (5yrs RFS rate: 70.7% vs 65.3%, Figure f)
Conclusion: Our pre-operative serum fingerprint is powerful in predicting post-transplant recurrence risk and will be helpful guiding candidate selection and anti-cancer treatments.



[A plasma fingerprint for hepatocellular carcinoma in liver transplantation]

0-026

Human mesenchymal stem cells for the treatment of steatohepatitis

Perroud E.[1], Montanari E.[1], Gonelle C.[1], Muller Y.[2], Gerber S.[3], Modarressi A.[1], Laumonier T.[1], Negro F.[1], Buhler L.[1], Clement S.[1], Meier R.[1,2]

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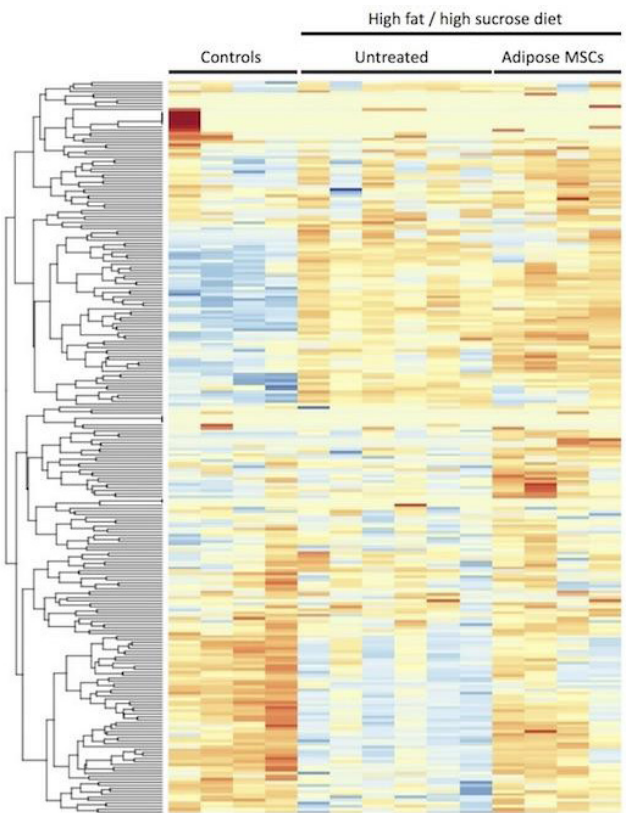
Background: Non-alcoholic steatohepatitis (NASH) is a fatty liver disease characterized by inflammation of the liver, eventually leading to complications such as cirrhosis and hepatocellular carcinoma. Factors secreted by mesenchymal stem cells (MSCs) have potential anti-inflammatory effects for liver repair and regeneration. We thus hypothesized that the anti-inflammatory molecules secreted by human MSCs may decrease liver inflammation in the context of NASH.

Methods: Hepatic stellate cells were cultured in conditioned medium of human bone marrow or adipose tissue-derived MSCs and alpha-smooth muscle actin (α-SMA) expression was assessed. NASH was induced by 25 weeks of high-fat high-sucrose diet in mice and animals were treated with human adipose tissue- or bone marrow-derived MSCs encapsulated in calcium-alginate microspheres. Untreated mice were used as control. Weight change and insulin resistance profile were assessed in the livers of these mice. The expression of 278 genes related to inflammation, lipid metabolism and fibrosis was assessed using microarray.

Results: Activated stellate cells exposed to MSC-conditioned medium showed reduced α-SMA expression. *In vivo*, transplantation of encapsulated adipose tissue-derived MSCs in high-fat high-sucrose fed mice reduced weight gain (+80±17% vs. +106±9%, p< 0.001) and plasma insulin (35±16mIU/L vs. 158±59ug/L, p< 0.001) as compared to untreated high-fat high-sucrose fed mice. The treatment with encapsulated adipose tissue-derived MSCs could partially reverse the gene-expression signature associated with high-fat high-sucrose diet (Figure). Encapsulated bone marrow-derived MSCs had similar effects.

Conclusion: Transplantation of encapsulated human MSCs appears to have a protective effect in a mouse model of NASH.



[Heatmap showing the expression of 278 genes related to nflammation, lipid metabolism and fibrosis]

0-027

Rat liver scaffolds selectively re-endothelialized with human vascular endothelial cells support perfusion with human blood

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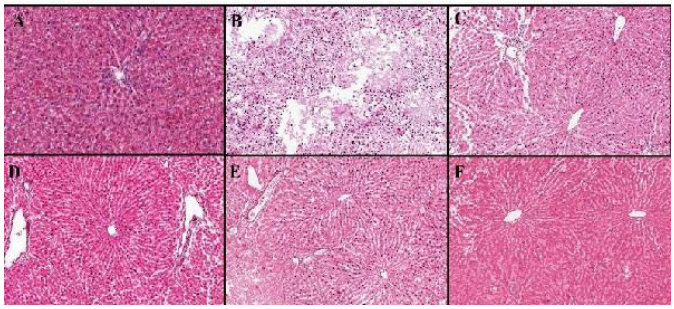
Background: The endothelium lining the vasculature tree of a transplanted liver provides the site of the initial interaction between the recipient immune system and the transplanted organ. This interaction is particularly critical in xenotransplantation, where preformed antibodies to donor antigen elicit hyperacute rejection in most instances. Replacement of the donor endothelium with recipient-type endothelium could attenuate this reaction and have profound implications on immunosuppression following transplantation.
Methods: Rat livers were procured using aseptic technique (n=10). Native endothelium was stripped while leaving hepatocytes intact utilizing a brief exposure to 0.1% SDS perfusion using our established bioreactor perfusion system. Human umbilical vein endothelial cells (HUVECs) were then introduced into the de-endothelialized livers, and perfused with culture media for 24 hours. Re-endothelialized grafts were then perfused with human blood, and examined at 1, 6, and 18 hours.
Results: Livers treated briefly with 0.1% SDS showed complete de-endothelialization without massive disruption of hepatic structure or affecting viability of the majority of hepatocytes as compared to native liver (Figure 1A, 1B). HUVECs engrafted successfully onto the de-endothelialized construct (1C). The re-endothelialized rat liver supported perfusion with human blood at 1, 6, and 18 hours without thrombosis (1D, 1E, 1F). CD-31 staining demonstrated human cells lining the vascular endothelium after re-endothelialization.
Conclusions: Rat liver endothelium can be manipulated to support human endothelial cells. These constructs support perfusion with human blood. This method demonstrates the ability to alter a key component of the immune response to xenogeneic antigen.



[Figure 1]

0-028

Early reduction of regulatory T cells by calcineurin inhibitor predicts acute graft rejection in liver transplantation

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Background: Regulatory T cells (Tregs) are important in preventing acute rejection in solid organ transplantation, but different kinetics of Treg population after liver transplantation (LT), and its clinical relevance are still unclear.
Method: We longitudinally investigated frequency and phenotypes of Tregs in the discovery and validation cohorts of LT under the tacrolimus-based immunosuppression using flow cytometry.
Results: We found that Treg and activated Treg (aTreg) frequency in CD4+ T cells were significantly reduced at D7 only in the rejectors, and their frequency at D7 was lower in the rejectors than in the non-rejectors. Treg and aTreg frequency at D7 could predict acute rejection, and recipients with the lower Treg and aTreg frequency at D7 were at high risk of acute rejection in the discovery and validation cohorts. Early reduced Treg frequency in the rejectors was associated with the reduced CD25 level of Treg at pre-transplantation, which was correlated with the reduced pSTAT5 level of Treg at D7, and increased Treg apoptosis at D7. Because Treg frequency was inversely correlated with serum tacrolimus level, we performed mixed lymphocyte reaction (MLR) assay using PBMCs from recipients and matched donors, and found that Treg reduction by tacrolimus was more prominent in rejectors, which was associated with compromised suppressive effect of tacrolimus on the allo-immune T-cell responses and could be complemented by rapamycin or IL-2 treatment.
Conclusion: Our results suggest that the Treg frequency should be monitored from the early time-point of LT not only for predicting acute rejection, but also for establishing more optimal recipient selection for Treg supporting therapies and more optimal immunosuppression protocols in LT.

0-029

RAPID enhances liver regeneration of small-for-size graft through upregulation of M1-type macrophage activation

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Background and purpose: The RAPID concept (Resection And Partial Liver Segment 2/3 Transplantation With Delayed Total Hepatectomy) is a novel transplantation technique utilizing an auxiliary segment 2+3 donor graft that expands to a sufficient size over 2-3 weeks and thereby allows a two stage hepatectomy in non resectable tumors of the liver[1]. Details of the underlying mode of liver regeneration in the RAPID protocol are still unclear. The aim of this study was to establish a simulated RAPID model in rats to explore the mechanism accounting for liver regeneration.
Methods: The previous ALPPS model with rats [2] was modified to mimic the procedure of RAPID, where a small FLR undergoes cold ischemia/reperfusion injury, and the rest liver is deportalized before the further resection (Group RAPID). Control animals were treated with 70% hepatectomy and the same size of FLR (Group Hepatectomy). In order to compare the profiles of sinusoidal injury and liver regeneration, samples of liver and blood were harvested before surgery, at day 1, 3 after step I surgery, and day 1, 3, 7, 21 after step II surgery in RAPID group for the further investigation.
Results: Sinusoidal injury following step I surgery in RAPID group was not notable compared with Hepatectomy group ($P< 0.05$) in Figure 1, indicating a well-preserved function of SFS liver after RAPID protocol. Regeneration parameters, KGR, LBW, Ki-67 and PCNA after step I surgery in RAPID group were higher than after Hepatectomy group. Phenotype of pro-inflammatory macrophage (M1), CD68 and iNOS, and plasma TNF-alpha and IL-6 were significantly up-regulated in RAPID.
Conclusion: The surgical model with rats provides a suitable model to simulate RAPID and to study the mechanism of liver regeneration in RAPID. Enhanced liver regeneration of SFS liver may be related with upregulation of M1-type macrophage activation.

0-030

HEMO2Life® attenuates the ischemia-reperfusion injury by decreasing ROS production during static cold storage in steatotic livers

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Background: Increase in the indications of liver transplantation, the organ shortage and the global epidemic of nonalcoholic liver disease have pushed innovation to develop new strategies to preserve steatotic livers. Great results in preserving other organs have been showed when $HEMO_2Life$® (natural oxygen carrier extracted from the marine invertebrate *Arenicola marina*) is used during static cold storage (SCS).
Methods: 36 livers from obese Zucker rats were procured and divided into three groups: sham, 24h SCS and 24h SCS + $HEMO_2Life$® at 1g/L, mimicking the gold standard of organ preservation. Ex situ machine perfusion for 2h was used to evaluate its quality. Regular perfusate sample for functional assessment and biochemical analysis (transaminases ALT-AST, Glutamate dehydrogenase -GLDH, lactate) and subsequent biopsies were done (Malondialdehyde -MDA, HMGB1, Nitrite-Nitrate -NO_2-NO_3, Bcl-1, Caspase-3).
Results: Transaminases, GLDH and lactate levels at the end of reperfusion were significantly lower in the group preserved with $HEMO_2Life$® ($p< 0.05$). Protection from reactive oxygen species (low MDA and higher production of NO_2-NO_3) and less inflammation (HMGB1) was also observed in this group ($p< 0.05$). Bcl-1 and Caspase-3 were higher in the 24h SCS group ($p< 0.05$) and presented more histological damage compared to those preserved with $HEMO_2Life$®.
Conclusion: These data demonstrate for the first time that the implementation of $HEMO_2Life$® to the preservation solution significantly protects steatotic livers during SCS by decreasing reperfusion injury and improving graft function.

0-031

Plasmacytoid dendritic cells promote hepatocellular carcinoma recurrence after liver transplantation

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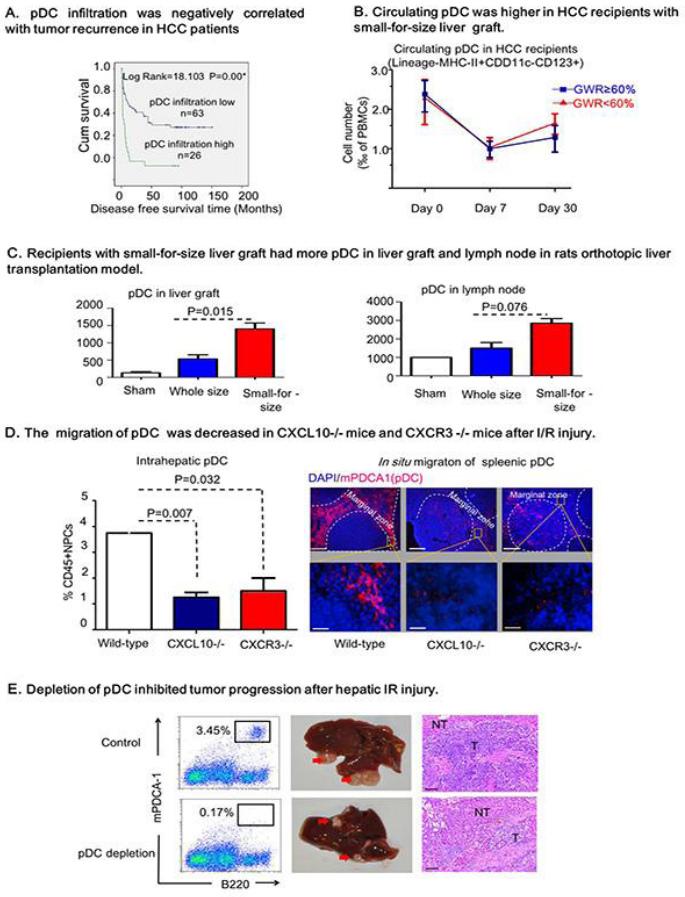
Background: Post-transplant tumor recurrence affects the long-term survival of recipients with hepatocellular carcinoma (HCC). However, its underlying mechanism remains largely unclear. Previously, we found early phase liver graft injury mediates post-transplant tumor recurrence via CXCL10/CXCR3 signaling. Plasmacytoid dendritic cell (pDC) is a unique DC subset that producing type I interferon, which has an immunosuppressive property in the tumor microenvironment. In this study, we aim to investigate the role and mechanism of pDC on tumor recurrence after liver transplantation.

Methods: The correlation between pDC and tumor recurrence was investigated in patients underwent curative HCC resection. The phenotype of pDC was studied in liver transplant recipients with HCC and rat orthotopic liver transplantation models. The direct role of CXCL10/CXCR3 signaling on pDC migration was investigated in CXCL10-/- mice and CXCR3-/- mice. The role of pDC on tumor progression was further investigated in mouse orthotopic liver tumor model.

Results: Clinically, pDC infiltration was negatively correlated with disease-free survival in HCC patients (5.65±2.30 vs. 50.53±8.89 months, P＜0.001, **fig 1A**), more circulating pDC was detected in recipients with GWR < 60% graft at day 30 after liver transplantation (**fig 1B**). In rats OLT model, there were more pDC both in liver graft (P=0.015) and draining lymph nodes(P=0.076) of the recipient with small-for-size liver graft (**fig 1C**). CXCR3 was predominantly expressed in pDC. Both of the intragraft infiltration of pDC and *in situ* migration of splenic pDC was significantly reduced after liver injury both in CXCR3-/- mice and CXCL10-/- mice compared to wild-type controls (**fig 1D**). The depletion of pDC attenuated orthotopic liver tumor growth in mice after hepatic IR injury with major hepatectomy (**fig 1E**).

Conclusion: pDC recruited through CXCL10/CXCR3 signaling at early phase liver graft injury may promote late phase tumor recurrence.



[pDC promote HCC recurrence after liver transplantation]

O-032

Hepamine 2.0

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Motivation: Throughout the past two decades, numerous gene expression profiling data on literally all liver diseases were stored in public databases. These data contain deep insights into the molecular development of liver diseases, support the development of molecular diagnostics and ultimately promote precision medicine in hepatology. However, once published most of these data remain idle. Only very few data were used for additional analyses or comparative projects. This may mostly be due to the limited bioinformatics knowledge of most biomedical research personnel. In order to overcome this barrier and to support an easy translation of bioinformatics data into translational hepatology research, we created Hepamine, a liver disease microarray database, visualization platform and data-mining resource.
Methods: Microarray data were obtained from the ArrayExpress Archive of Functional Genomics Data (http://www.ebi.ac.uk/arrayexpress). Pre-analysis of expression data was performed using R statistical software and microarray analysis packages from the Bioconductor repository (https://www.bioconductor.org). Expression data were stored locally in a MySQL database.
Results: We have generated Hepamine, a web-based repository of pre-analyzed microarray data for almost all common liver diseases. Further development was influenced by optimization the access and visualization of the data. Filtering and visualization options of the data were optimized and individual configuration enabled. We also provide predefined gene sets to select pathways from KEGG and Wikipathways. A simple three color visualization table is retained for getting a fast and intuitive impression on the data characteristics.
Conclusion: Hepamine provides comprehensive data and easy access to various hepatologic gene expression data. It will open this widely unused resource particularly to hepatologists without bioinformatics or microarray profiling experience and substantially facilitate the translation of these data to molecular hepatology research. Hepamine is accessible at: http://www.hepamine.de.

Concurrent Oral Abstract Session: Comorbidities and Complications

0-033

Small dense low-density lipoprotein cholesterol is a better predictor of future cardiovascular events than the traditional lipid profile in liver transplant recipients

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Introduction: Cardiovascular disease is an important cause of morbidity and mortality after liver transplantation (LT). Although LT is associated with dyslipidemia, particularly atherogenic lipoprotein sub-particles, the impact of these sub-particles on cardiovascular disease (CVD) related events is unknown. Therefore, the aim of the current study was to evaluate the impact of small dense low-density lipoprotein cholesterol (sdLDL-C) on CVD events.
Methods: Prospectively enrolled patients (N=130) had detailed lipid profile consisting of traditional lipid parameters and sdLDL-C and were followed for CVD events. The primary endpoint was a CVD composite consisting of myocardial infarction, angina, need for coronary revascularization, and cardiac death.
Results: The mean age of the cohort was 58±11 years and the most common etiology of liver disease was hepatitis C (N=48) and nonalcoholic steatohepatitis (N=23). A total of 20 CVD events were noted after median follow up of 45 months. The baseline traditional profile was not predictive of future CVD events. A serum LDL-C cutoff of 100 mg/dL was unable to identify individuals at future risk of CVD event (P=0.856). In contrast, serum concentration of atherogenic small dense LDL-C > 25mg/dL was highly predictive of future risk of CVD events with hazard ratio of 6.376 (95% confidence interval 2.65, 15.34, P< 0.001). This relationship was independent of diabetes, hypertension, dyslipidemia, obesity and immunosuppression use.
Conclusion: Small dense LDL-C independently predicted future CVD events while LDL-C did not. Thus, sdLDL-C may provide a useful clinical tool in risk-stratifying and managing patients after LT.

0-034

Proximal Splenic Artery Embolization (SAE) for refractory ascites and hydrothorax after liver transplant: analysis of factors associated with success

Lomaglio L.[1], D'Amico G.[1], Armanyous S.[1], Diago Uso T.[1], Hashimoto K.[1], Eghtesad B.[1], Fujiki M.[1], Aucejo F.[1], Sasaki K.[1], Kwon C.H.D.[1], Coppa C.[2], Bayona Molano M.D.P.[3], Lindenmeyer C.C.[4], Miller C.[1], Quintini C.[4]

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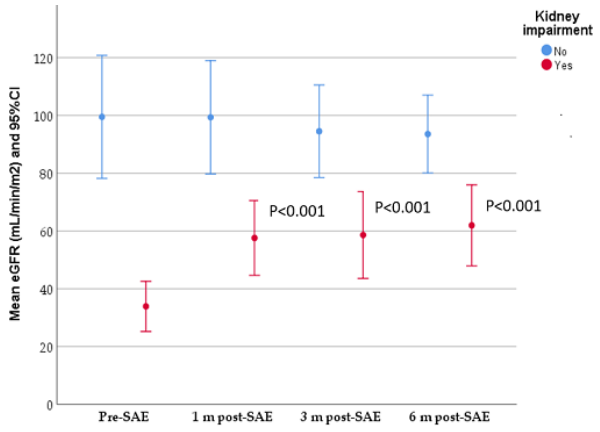
Background: The aims of this study were to
(1) assess the efficacy of proximal SAE for the treatment of RA and RH after LT and to
(2) identify clinical factors associated with clinical resolution.
Methods: A retrospective analysis of all patients who underwent SAE for RA and RH after LT between 2008 and 2017 was conducted. Independent t-test was used to test differences between the quantitative variables. Paired t-test was used to compare values before and after SAE. A linear model was built to study the effect of the operative intervention and follow-up duration on estimated glomerular filtration rate (eGFR).
Results: Thirty patients underwent SAE after LT. The mean interval of follow-up was 54 ± 34 months. Of these patients, 19 (64%) underwent SAE for RA, 1 (3%) underwent SAE for RH, and 10 (33%) underwent SAE for both RA and RH post-operatively. Timing of resolution of RA/RH was divided into early (< 3 months after SAE) and late (>3 months after SAE). The mean time to early resolution was 56 ± 11 days (24 patients); the mean time to late resolution was 135 ± 79 days (6 patients) (p< 0.034). Factors associated with early versus late resolution of symptoms were : age, pre-SAE eGFR, splenic/hepatic artery ratio, spleen/liver volume ratio, spleen volume, intraoperative portal vein (PV) flow, and pre-SAE PV velocity. Patients with kidney function impairment who underwent SAE after LT were noted to have improved eGFR (Figure 1).
Conclusions: The absence of renal insufficiency before SAE predicts early clinical resolution. However, SAE significantly improves renal function after LT in patients with pre-existing renal insufficiency. We suggest that a predictive model for successful SAE for the therapy of RA/RH after LT be built based on factors we identified.



[Figure 1. Kidney function in the first semester after proximal splenic artery embolization]

0-035

Defining adipose tissue redistribution in decompensated cirrhosis: visceral adiposity in severe hepatic dysfunction does not correlate with BMI and is associated with chronic kidney disease

Sharma R.[1], Schluger A.[1], Ahmed F.[2], Guo X.[2], Zhao B.[2], Verna E.[1]

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Background: Obesity adversely impacts outcomes in end-stage liver disease (ESLD). However, how the quantity and distribution of abdominal adipose tissue changes in decompensated cirrhosis is unknown, and no validated methods exist to adjust anthropometric measures (BMI) for ESLD-related changes in body composition.
Methods: Adults with liver transplant (LT) 1/08-8/17 and pre-LT abdominal MRI were retrospectively assessed. Visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and skeletal muscle (SM) area (cm^2) were determined at L3. VAT/SAT ratio (VSR) was calculated, reflecting adipose redistribution. Elevated VSR=VSR >1.0. Chronic kidney disease (CKD)=eGFR>60ml/min per 1.73m^2. VSR and BMI correlation was tested with Pearson. Body composition measures were compared by Child-Turcotte-Pugh (CTP) class, and evaluated as predictors of LT outcomes.
Results: 228 patients were analyzed. VSR was poorly correlated with BMI in CTP A (r=-0.09), B (r=-0.07), and C (r=-0.003) cirrhosis. VSR (1.4v1.0, p< 0.01) was significantly higher in CTP C compared to CTP A/B cirrhosis, but there were no differences in SM (p=0.49) and SAT (p=0.37). In adjusted analysis, patients with CTP C cirrhosis had a 2.7 times higher odds of elevated VSR compared to CTP A cirrhosis (p=0.02). Elevated VSR was also associated with CKD pre-LT (67v45%, p=0.01) and post-LT (57v43%, p=0.05). In adjusted analysis, patients with elevated VSR had a 2.5 times higher odds of pre-LT CKD compared to those without (p=0.03). Death was rare (n=6), and was not significantly associated with elevated VSR.
Conclusion: BMI does not adequately represent adipose stores and is a poor surrogate for metabolic risk in ESLD. Despite similar SM values, patients with CTP C cirrhosis had the most profound increase in VSR, suggesting that assessment of sarcopenia alone is not sufficient to understand metabolic derangement in ESLD. VSR was also associated with pre-LT CKD indicating that redistribution to the visceral compartment is more harmful than increased VAT alone.

0-036

Arterial stiffness in the assessment of cardiovascular risk after liver transplantation

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Background: Liver transplant (LT) recipients have a high cardiovascular risk (CVR). Early atherosclerosis induces asymptomatic vascular lesion that can be quantified through the estimation of arterial stiffness or by measuring the ankle-arm index (AAI). We aimed to evaluate these markers and their association with clinical CVR factors after LT.
Method: Cross-sectional single-center study that included all LT recipients with a follow-up of 12, 60 and 120 months after LT. The presence of CVR factors and their control was assessed, and the algorithms SCORE and REGICOR were calculated. Arterial stiffness was estimated by measuring wave pulse velocity (Mobil-O-Graph®), and AAI was calculated with a double digital oscilometer (WatchBP OfficeABI®).
Results: We included 122 LT recipients with 12 (n=39), 60 (n=45) y 120 (n=38) months of follow-up, at a median age of 58, 60 and 66 years, respectively (p=0.02). The prevalence of arterial hypertension increased significantly with the time of post-LT follow-up (51%, 67% and 82% at 12, 60 and 120 months, p=0.01). We did not find significant differences in the prevalence of the remaining CVR factors. Similarly, there were no significant differences either in clinical algorithms or in AAI according to the time of transplant follow-up. Wave pulse velocity significantly increased, being 8.2 m/s at 12 months, 8.9 m/s at 60 months and 9.4 m/s at 120 months (p=0.014). Wave pulse

velocity was significantly associated with age (p< 0.001), time of transplant follow-up (p=0.007), the REGICOR algorithm (p=0.05), and the grade of control of blood pressure (p=0.02).
Conclusion: Estimation of arterial stiffness by wave pulse velocity is associated with variables related to cardiovascular risk and its grade of control after LT and thus it may be a good marker of such risk in this population. Longitudinal studies are required in order to test its capacity to predict major cardiovascular events.

0-037

Presence of Class II DSAs is associated with development of fibrosis, chronic rejection and graft loss more than 10 years after liver transplantation

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Introduction: For decades, donor-specific antibodies (DSA) have been thought not to be clinically relevant in orthotopic liver transplantation (OLT). However, recent studies have shown a negative impact of Class II DSA in short term follow-up of OLT recipients. So, aim of this study was to assess the long-term graft outcome with respect to the presence of DSA classII.
Methods: OLT recipients presenting to the outpatient clinic with a 10-20 years post op follow-up were included in the study. Patients with HCV were excluded. Liver function tests, liver elastography and HLA antibodies were determined. DSA class II antibodies with a MFI > 1500 U were regarded as positive.
Results: Altogether 132 patients with a mean follow-up of 5699 days post OLT were analysed. DSA Class II were positive (DSA+) in 55/132 (42 %) patients. There was no significant difference between DSA + and DSA- patients in terms of sex, length of follow-up post OLT, indication for OLT (Re-OLT, autoimmune, viral, alcoholic disease or other), CIT, WIT, and type of transplantation (split vs full organ). However, DSA + patients were significantly younger (42y vs 59y; p < 0.001). Most importantly, the median liver stiffness on elastography of DSA+ patients was significantly higher than of DSA- patients (9.4 ± 9.7 kPa vs 6.9 ± 7.1; p < 0.01). Also a significant higher incidence of chronic rejections (12.7% vs 2.6%; p=0.03) and graft losses (5.5% vs 0%; p=0.04) were found in DSA + as compared to DSA- patients. However, there was no significant difference between DSA+ and DSA - patients with regard to early or late acute rejection episodes.
Conclusion: Presence of DSA class II was associated with increased fibrosis grade, high incidence of chronic rejection and graft loss in long-term liver transplant recipients.

0-038

Allosensitization is associated with increased morbidity and mortality in liver alone and simultaneous liver kidney transplantation

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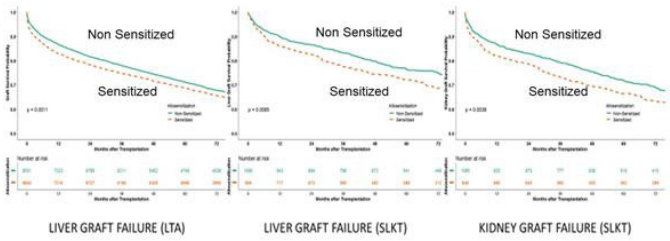
Background: Aloensitization is thought to have marginal impact among patients that undergo liver transplantation (LTA); further among simultaneous liver kidney transplantation (SLKT), livers may protect organs transplanted simultaneously from the same donor from HLA allosensitization. We hypothesized that allosensitization has significant clinical impact in transplant recipients.
Methods: We examined all LTA and SLKT transplanted in the US (1995-2016). Patients were stratified by presence of allosensitization (positive T cell cross match &/or Panel Reactive Antibodies > 20%). Patients missing XM or PRA data were excluded from the study.
Results: 17,371 LTA and 1943 SLK were performed in the study period and met inclusion criteria. Compared to non-sensitized LTA recipients, allosensitized counterparts had longer median initial hospital stay (13 vs. 11, p < 0.001). Similarly, allosensitized SLK had longer median initial hospital stay (21 vs. 15, p < 0.001). Allosensitized LTA and SLK recipients also had higher rate of readmission in the first 6 months after LTA (14% vs. 10%, p < 0.001) and SLKT (12 vs. 9%, p < 0.001, respectively). Rates of rejection at discharge were higher for allosensitized recipients after LTA (6.7 % vs. 5.8%, p=0.03) as well as SLKT (3.9% vs. 1.8%, p=0.01). Rates of liver graft failure were higher for sensitized patients both after LTA and SLKT. (**Figure 1a and b**). Further, rates of kidney graft failure were higher for sensitized patients after SLKT (**Figure 1c**). After adjusting for donor, recipient and transplant related characteristics, allosensitization was associated with increased mortality after LTA (AHR=1.06, 95% C.I. 1.00-

1.12) and SLKT (AHR=1.07, 95% C.I. 1.01-1.13).
Conclusion: Both liver and kidney graft failure is impacted after LTA and SLKT in allosensitized recipients. Beyond the absolute increase in mortality, the economic impact (LOS, resource utilization, readmissions) also should not be ignored.



[Figure: Sensitized versus non sensitized recipients]

0-039

Deficiencies in reproductive health counseling and practices in liver transplant patients

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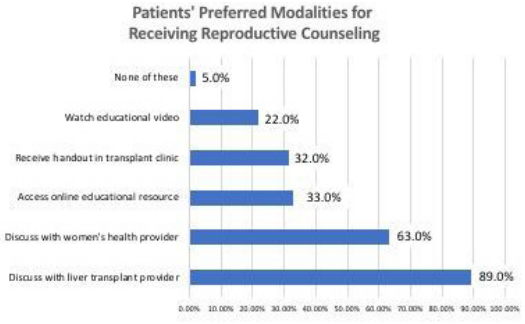
Introduction: Over 30% of female liver transplant patients are reproductive-aged. Fertility recovers quickly after transplant, and unplanned pregnancies are common. However, data on reproductive counseling in female transplant patients are lacking.
Methods: Women ages 14-45 years who were listed, or received a liver transplant (n=148) at an academic medical center were sent an online survey in 2018. Questions explored contraception/pregnancy counseling and contraception use post-liver transplant (post-LT).
Results: Seventy-three (49%) women completed the survey; 15 pre-LT, 58 post-LT. Median age was 32 years; 59% were white, 22% Hispanic. 40% (29/73) desired future pregnancy. Pregnancy counseling occurred in 83% (49/58) of post-LT patients and in 40% (23/58) of waitlisted women. However, less than half (47%) felt counseling received was sufficient. No pregnancy recommendations were provided to 5 pre- and 9 post-LT women; 2 pre-LT and 5 post-LT women were advised never to conceive, and 3 post-LT women were told pregnancy was not possible. Approximately 60% (44/73) received counseling from transplant providers.
Of 9 reported pregnancies, 20% occurred within 3 months post-LT; 30% were unplanned, including two miscarriages. In the first year post-LT only 36% of sexually active women used contraception, including 37% using high failure methods (ie withdrawal, rhythm, or condoms).
Most (72%) women considered reproductive counseling as "very important" to their post-LT care, and most (89%) preferred counseling to come from their transplant providers (89%)(Figure).
Conclusion: Reproductive counseling is inadequately provided to transplant patients. Most women consider this high priority to their transplant care, and desire information from transplant providers. Reproductive practices are also inadequate, with most women using no contraception in the first year following LT. Given risks of unplanned pregnancies to fetal and graft health, systems-based interventions are needed in transplant clinics to improve observed gaps in care.



[Figure. Patients' Preferred Modalities for Receiving Reproductive Counseling]

0-040

Efficacy and superiority between ERCP and PTBD as first line intervention of biliary complication after liver transplantation

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Introduction: Biliary complications after liver transplantation(LT) are most common complications and associated with morbidity and mortality. Currently, the generally applied first intervention for post-LT biliary complications is Endoscopic retrograde cholangiopancreatography(ERCP) because of less invasiveness and patient convenience. However, there has not been a uniform conclusion published on superiority of the two types of intervention as first trial. Therefore, we compared the efficacy of ERCP and percutaneous transhepatic biliary drainage(PTBD) as a first line treatment of post-LT biliary problems.

Method: From January 2013 to December 2016, 565 patients underwent LT in Seoul National University Hospital(SNUH). Medical records of LT recipients with biliary complications retrospectively reviewed. Long-term follow-up was evaluated using cholangiogram, computed tomography(CT) scan and laboratory parameters.
Results: Among 565 LT patients, 85 patients(15.0%) were treated by intervention including ERCP and PTBD with diagnosis of biliary complications. Successful intervention on the first attempt was achieved in 36 of 60 patients(60.0%) with ERCP, and 19 of 25 patients(76.0%) with PTBD, respectively(p=0.16).
We also classified the groups based on the location of the biliary complications and compared the success rate; one with anterior bile duct problems (a-BD, n=29) and another with posterior bile duct (p-BD, n=14). In a-BD, there was no difference in the intervention success rate of PTBD and ERCP(25% vs.24%, p=0.692). However, in p-BD, PTBD success rate was significantly better than ERCP(75% vs.18%, p=0.002).
Conclusions: PTBD could be considered as more effective procedure for termination of treatment in patients with post-LT biliary complications, especially posterior duct problems.

O-041

Impact of frailty on short term outcome after liver transplantation; a retrospective, single-center study

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Introduction: Key components of frailty, a generalized condition of poor health, functionality, and compromised reserve across multiple physiologic systems, include decreased skeletal muscle mass, deconditioning, and malnutrition. The purpose of the study was to assess the association between decreased skeletal muscle mass, physical performance, and nutrition status with postoperative outcomes in liver transplant recipients.
Methods: This retrospective, single-center study includes 142 liver transplants (≥ 18 years old) performed at University of Miami/ Jackson Memorial Hospital from 2016 to 2017 who had computed tomography scans available within six prior to liver transplant. We analyzed the relationship between Lumbar 3 Psoas Muscle Index, Karnofsky Performance Status Scale (KPS) score, and Academy/ ASPEN nutrition criteria and postoperative outcomes (including major complications within first 6 months, duration of mechanical ventilation, length of stay, and 1-year mortality).
Results: The combination of decreased muscle mass, low KPS score, and malnutrition was statistically associated with major complications (Clavien-Dindo grade III and above) during first 6 posttransplant months (P=0.01). Two risk factors were associated with 1-year mortality: male gender and Karnofsky score < 50 (the whole model was statistically significant (χ2=8.3, P=0.01)).
Conclusions: Decreased muscle mass combined with low functional status and malnutrition, as markers of patient frailty, is associated an increase in major complications after liver transplant. Low physical performance status is associated with increased 1-year post-transplant mortality.

Concurrent Oral Abstract Session: Donation after Cardiac Death

O-042

Proportions of EAD criteria in donation after circulatory death liver transplantation

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Background: Early allograft dysfunction (EAD) was defined by the presence of 1 or more of the following variables:
(1) total bilirubin (TB) ≥ 10 mg/dL on postoperative day 7;
(2) an international normalized ratio (INR) ≥ 1.6 on postoperative day 7, or
(3) alanine aminotransferase (ALT) or aspartate aminotransferase (AST) levels > 2000 U/L within the first 7 postoperative days.
EAD is associated with inferior graft and patient survival. We aimed to analyze the proportions of recipients based on the EAD diagnostic criteria in donation after circulatory death (DCD) liver transplantation.
Method: Donor, recipient and operative data associated with EAD were analyzed to identify numbers and proportions of each criteria of EAD.
Results: A total of the 123 liver transplantation recipients who developed EAD were analysed retrospectively, One hundred (81.30%) recipients met the only ALT/AST criteria, while only 4 (3.25%) and 1 (0.81%) recipients satisfied the only TB and INR criteria respectively. The other 18 (14.63%) recipients are diagnosed by two or three criteria of EAD.
Conclusion: The ALT/AST criteria of EAD accounts for a large proportion while only a small part of recipients who met TB or INR criteria. Further refinement of the EAD criteria are needed.

O-043

Clinical outcomes of DCD type V liver transplantation: Donation after euthanasia

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Background: Due to shortage of donor organs, physicians and surgeons are forced to accept livers from donation after circulatory death (DCD) donors. One special group of DCD organs are those obtained after euthanasia (DCD type V). To create more awareness on the possibility of organ donation after euthanasia, it is important to evaluate the results of transplantation with this type of graft. Aim of our study was to evaluate the outcome of DCD type V liver transplantation (LT) in the Netherlands and Belgium.
Methods: DCD type V LT performed until 2018 in all three Dutch LT centers and in four out of six Belgian LT centers, were included in this study. Grafts that have been preserved with machine perfusion were excluded. Continuous data are expressed as median (IQR), categorical data as number (percentage).
Results: Until 2018, 44 DCD type V LT have been performed. Five cases in which the liver was preserved by machine perfusion were excluded. Median age of donor and recipient was 50 years (45-56) and 56 years (48-64), respectively. A neurological disease was the most common underlying disease in donors requesting euthanasia, followed by psychiatric disorders. Median time between administration of the euthanaticum and cold perfusion was 21 minutes (14-26). Peak AST and ALT levels in the recipients were 904 U/L (586-2478) and 709 U/L (448-1841) respectively. One- and three-year patient survival were 89% and 83%, respectively. Five patients (12.8%) required a retransplantation, due to PNF (n=1), HAT (n=1) or post-transplant cholangiopathy (n=3), the majority within the first year after the prior LT.
Conclusion: Liver transplantations with grafts from donors who

underwent euthanasia yield satisfying results during the relatively short follow up period that is currently available. Comparison of these results with DCD type III LT and donation after brain death (DBD) LT is currently ongoing.

0-044

The utility of intraoperative vascular anastomotic inflow measurements in donation after circulatory death (DCD) liver transplantation

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Background: The use of flow probes to measure hepatic inflow at the conclusion of vascular anastomoses in Donation after Circulatory Death (DCD) liver transplantation is not routine and its value not clearly defined.
Methods: A single-institution retrospective review of DCD liver transplant case records from 2005-15 was conducted. Intraoperative vascular flow data (Portal vein and Hepatic artery) was collected prior to initiation of biliary anastomosis. These measurements were then compared against pertinent clinical variables and graft survival.
Results: A total of 118 DCD transplants were performed during the study period. Median recipient age was 57 years, with male preponderance (71%). Hepatocellular carcinoma was the indication for transplantation in 36% cases. Mean follow up was 4.4 years. Four patients (3.4%) developed primary non-function, and intraoperative portal vein flow was found to be significantly less in these instances (p= 0.002). Graft loss was observed in 11 patients (9%). The rates of ischemic cholangiopathy, bile leak and anastomotic biliary stricture were 4.2%, 2.5% and 30% respectively. Flow data was available in 107 cases. Median (inter-quartile range) values/100gms liver tissue/min for total hepatic inflow, portal vein flow and hepatic artery flow were 107 (84-138), 93(64-122) and 14(10-23) mls respectively. Poor correlation of flow rates with peak liver enzyme activity was observed. Anastomotic biliary stricture was however associated with significantly lower total hepatic flow/100g/min and portal vein flow/100g/min (p= 0.011 and 0.004 respectively), but not with hepatic artery flow/100g/min. Portal vein flow < 52.9mls/100gms/min was significantly associated with risk of graft loss (p=0.01).
Conclusion: Measurement of intraoperative vascular inflow can provide prognostic information on biliary stricture potential and graft outcomes in DCD liver transplantation.

0-045

Conditional probability of graft survival in liver transplantation using donor after circulation death

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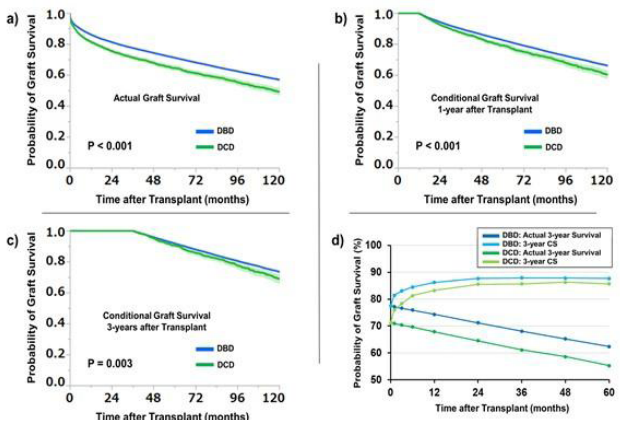
Objective: The use of livers from donors after circulation death(DCD) is generally characterized by increased rates of biliary complications and inferior graft survival(GS) compared with donation after brain death(DBD) donors. Although, previous studies focused on short-term outcomes after LT, the long-term outcomes of LT using DCD is unclear. This study aimed to evaluate the dynamic prognostic impacts of DCD to reveal whether it is an adverse factor for patients surviving a certain period after LT.
Methods: This study used adult patients who had deceased donor LT in the Scientific Registry of Transplant Recipients from 2002-2017. 1- and 3-year conditional GS rate and conditional hazard ratio(HR) using Cox regression were calculated.
Results: Of the 80,520 patients identified, 4045 patients received DCD livers(5.0%). The donor age of DCD was significantly younger than DBD (34.0 y.o vs. 43 y.o, P< 0.001). The MELD score at the time of LT was also significantly lower in the DCD patients(17 vs 20, P< 0.001). The actual 1-, 3-, and 5-year GS of DCD patients were 81.5%, 71.3%, and 64.5%, which were significantly worse than those of DBD(all P< 0.001, Figure a). Although the GS differences compared to DBD decreased, DCD patients still had worse GS even after surviving 1- and 3-years (Figure b and c). The 3-year actual and conditional 3-year GS were plotted in Figure d. Conditional 3-year GS of DCD did not reach those of DBD even 5-years after LT. Actual, 1- and 3-year conditional HR of 1-year GS in DCD were 1.83, 1.43, and 1.28, respectively. Of the 619 known-causes of graft loss after 1-year from LT, 70 patients had biliary complication related to biliary duct including ischemic cholangiopathy(median 24.7 months, range 12.0-88.6 months).
Conclusions: Adverse influences of DCD organ stay in long-term after LT.



[CS DCD figures]

0-046

Donor hematocrit is an independent predictor for the development of non-anastomotic biliary strictures after donation after circulatory death liver transplantation

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Background: Donation after circulatory death (DCD) livers are increasingly used for transplantation to overcome donor organ shortage. These livers, however, develop non-anastomotic biliary strictures (NAS) in up to 30%, frequently resulting in graft loss or even death. The high incidence of NAS cannot be completely explained by the currently known risk factors. Blood hematocrit is a determinant of blood viscosity and might therefore affect graft flush out during procurement. We aimed to investigate the impact of donor hematocrit (among other known risk factors) on the development of NAS after DCD liver transplantation.
Method: DCD liver transplantations performed between 2003 - 2017 in the two participating centers were included. Exclusion criteria were retransplantation, use of machine perfusion, and unknown donor hematocrit. NAS was defined as donor bile duct strictures at any location but the anastomosis. Continuous data are expressed as median (interquartile range). Uni- and multivariate logistic regression analysis were used to identify risk factors for the development of NAS. Variables with a p-value below 0.2 in the univariate analysis were included in a multivariate analysis.
Results: A total of 235 DCD liver transplantations were included. Median donor hematocrit was 34 (30-39) %, donor age 47 (36-54) years, time between withdrawal of life support and cold perfusion 31 (26-38) min, and cold ischemia time (CIT) 408 (356-460) min. Univariate analysis identified donor age (p=0.005), CIT (p=0.102), time between withdrawal of life support and cold flush (p=0.107) and donor hematocrit (p=0.045) as (near) significant risk factors for NAS. After multivariate analysis only donor hematocrit (OR 1.054, 95%CI: 1.003-1.108, p=0.039) remained as an independent risk factor for NAS. Livers from DCD donors with a hematocrit ≥37% had a more than 2-fold higher risk to develop NAS.
Conclusion: Donor hematocrit is a strong risk factor for the development of NAS after DCD liver transplantation.

0-047

Variations in DCD procurement procedures across OPOs and their effects on liver transplant outcomes

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Introduction: Variations in procurement procedures across Organ Procurement Organizations (OPOs) may account for discrepancies in outcomes of donation after cardiac death (DCD) liver transplants. We investigated the association between procedure variations and liver transplant outcomes by linking procurement survey results from OPOs to UNOS data.
Materials and methods: A survey of all 58 OPOs inquiring about their practices of DCD organ procurement was conducted. The final data included transplants of liver between 2000 and 2016 (n = 3,613). Bivariate cox regressions and log-rank tests were done to examine the impact of procurement practices on transplant outcomes using death-censored graft failure rate.
Results: The survey indicated substantial differences across OPOs in DCD procedures. Cox regression analysis of the data showed that policy variations in the perfusion protocol, use of vasodilators and mandatory postmortem wait times had a statistically significant impact on transplant outcomes. The impact of policy variations in heparin use, location support withdrawal, and BMI cutoffs did not have a statistically significant impact on outcomes. The use of pre-mortem cannulation over rapid laparotomy was positively associated with increased graft mortality (HR = 1.210, p=0.000). Similarly, the use of vasodilators was associated with decreased graft failure (HR = 0.785, p = 0.002). Although the log-rank test did not show a significant difference in survival curves for pre-mortem cannulation and vasodilator use, a longer mandatory wait time presented with increased mortality at a 10% significance level. A waiting period of 5 minutes or longer was associated with increased post-operative graft failure (HR = 1.228, p = 0.022).
Conclusion: There are substantial variations across OPO protocols for procuring DCD organs that affect transplant outcomes and patient mortality. Identification of factors associated with positive DCD liver transplant outcomes can improve the understanding of risk factors and influence informed policy reforms in OPO protocol.

0-048

Impact of center volume on donation after cardiac death liver transplant outcomes. A retrospective scientific registry of transplant recipients analysis

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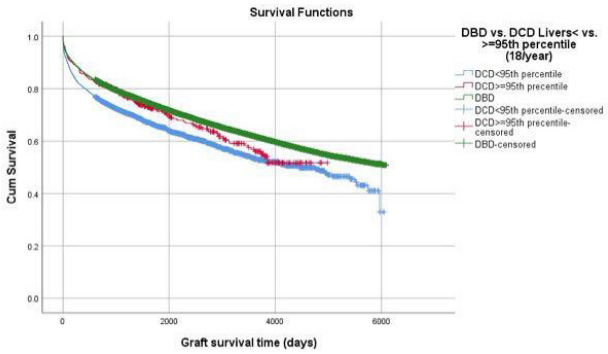
Background: Organ shortage necessitates the optimization of the utilization and outcomes of donation after cardiac death (DCD) liver allografts. Aim of the study was to assess the center volume effect on graft survival in DCD liver transplantation (LT).
Method: Retrospective SRTR analysis on deceased donor LTs performed during period 2001-2015. Exclusion criteria: age< 18 years, partial grafts, retransplants, multivisceral transplants, < 5 LTs per year. Cohort was sorted by time and location. Transplant centers were ranked in order of annual case volume. Center rank and group designation were annually recalculated. The observations were split into tertiles and then further subcategorized into annual DCD volume deciles. Log-rank analysis was performed comparing LT graft survival. Multivariate backward cox-regression analysis was performed.
Results: N=69,387 LTs. DCD LTs were 3,536 (5.1%). 60% of DCD allografts were used by centers performing < 5 DCD/year; their survival was inferior to higher volume centers (p=0.024). Low DCD volume center outcomes were consistently inferior to the outcomes of higher volume centers or DBD grafts, until the 95th percentile (≥18DCD/year); beyond this threshold, DCD graft survival became equivalent to DBD (p=0.224). Adjusted cox-regression analysis indicated that < 5 DCD/year, prolonged cold ischemia time, increased warm ischemia time, older donor age and ICU status at the time of transplant were predictors of inferior DCD graft outcome.
Conclusion: Presently, the majority of DCD allografts are transplanted at low DCD volume centers. DCD outcomes are persistently higher in busier DCD centers, becoming equivalent to DBD at centers performing ≥18 DCD/year. Expedited offering and allocation of potential DCD allografts to accredited regional DCD centers of excellence may therefore optimize DCD graft utilization and outcomes.



[K-M curve]

0-049

Single center experience in 157 controlled DCD-liver tranplantation

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Introduction: Donation after circulatory death (DCD) have been proposed to partially overcome the organ donor shortage. DCD-LT remains controversial, with reported increased risk of graft loss and retransplantation. The authors retrospectively reviewed a single centre experience with controlled DCD-LT in a 15-year period.
Patients and Methods: 157 DCD-LT were consecutively performed between 2003 and 2017. All donation and procurement procedures were performed as controlled DCD in the operating theatre. Data are presented as median (ranges). Median donor age was 57 years (16-83). Median DRI was 2.242 (1.322-3.554). Allocation was centre-based. Median recipient MELD score at LT was 15 (6-40). Mean follow-up was 37 months. No patient was lost to follow-up.
Results: Median total DCD warm ischemia was 19 min (7-39). Median total ischemia was 313 min (181-586). Patient survivals were 89.8%, 75.5% and 73.1% at 1,3 and 5 years, respectively. Graft survivals were 89%, 73.8% and 69.8% at 1,3 and 5 years, respectively. Biliary complications included mainly anastomotic strictures, that were managed either by endoscopy or hepatico-jejunostomy. Two patients were retransplanted due to intrahepatic ischemic lesions.
Conclusion: In this series, DCD LT provides results similar to classical LT. Short cold ischemia and recipient selection with low MELD score may be the keys to good results in DCD LT, in terms of graft survival and avoidance of ischemic cholangiopathy.

0-050

Qualitative evaluation of short- and long-term outcomes in liver transplantation using deceased after cardiac death (DCD) donor grafts

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Objectives: Prediction model of graft utilization and patient outcome in liver transplantation from DCD grafts.
Methods: Study population was from a single institute (King's College Hospital, London 2001-2018). The long-term outcome of a total of 968 patients was analyzed. Each DCD transplant was matched with 1 DBD graft according to the period of transplantation. Primary outcome measures were early allograft dysfunction (EAD), biliary complications, graft and patient survival. Minimum follow-up was 6 months.
Results: A slight trend of inferior patient and graft 1- 3- 5- yrs survival was observed in the DCD group(p 0.001). DCD recipients were more often affected by PNF (2.6%, p=0.028), ischemic cholangiopathy (4.1%, p=0.017), biliary stricture (16.2%, p=0.001) and required re-transplantation (6.9%, p=0.022). The rate of early allograft dysfunction was higher in the DCD group (51%, p 0.001). On univariate analysis graft variables of type (DCD vs DBD), donor gender, steatosis, MELD>20, cold ischemic time>8hrs, type of reperfusion (portal vs arterial) were predictor of development of EAD. On multivariate analysis donor gender, steatosis, CIT> 8 hrs, portal reperfusion, intraoperative blood loss>5 lt were positively correlated with EAD, while donor age> 45 years, donor WIT and hepatectomy time were negatively associated with EAD.
Conclusion: DCD grafts are more subjected to several complications, including biliary complications compared to DBD. The severity of graft dysfunction is an independent risk factor for allograft loss. Grading EAD by simple criteria based on the peak of aminotransferases, bilirubin and INR during the first postoperative week might not be sufficient as it appears to be correlated to intraoperative variables. As such, mitigating donor and recipient risk factors such as type of reperfusion, CIT and blood loss are of prime importance. Future studies should be directed to identify early markers of EAD and interventions that could minimize or reverse graft damage and loss.

Concurrent Oral Abstract Session: Immunosuppression and Tolerance Induction

0-051

Incidence and treatment of rejection in patients converted to Everolimus (EVL) after liver transplantation (LT): longterm histological data from the Everoliver multicenter observational French registry

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The aim of this multicenter observational study is to analyze incidence, histological features and treatment of rejection under EVL regimen.
Patients and methods: From 2006 to 2017, LT patients from 9 centers who were converted to EVL were recruited in the study. Data from last liver biopsy performed prior to conversion and from all biopsies performed after conversion were collected.
Results: 1045 adult recipients (75.1% male) had a mean age of 54.3±10.3 years. EVL was introduced in 45% of the patients during the 1rst year post-transplant. Main reasons of introduction of EVL were chronic renal failure (36.2%) treatment of recurrent HCC (6.2%) or de novo cancer (21.1%) and prevention of HCC recurrence (41.5%). Mean through EVL levels were respectively 5.6±3.7, 6.3±3.1 ng/mL at M1 and M36. CNI were withdrawn in 49.8% at M12. Under CNI regimen, 480/1045 (46%) patients had at least 1 liver biopsy prior to conversion to EVL. Biopsy-proven acute rejection (BPAR), treated BPAR and BP chronic rejection (BPCR) were respectively 9.6%, 6.9% and 2.1%. Under EVL regimen, 527/1045 (50.4%) patients had at least 1 liver biopsy after conversion to EVL with a median delay of 25.2 (0.4-359) months. BPAR, treated BPAR and BPCR were respectively 8.9%, 5.5% and 3.1%. In the 329 patients who had at least 2 biopsies prior and after conversion, 14 patients (4.2%) without BPAR prior to conversion developed BPAR after conversion. Eight patients (0.8%) underwent retransplantation.
Conclusion: This real life registry showed in more then 1000 liver biopsies from patients converted to EVL, that the risk of treated BPAR under EVL based regimen with a long follow-up is low (≤ 5%). Conversion from CNI to EVL allowed a weaning of CNI in 50% of the patients at 1 year and a minimization of CNI in the others without increasing chronic rejection (3%).

0-052

PIRCHE-II algorithm may predict allograft dysfunction in calcineurin inhibitors (CNI) free maintenance immunosuppression liver transplant patients

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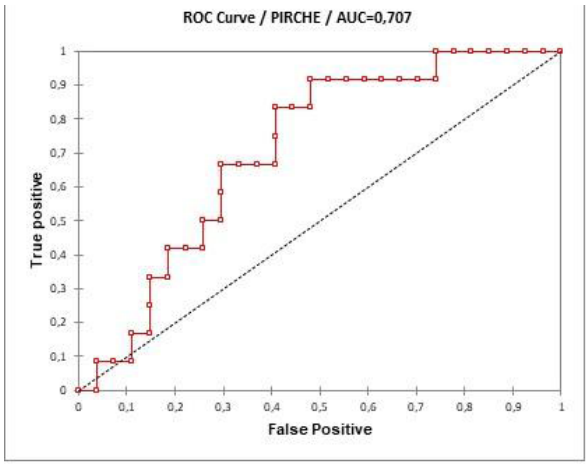
Background: The PIRCHE (predicted indirectly recognizable HLA epitopes) score is a novel HLA epitope matching tool able to predict the alloimmune response, de novo donor specific antibodies (dnDSA) formation and graft dysfunction following kidney transplantation. Recently our team reported the use of PIRCHE-II algorithm to predict de novo DSA following liver transplantation.
The aim of our study was to corelate for the first time the PIRCHE-II score to the liver biopsy to predict allograft dysfunction in a cohort of CNI free maintenance liver transplant patients.
Methods: A total of 39 liver transplant patients having a CNI-free immunosuppression regimen were analyzed. HLA typing of the donor and recipient was achieved by molecular techniques. Missing typings were extrapolated from HLA-ABCDRDQ-haplotype frequencies based on the National Marrow Donor Program Database. Low-resolution typing data of patients and donors was extrapolated using a multiple imputation approach. The HLA-derived mismatched peptide epitopes that can be presented by the recipient's HLA-DRB1 molecules were calculated using the latest version of the PIRCHE algorithm. Every patient had a liver biopsy and dnDSA were screened using Luminex SAB (One Lamda).
Results: Patients having an abnormal liver biopsy had a mean PIRCHE score of 112.6 versus 84.9 in case of normal liver biopsy (p=0.06). A PIRCHE score ≥68 was predictive of liver allograft dysfunction (AUC=0,70 ;p=0,05) (Figure1).
Conclusion: PIRCHE score could be predictor of liver graft dysfunction in CNI-Free patients following liver transplantation. Larger studies are needed to validate PIRCHE score to predict graft dysfunction following liver transplantation.



[Figure 1: Sensitivity analysis of PIRCHE score (>68) in predicting liver allograft dysfunction]

Results: At the last control, of the 22 TP involved in the WP, none were diagnosed with DNM, while in the NTP group, two patients (6.4%) developed DNM. In the standard immunosuppression group, 32 recipients (13%) were diagnosed with DNM, highlighting the connection between immunosuppression and DNM in the long term, with a 3.8 fold higher risk ratio of DNM onset when compared with the weaned patients.
Conclusion: The withdrawal of immunosuppression was shown to greater positive outcomes in weaned LTR, while immunosuppressed patients expressed a greater DNM incidence. Thus, LTR under immunosuppression face a higher risk of developing DNM than recipients under WP, which proved to be protective from DNM and demonstrated his efficacy and feasibility over time. Nevertheless, strict long-term follow-ups are still mandatory as well as extensive investigations with bigger groups of patients to acquire further knowledge.

0-053

Weaning immunosuppression protocol and *de novo* malignancies in liver transplanted recipients: observational study

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Background: In the liver transplant setting, *de novo* malignancies (DNM) still remain a serious threat. A key role is played by immunosuppression, however the withdrawal seems to reduce tumor incidence. Clinical operational tolerance has been shown in almost 40% of well-selected recipients. Our primary endpoints are to analyze whether there is evidence of DNM in weaned liver transplanted recipients (LTR), and to evaluate the feasibility and safety of the weaning protocol (WP) in order to broaden our understanding of it.
Method: From April 1998 to 2014 at our institution 299 liver transplants have been performed. We consented 53 patients for the WP: this cohort included 22 (41.5%) tolerant patients (TP) and 31 (58.5%) non-tolerant patients (NTP) who needed immunosuppression resumption after clinical or biopsy-proven rejection. In parallel, we considered all the patients receiving standard immunosuppression (n=246). Furthermore, we compared the data to assess the differences in DNM incidence after a 4-year follow-up.

0-054

Are only pre-transplant rituximab and plasma exchange sufficient for desensitization protocol of ABO incompatible LDLT?

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Backgrounds: ABO incompatible living donor liver transplantation (ABOi LDLT) has become a feasible option because of improved outcomes by various desensitization strategies. However, the protocol of ABOi LDLT has not been established worldwide. Nevertheless, the results after transplantation are homogenous. The reports for the results of ABOi LDLT using only rituximab and plasma exchange are scarce. We present the outcomes of our desensitization protocol for ABOi LDLT.
Methods: From January 2015 to August 2018, we performed 117 LDLTs. Of them, 29 patients (25%) received ABOi LDLT. We used only a single dose of rituximab(300 mg/m^2) and several plasma exchanges for pre-transplant desensitization in ABOi LDLT and post-transplant immunosuppression consisted of basiliximab, tacrolimus, mycophenolate mofetil and steroid. The target iso-agglutinin IgG titer before transplantation and during post-transplant period were 1:32 and 1:64.
Results: The mean initial iso-agglutinin IgG titer was 131 (range, 4~512) and initial iso-agglutinin IgG titer in recipient blood type O was higher than in another blood types. Pre-transplant plasma exchanges were performed in all recipients with more than target titer (mean number of sessions, 2.32 (range, 1~5)). Post-transplant

plasma exchanges were performed in 3 patients because of higher target isoaaglutinin titer (> 1:64), but none had antibody mediated rejection. Biliary complications were identified in 8 patients, but all was anastomotic site stricture. Acute cellular rejection was confirmed in one patient and resolved by steroid pulse therapy.
Conclusions: Both rituximab and plasma exchange along are one of desensitization strategies to eliminate the risk of antibody mediated rejection and our results were also comparable to ABO-identical or compatible LDLT. Hence, we believe that complex protocols including splenectomy, intravenous immunoglobulin, and local infusion therapy are not necessary in most ABOi LDLT.

0-055

Donor dominant one way HLA matching - a risk factor for lethal GVHD after LRLT

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Introduction: GVHD is a rare but serious complication that may occur after living donor liver transplantation.In the literature, it has been shown that transplant from an HLA-homozygous donor resulting in donor-dominant one-way HLA matching significantly increases the risk of developing GVHD and it has been advised that these potential grafts should be refuted upfront in order to prevent the devastating GVHD
Methods and results: We present our experience of 7 cases of fatal GVHD (out of 2500 liver transplants) in the past one decade and their HLA results. All the 4 patients had proven GVHD based on either the skin biopsy or donor derived chimerism in peripheral blood, apart from having typical clinical features of GVHD with involvement of skin , GI and bone marrow. On analysis of HLA report it was found that 4 out of 7 patients had one way matching at all the 3 loci of HLA A, B and DR , while other three had one way matching only in 2 loci of HLA - A and B. CMV was ruled out in all four patients All 7 patients eventually died because of multi organ failure. Sepsis was predominant cause of mortality in two of the recipients.
Conclusion: The use of a graft from a donor having donor dominant one way matching at all the three loci is extremely high risk for development of lethal GVHD, especially in the Asian subcontinent where most of donors are the family members and consanguineous marriages are also common. Hence these grafts must not be used except for emergency situations. Prevention is the key in such situation.

0-056

Immunoprotective effect of human gingiva marrow-derived stromal cells on rat liver transplantation model via FAS/FASL pathway

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Background: Marrow mesenchymal stem cells (MSCs) play an important role in immune regulation of graft rejection especially bone MSCs (BMSCs). However, the shortcomings of BMSCs limit its application. MSCs from gingiva (GMSCs) also possess immunomodulatory properties. Our study is to evaluate the regulatory role of GMSCs in the rejection of rat liver transplantation model and explore the possible mechanism.
Methods: GMSCs were obtained from human gingival tissues and BMSCs were harvested from Brown Norway (BN) rats. The shRNA mediated knockdown of Fas ligand (FASL) expression in GMSCs (FASL-/-GMSCs) was transfected by lentivirus plasmid method. Rat orthotopic liver transplantation model was established based on the “double-cuff technique”. BN rats were used as recipients and divided randomly into four groups: normal saline (NS) group, FASL-/-GMSCs group, BMSCs group, and GMSCs group. All of the groups were injected the solution into the rat rejection model via vena dorsalis penis. Graft survival was assessed and liver function indexes were detected. The immunological reactions of recipients including immunocytokines and regulatory T cells (Treg) were also evaluated by flow cytometry.
Result: The graft survival of recipient rats in the GMSCs group (38 days) was significantly prolonged in comparison with that of the NS group (18 days), FASL-/-GMSCs group (15 days), and BMSCs group (25days). GMSCs group remarkably decreased the levels of AST, ALT and TBIL. As for immunocytokines, recipient rats in the GMSCs group had significantly reduced serum levels of IL-2, IL-17, IL-23, and TNF-α in comparison with that of the other three groups, while increased the serum IL-10 and TGF-β expressions as well as peripheral serum Treg.
Conclusion: GMSCs exert immunoprotective effect on liver transplants in allotransplantation model by FAS-FASL pathway, which provides basis for GMSCs to be used in clinical anti-rejection after liver transplantation.

0-057

An open-label proof-of-principle Phase 2a study to evaluate Autologous Hematopoietic Stem Cell Transplantation for Allogeneic Organ Transplant Tolerance (ASCOTT)

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Background: Long-term survival of recipients of solid organ transplants is hampered by chronic rejection, disease recurrence and immunosuppression-induced toxicity. We are now studying whether hematopoietic stem cell transplantation (HSCT) can induce tolerance in liver transplant recipients with recurrent primary sclerosis cholangitis (PSC).
Methods: Patients with recurrent PSC treated with liver transplantation who are > 3 months post-transplant and 18 to 55 yrs old were eligible for the trial. Busulfan, cyclophosphamide and rabbit antithymocyte globulin were administered to ablate auto- and allo-reactivity followed by HSCT. Immunosuppressive medications were discontinued at the time of HSCT and everolimus was given to promote regulatory T cell expansion for the first 6 months. Patients were followed for evidence of tolerance or rejection.
Results: 75 liver transplant patients were screened and 13 patients were evaluated. 6 patients were enrolled and 5 have undergone HSCT. All patients had evidence of recurrent PSC with moderate to severe ductopenia and fibrosis at a median of 98 months (15-233 mo.) prior to HSCT. The median age was 40 (36-44) yrs. Immunosuppression was discontinued in 3 patients post HSCT: 2 are alive at greater than 2 years after HSCT and one died at 212 days post-HSCT of heart failure. Of the other two patients who received HSCT, one patient developed veno-occlusive disease and required repeat liver transplantation, and one patient died of hemophagocytosis. Tolerance induction with HSCT was associated with both deletional events and evidence of peripheral regulation. HSCT led to deletion of T cell clones and autoantibodies while promoting circulating Treg and transitional B cells.
Conclusion: These results suggest that HSCT can induce tolerance in liver transplant recipients, although toxicity is a significant problem that needs to be addressed.

0-058

Azathioprine or mycophenolic acid after liver transplantation: A tailored immunosuppression is key

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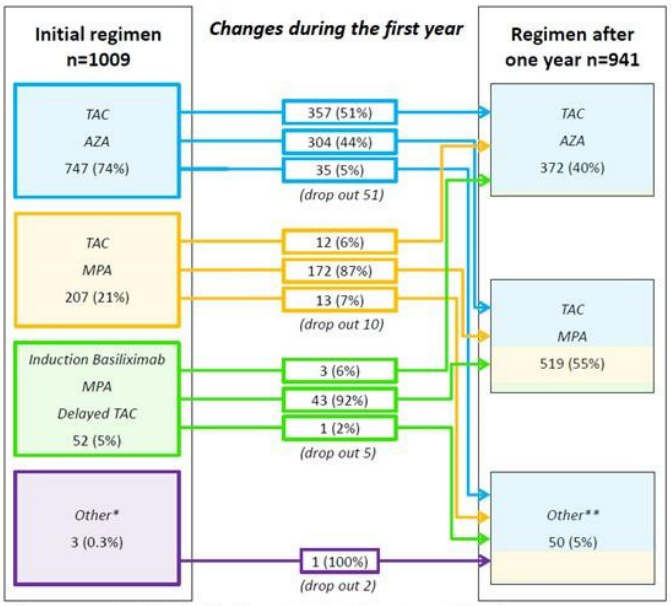
Background: Today no analysis comparing immunosuppressive regimens with Azathioprine (AZA) or Mycophenolic Acid (MPA) after liver transplantation (LT) exists. At our centre, both immunosuppressive drugs are regularly combined with steroids and tacrolimus (TAC) and adapted to graft quality and the potential risk for allograft rejection and renal complications after LT. The aim of this study was to assess the impact of such immunosuppression regimens on acute rejection (AR) and other complications according to the underlying liver disease.
Methods: All patients undergoing primary LT for chronic liver disease at our centre (2007-2015) were included. Initial immunosuppression regimens were divided into 4 groups: TAC-AZA, TAC-MPA, MPA-IL2-blocker-delayed TAC-introduction, and other regimens.
Results: Overall, 1009 patients were included. TAC-AZA was the most common used initial regimen (74%), followed by TAC-MPA (21%), MPA-IL2-blocker-delayed-TAC (5%) and other regimens (0.3%). Overall, 24% developed AR, which was more frequently observed in the TAC-AZA group (26%vs.18%; p=0.005). Consequently, there was a major shift towards TAC-MPA within the first year: TAC-MPA: 55%; TAC-AZA: 40%; other regimens: 5% (Figure 1). Multiple logistic regression identified younger recipient age, primary sclerosing cholangitis (PSC), post-transplant early allograft dysfunction and initial use of TAC-AZA immunosuppression as risk factors for development of AR. Patients with PSC developed more frequently AR if a TAC-AZA regimen was used (47%vs.21%:p=0.021). Importantly, AR was associated with a decreased long-term graft survival (78%vs.70%;p=0.005), due to a higher incidence of hepatic artery thrombosis, chronic rejection and the development of de novo cancers.
Conclusion: This study shows, that a TAC-AZA Immunosuppression remains a good option for a large group of recipients. However, AZA combinations should be applied with caution in younger patients with PSC or post-transplant early allograft dysfunction, to avoid development of acute rejection and protection from subsequent graft loss.



[Figure 1]

0-059

Comparable efficacy-safety and better renal function with everolimus and reduced-exposure tacrolimus versus standard-exposure tacrolimus in liver transplant recipients: H2304 and H2307 pooled analysis

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Background: Use of everolimus (EVR) with reduced-exposure tacrolimus (rTAC) may be helpful to avoid long-term complications, such as nephrotoxicity and increased risk of hepatocellular carcinoma (HCC) recurrence, after liver transplantation (LTx). The EVR+rTAC versus tacrolimus control (TAC-C) has shown comparable efficacy and safety with better renal function in both deceased- (H2304 [NCT00622869]) and living- (H2307 [NCT01888432]) donor LTx studies. Here we present the 24 months (M) pooled data from both the studies.

Methods: Both H2304 and H2307 were 24M, multicentre, randomized, controlled studies. This pooled analysis included 772 LTx recipients (LTxRs) who received EVR+rTAC (N=387; EVR trough levels [C_0]: 3-8 ng/mL, rTAC ng/mL C_0: 3-5 ng/mL, from M1 to M24) or TAC-C (N=385; TAC C_0: 8-12 ng/mL from M1 to M4, and 6-10 ng/mL thereafter). The efficacy endpoints included incidence of composite efficacy failure (CEF) of treated biopsy-proven acute rejection (tBPAR), graft loss, or death, and its individual components. Other endpoints included renal function by estimated glomerular filtration rate (eGFR; MDRD4), incidence of HCC recurrence and *de novo* malignancy at M24.

Results: Baseline patient characteristics were well-balanced between EVR+rTAC versus TAC-C with mean baseline eGFR (98.6 vs 98.7 mL/min/1.73 m²). At M24, CEF was comparable between both arms; tBPAR was lower with EVR+rTAC versus TAC-C. Renal function was better maintained with EVR+rTAC than TAC-C (Table 1A). At M24, EVR+rTAC versus TAC-C showed numerically lower HCC recurrence overall and in a subset of patients with HCC beyond Milan. EVR+rTAC versus TAC-C showed numerically lower incidence of *de novo* malignancies at M24 (Table 1B).

Conclusion: In this large population of LTxRs, EVR+rTAC compared to patients who received TAC-C showed comparable immunosuppressive efficacy, better renal function and a trend towards lower HCC recurrence up to 24 months after LTx.

Table 1. (A) Efficacy and renal function (B) HCC history and recurrence and *de novo* malignancy with EVR+rTAC versus TAC-C in pooled analysis – Full analysis and safety set (M24)

(A)

	EVR+rTAC (N=387)	TAC-C (N=385)	*P*-value*†
Efficacy‡, n (%)			
CEF (tBPAR, graft loss, or death)	36 (9.8)	40 (10.8)	0.641
tBPAR	15 (4.2)	24 (6.4)	0.168
Graft loss	9 (2.5)	8 (2.3)	0.862
Death	20 (5.5)	14 (3.9)	0.305
On-treatment Death	9 (3.0)	11 (3.4)	0.752
Renal function			
eGFR (MDRD4; mL/min/1.73 m²) at M24, mean ± SD	76.7 ± 27.38	70.7 ± 22.72	-
Change in eGFR from randomization (mL/min/1.73 m²), mean ± SD	−7.5 ± 28.43	−12.7 ± 24.98	0.002
Proportion of patients with eGFR <60 mL/min/1.73 m² at randomization	**n=78**	**n=69**	-
Shift in eGFR to ≥60 mL/min/1.73 m² at M24, n (%)	37 (47.4)	15 (21.7)	-

*P-value for efficacy based on Z-test for EVR+rTAC – TAC-C = 0; †P-value for change in eGFR from randomization based on Wilcoxon Rank-sum test; ‡KM incidence rate of efficacy endpoints
CEF, composite efficacy failure; eGFR, estimated glomerular filtration rate; EVR, everolimus; KM, Kaplan Meier; M, month; MDRD4, Modification of diet in renal disease formula; rTAC, reduced tacrolimus; TAC-C, standard tacrolimus; tBPAR, treated biopsy proven acute rejection

(B)

	EVR+rTAC (N=387)	TAC-C (N=383)	Risk difference (95% CI), *P*
Patients with HCC at Tx, n (%)	**123 (31.8)**	**128 (33.4)**	
Within Milan	102 (82.9)	96 (75.0)	
Beyond Milan	17 (13.8)	26 (20.3)	
Missing	4 (3.3)	6 (4.7)	
HCC recurrence rate at M24, n/m (%)			
Overall	4/123 (3.3)	8/128 (6.3)	−3.0 (−15.4, 9.4), *P*=0.377
Within Milan	3/102 (2.9)	2/96 (2.1)	0.9 (−13.2, 14.8), *P*=1.000
Beyond Milan	1/17 (5.9)	6/26 (23.1)	−17.2 (−45.6, 13.0), *P* = 0.215
Missing	0/4	0/6	-
HCC recurrence by AFP level (µg/mL) prior to Tx, %			
< 400	2/90 (2.2)	5/104 (4.8)	−2.6 (−16.6, 11.5), *P*=0.453
≥ 400	1/5 (20.0)	2/3 (66.7)	−46.7 (−92.3, 30.1), *P*=0.464
Missing	1/28 (3.6)	1/21 (4.8)	−1.2 (−29.4, 27.1), *P*=1.000
***De novo* malignancies, %**	**N=264***	**N=255***	
	7 (2.7%)	10 (3.9%)	0.68 (0.26, 1.75)†

*patients who did not had HCC at Tx; †data presented as Risk ratio (95% CI)
n, number of patients with HCC event; m, total number of patients who had HCC at Tx
AFP, alpha-fetoprotein; EVR, everolimus; M, month; HCC, hepatocellular carcinoma; rTAC, reduced tacrolimus; TAC-C, standard tacrolimus; Tx, transplantation

[Table 1]

Concurrent Oral Abstract Session: Living Donor

0-060

Five thousands living donor liver transplantation in single center

Song G.-W., Lee S.-G., Hwang S., Kim K.-H., Ahn C.-S., Moon D.-B., Ha T.-Y., Jung D.-H., Park G.-C., Yoon Y.-I., Kwon J.-H., You S.-E., Kang S.-H., Choi J.-W.

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From Dec 1914 to Aug 2018, we've done 5000 LDLT including 4,726 adult and 274 pediatric LDLTs. The mean age of recipients was 48.8 years (3 months~72 years) and 72.9% were males. In adult patients, HBV was the most common original disease accounting for 70%. ALC was 2nd (12%) and HCV 3rd (6%). In the pediatric group, BA was the most common cause (47%). The mean PELD and MELD was 19 and 17.7, respectively. And, 8% of patients showed high MELD over 34. The most common graft type used was MRL (75%). The mean GRWR was 1.10% in RL, 1.06% in dual and 0.87% in LL. The mean OP time and transfusion requirements was 13.8 hours and 11.2 units of RBC. The overall in-hospital mortality was 4.2%. The 1, 5 and 10-year overall graft survival rate was 92.4, 86.4 and 83.6%, respectively. The 1,5 and 10-year patient's survival rate was 93.0, 87.0 and 84.8%, respectively. In the early death (within 1year), infection was the most common cause. In the multivariate analysis, MELD, preoperative patient's conditions including ICU stay, preoperative use of ventilator, hemodialysis and vasopressor were significant risk factors for survival. But, HCC recurrence, de novo malignancy and recurrence of HCV were independent risk factor for long-term survival. The most common surgical complication was biliary stricture (18.2%). The postoperative bleeding was 2nd common (16.9%) and hepatic vein stenosis was 3rd (5.3%). The overall incidence of biopsy-proven in 5,000 LDLT was 18%. Among 5,499 living donors, 67.3% were males. The mean age was 29.4 years. In the relationships between donor and recipients, 62.7% were sibling in adult LDLT and 84.4% were parents in pediatric LDLTs. The overall incidence of major complication in living donor hepatectomy including 91 pure laparoscopic donor hepatectomies were 3.2% and we had no donor mortality.

0-061

Risk factors for long-term mortality in live liver donors

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Background: More than 700 healthy individuals every year undergo hepatectomy for the purpose of liver donation in Korea. However, long-term outcome in live liver donors remains in question. The aim of this study was to evaluate the long-term survival outcome and related factors of live liver donors in Korea.
Methods: Liver donors who were registered in the Korean Network Organ Sharing (KONOS) between February 2000 and December 2015 were included in this study. KONOS of the Korea Center for Disease Control and Prevention (KCDC) is responsible for properly managing the transplantation. Post-donation death was ascertained by linkage to the data of Statistics Korea as of December 31, 2015.
Results: During the observation period, there were 52 deaths among 10,116 live liver donors. Median (interquartile range) follow-up was 5.71 (2.88-9.35) years. Univariate analyses showed that factors significantly associated with mortality after donation were individuals aged 50 to 59 years (HR 6.19, 95% CI 2.78-13.79, P< 0.001), aged 60 years or older (HR 16.49, 95% CI 3.82-71.17, P< 0.001), and divorced people (HR 7.13, 95% CI 2.81-18.10, P< 0.001). Unemployed people (HR 9.39, 95% CI 2.51-35.09, P=0.001) and office workers (HR 3.82, 95% CI 1.27-11.52, P=0.017) were also associated with higher rates of long-term death compared with students. Donor sex, blood type, BMI, smoking or alcoholic habit, level of education, center volume, graft type, donor operation time, year of operation, recipient age, and recipient death were not significantly associated with mortality after donation (P>0.05). Multivariate analyses showed divorce (HR 7.075, 95% CI 2.57- 19.51, P< 0.001) and unemployment (HR 6.969, 95% CI 1.73- 28.1, P=0.006) were significant factors of mortality after donation.
Conclusion: Careful health checkup should be continued and long-term risk information and informed consent should be given especially in live liver donors with risk factors.

0-062

Pure laparoscopic donor hepatectomy: Korean multicenter experience

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Background: Due to increased experience and knowledge in laparoscopic surgery in the era of minimally invasive surgery, laparoscopic donor hepatectomy is also being increasingly performed at some centers, especially in Korea where more than 700 cases of living donor liver transplantation (LDLT) are performed. The aim of this is to present the outcomes of experiences of 5 large volume LDLT centers in Korea.
Methods: Data from live liver donors who underwent pure laparoscopic hepatectomy at 5 centers in Korea until June 2018 were retrospectively analyzed.
Results: Among 511 donors, 54.0% were male. Mean age at donation was 31.9 years and mean body mass index was 23.4 kg/m^2. 91.2% underwent right hepatectomy without middle hepatic vein (MHV), 2.9% right hepatectomy with MHV, 1.8% left hepatectomy without MHV, 2.3% left hepatectomy with MHV, and 1.8% left lateral sectionectomy. Mean operative time was 395.8 minutes and mean warm ischemic time was 9.0 minutes. Mean graft weight was 682.3 g and mean graft-to-recipient weight ratio was 1.1. Mean estimated blood loss was 316.8 cc and there were 10 cases (2.0%) of open conversion. Mean peak bilirubin level was 3.5 mg/dL, AST 227.6 IU/L, and ALT 233.5 IU/L. Mean hospital stay was 9.4 days. There were 15 donor who experienced minor complications (7 donors with wound complication, 3 donors with pleural effusion, 4 donors requiring antibiotics for fluid collection, and 1 donor with pulmonary embolism). There were 19 donors who experienced biliary complication requiring procedure or reoperation. Four donors experienced vascular complication recovered by vascular intervention or reoperation. There were 4 donors with postoperative bleeding requiring reoperation for bleeding control. All donors recovered well.
Conclusion: Pure laparoscopic donor hepatectomy is a feasible procedure and can be established as the new gold standard of practice.

0-063

Donor right hepatectomy: Is robotic approach the way forward?

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Introduction: Robotic donor right hepatectomy, a highly technophilic surgery, is performed only by a handful of centres around the world. Studies comparing pure robotic donor hepatectomy with open approach are limited. We present the first comparative study of robotic versus open right donor hepatectomies from India.
Methods: Prospectively collected data of 20 (M:F=6:14, Age-38.95±10.13) consecutive pure robotic donor right hepatectomies were compared with 62 (M:F=16:46, Age-40.61±10.02) open donor hepatectomies.
Results: Donor biliary anatomy, graft weight (701.85±166.96 Vs 653.53±144.16), GRWR (0.98±0.20 vs 1.00±0.26) and recipient MELD 22.85±5.74 vs 23.89±6.83) were comparable between the robotic and open group respectively. Compared with the open group, operative duration (579.00±61.81 vs 458.23±99.16min, P< 0.001), blood loss (557.50±229.57 vs 390.65±175.88ml, P< 0.001) and primary warm ischemia (15.00±4.38 vs 7.90±3.61min, P< 0.001) were more in the robotic group. However, the robotic group had significantly lower peak postoperative bilirubin (2.88±1.02mg/dl vs 4.09±1.79mg/dl, P< 0.001) & liver enzymes (AST/ALT 290.60±87.99/311.10±105.09IU/ml vs 511.21±369.38/459.53±262.49IU/ml, P< 0.001) with shorter hospital & ICU stays (7.50±1.47 & 3.15±0.75 vs 10.00±2.64 & 3.66±0.60days, P< 0.001, P=0.002). Among recipients, complications rates (bile leak/HAT/infections), graft function (Peak & Day7 Liver functions/SFSS/EAD) and mortality rates were similar between the two groups.
Conclusion: Robotic donor hepatectomy takes significantly longer to perform compared to open hepatectomy. Neverthelss the ICU and hospital stay were signifcantly shorter following robotic surgery. Recipient outcomes were similar in both groups. Future studies should concentrate on whether robotic donor hepatectomy offers better long term quality of life to the donors.

0-064

Is portal inflow modulation always necessary for successful utilization of small volume live donor liver grafts?

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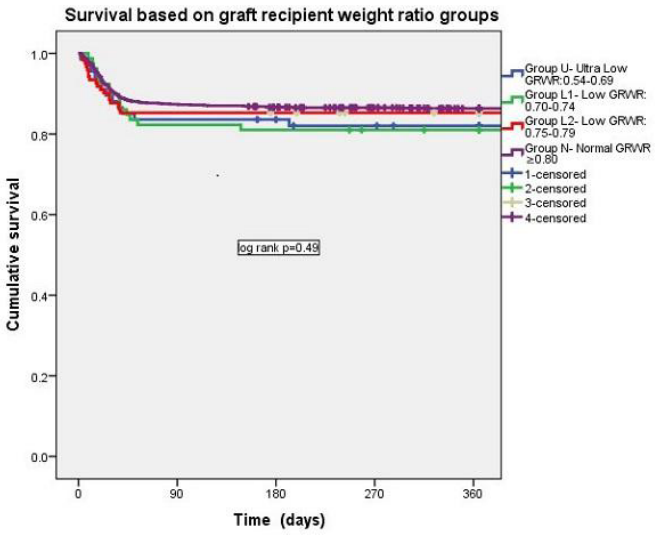
Introduction: While well accepted lower limit of graft to recipient weight ratio (GRWR) for successful living donor liver transplantation (LDLT) remains 0.8%, many believe grafts with lower GRWR may suffice with portal inflow modulation (PIM) with equally good recipient outcomes.
Aim: To evaluate the outcomes of LDLT with small for size graft (GRWR < 0.8) with our PIM protocol based on GRWR and Portal-pressure (PP).
Methods: Of 1321 consecutive adult LDLT from January 2012-December 2017, 287 (21.7%) had GRWR < 0.80%. PIM was performed (HPCS-109, SAL-14) in 42.8% patients according to following protocol: ≥0.8% (Group N) - no PIM; 0.75-0.79% (Group L1) - SAL; 0.70-0.74% (Group L2) - SAL or HPCS; < 0.7 (Group U) - Hemi-portocavalshunt (HPCS). No PIM was done if PP in the dissection phase was < 16 mmHg.
Result: Mean age of cohort was 49.3±9.1 years, 263 were males. Median CTP and MELD scores were 10 and 14 respectively. Majority 50.2% received right lobe graft with subtotal MHV. The lowest GRWR was 0.54%. There were 72 recipients in group U, of whom 58 underwent HPCS and 14 underwent no PIM, while 215 had GRWR between 0.70-0.79%, of whom 51 and 14 underwent HPCS and SAL respectively. During the same period, 1034 had ≥ 0.80% and did not undergo PIM. Median post-reperfusion PP for grafts in group U were 12 (IQR=10-15) while those for groups L1+L2, were 14(IQR=11-17). SFSS developed in 4.2% and 2.3% patients in groups U, and L1+L21 respectively. Three patients needed shunt closure at 0.25, 1 and 60 months. The one year patient survival were shown in figure-1.
Conclusion: With good venous outflow and PIM protocol that optimizes post-perfusion portal pressure, low GRWR grafts can be safely used for appropriately selected LDLT recipients.



[Figure-1 Kaplan Meier survival curve]

0-065

Left lobe living donor liver transplantation - evolving paradigm for the double equipoise

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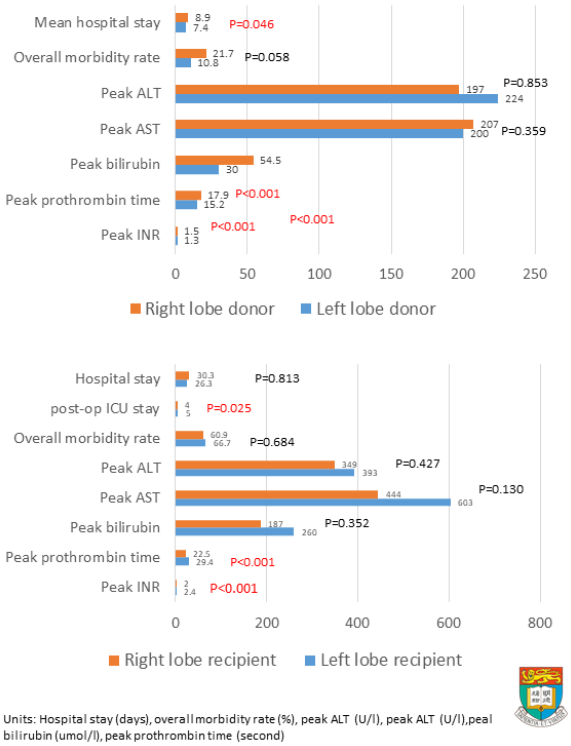
Background: Despite lower morbidity and mortality in left lobe (LL) donor hepatectomy, right lobe (RL) graft remains the preferred choice for living donor liver transplantation(LDLT) in many transplant centres for fear of shifting donor risk to the recipient. However, solid evidence to support such concern is lacking.
Method: Consecutive cohort of adult-to-adult LDLT from 1994-2017 was analysed. Propensity score matching (PSM) was performed before donor and recipient outcomes analyses. Paediatric patients, LDLT using graft types other than hemi-liver graft were excluded.
Results: This retrospective analysis involved 1478 patients. The median follow-up for donor and recipient was 124 and 92 months respectively. After PSM, LL donors were found to have significantly lower peak post-operative bilirubin (30 vs 55 mmol/l), international normalization ratio (INR) (1.3 vs 1.5), and shorter prothrombin time (PT) (15.2 vs 17.9s) (all P < 0.001). In addition, LL donors had significantly shorter hospital length of stay (7.4 vs 8.9) days

when compared to the RL donors (P = 0.046). Though statistically insignificant, there was a trend of lower overall (10.8% vs 21.7%, P=0.058) and severe (Clavien IIIa or above) (0% in LL vs 5% in RL, P=0.337) operative morbidity. There was no donor hospital mortality in this cohort. Concerning the recipient analyses, the median MELD was 16.4. Despite higher prevalence of small-for-size (SFS) graft in LL group (83% vs 23%, P< 0.001), there was no statistical difference in terms of SFS syndrome (15.4% vs 5.6% P=0.081) and in-hospital mortality rate (7.1% vs 1.6%, P=0.100). The 5-year graft survival for LL and RL recipients were 81% vs 83% (P=0.327) respectively.
Conclusion: LL graft is a safe option for both donor and recipient in LDLT and should be the first choice if both LL and RL are suitable.



Units: Hospital stay (days), overall morbidity rate (%), peak ALT (U/l), peak ALT (U/l),peal bilirubin (umol/l), peak prothrombin time (second)

[Left vs Right Lobe Living Donor Liver Transplantation (PS matched comparison)]

0-066

Outcomes after robotic donor hepatectomy in 46 consecutive live donors

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Background: Laparoscopic donor right hepatectomy has been performed in a few centers by expert surgeons. Robotic system is one of the tools for laparoscopic liver resection, however, there have been few studies about surgical outcomes after robotic living donor hepatectomy, especially for a right graft.
Method: From Apr. 2016 to Oct 2018, 46 liver donors received robotic donor hepatectomy (43 right grafts, two left grafts and one left lateral graft) in our institute. Short-term outcomes were evaluated in a prospective way.
Results: The median age of donors was 28.9 years and 22 donors were male. The mean right graft volume was 712.9 ml (range, 517-919). The mean operative time and blood loss were 503 min and 109 ml, respectively. The median warm ischemic demarcation time was 15.1 min. There was no perioperative transfusion. The first case was converted to mini-laparotomy (2.2%) due to injury to the left bile duct and Roux-en-Y hepaticojejunostomy was performed. There were three events related to hem-o-lok including dislodgement from the right bile duct, the inferior hepatic vein and the right hepatic artery. The first two events were managed during the operation, but an emergency laparotomy was needed to control bleeding from the right hepatic artery. Postoperative complications occurred in eleven patients (24.4%) and severe complication more than grade III occurred in two patients (one hepatic artery bleeding and one bladder injury). The mean hospital stay was 9 days.
Conclusion: From our experience, robotic living donor hepatectomy is feasible and safe at expert hands in selected liver donors. However, hem-o-lok should be cautiously used due to the possibility of the dislodgement.

0-067

A proposal of indication for splenectomy in living donor liver transplantation

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Background: In Living Donor Liver Transplantation(LDLT), it has been controversial whether splenectomy should be performed or not. The aim of this study is to identify the indication of splenectomy to prevent Small-For-Size syndrome(SFSS).
Methods: This is a retrospective chart review study. Adult LDLT performed in our institute from 1998 to 2018 were included in this study. Exclusion criteria were the cases with surgical complications within 2 weeks, or the cases with rejection within 2weeks.

Definition of SFSS was total bilirubin more than 5 mg/dL and ascites more than 1.5L/day at post-operative day 14.
Results: 139 patients were included in this study. 13.67%(19/139) developed SFSS. Multivariate logistic regression model showed that Graft Volume/Standard liver Volume (GV/SV) ratio less than 40%(P=0.000), Portal Vein Flow volume/ Graft Volume (PVF/GV) >250ml/min/100g (P=0.036), and donor age>35 (P=0.049) were the independent risk factors for SFSS. Recipient age, etiology, MELD score, and portal vein pressure were not the risk factors.
The incidence of SFSS with or without splenectomy, stratified by GV/SV ratio, were as follows; in GV/SV ratio < 30%, 9.09% vs. 40.0%(with splenectomy vs without splenectomy;P=0.089); in GV/SV ratio 30% to 35%, 7.69% vs. 28.57%(P=0.150); in GV/SV ratio 35% to 40%, 0% vs. 30.0%(P=0.056). In patients with GV/SV ratio >40%, no SFSS was observed in both groups.
Subgroup analyses were performed in patients with GV/SV ratio less than 40%. Among the patients with PVF/GV less than 250ml/min/100g, there was no significant differences in the incidence of SFSS between with or without splenectomy (16.67% vs 15.38%;P=0.930). On the other hands, the patients with PVF/GV more than 250ml/min/100g, the incidence of SFSS was lower in splenectomy group than non-splenectomy group (10.0% vs 38.24%;P=0.031).
Conclusions: In LDLT, Splenectomy is indicated those who with GV/SV ratio less than 40% and PVF/GV more than 250ml/min/100g to prevent SFSS.

0-068

Inferior graft and patient survival following offspring to parent living donor liver transplantation

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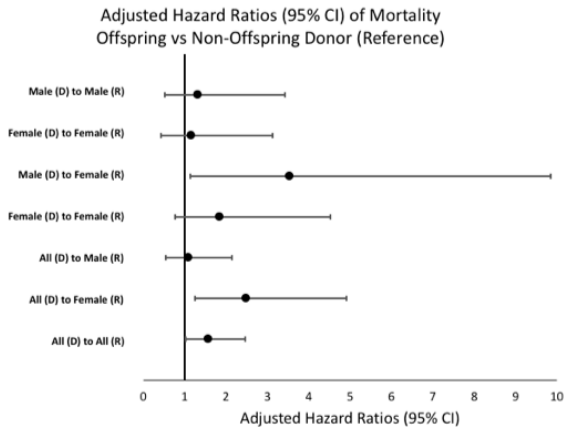
Background: Offspring (donor) to parent (recipient) transplant is the most common form of living donor liver transplant in the United States. Following living donor kidney transplantation Female recipients of offspring living kidney allografts have been demonstrated to have inferior outcomes, which is believed to be related to issues of female recipient to offspring alloimmunization during pregnancy. It is unknown whether this same phenomenon occurs following liver donor liver transplantation.
Methods: A retrospective analysis was completed including all recipients of a living donor liver transplant from January 1990 to January 2018 in the OPTN/UNOS database. Patients were grouped as having received a donor liver allograft from an offspring or a non-offspring, with exactly three HLA matches, as would be expected between an offspring and parent. Graft and patient survival were analyzed using Cox proportional hazards modeling.
Results: Among recipients with exactly three HLA matches with their donor, 282 offspring to parent and 251 non-offspring donor liver transplants were performed. Female recipients of offspring liver allografts had both inferior 10-year graft (52% vs 72%, P< 0.001) and patient survival (52% vs 81%, P< 0.001) compared with female recipients of non-offspring allografts. No such difference in outcomes was discovered amongst male recipients. A stratified analysis of sex of offspring donors to female recipients demonstrated that male gender was associated with graft failure (HR=2.99, P=0.02) and mortality (HR=3.54, P=0.03). Again, this association was not seen with male recipients.
Conclusions: Among female recipients, offspring to parent living donor liver transplantation yields inferior long-term graft and patient survival. Furthermore, among offspring donors, male gender was strongly associated with inferior outcomes. It is unclear to what extent alloimmunization during pregnancy is associated with these findings. If available, non-offspring to recipient living donor liver transplant should be favored.



[Adjusted Hazard Ratios of Mortality Offspring vs. Non-Offspring (Reference)]

Plenary Abstract Session I

0-069

Predicting early post-operative sepsis in liver transplantation applying artificial intelligence

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Background: Artificial intelligence (AI) and machine learning can be used to identify patients at risk for events earlier, thereby reducing risk of consequences. In liver transplantation, early systemic infection leads to severe recipient complications. Early identification and prompt intervention may improve outcomes.
Data: This pilot study is part of a larger project, identifying 'physiomarkers' in continuous minute-by-minute physiologic data streams to predict the onset of sepsis. A total of 5,748 ICU patients across the Methodist University Hospital and Transplant Institute (UTHSC) were monitored over 8-months. 604 patients developed sepsis, identified using the "Sepsis-3" criteria. We further collected continuous data from 48 deceased donor liver transplant patients (ICU-stay), of which 13 transplant patients developed early sepsis.
Results: Using AI and an alert timestamp generated by the Sepsis-3 definition as a reference point, we studied up to 24 prior hours of continuous physiologic data totaling 8.35 million data points. 150 features were generated using signal processing and statistical methods. Recursive feature elimination identified 22 highly ranked features (Figure 1), all of which were derived using only the systolic BP stream. A Random Forests classifier was then trained on the ranked features using 5-fold cross validation on all non-transplant patients (n=5,748) and the optimal model was subsequently evaluated on the transplant patients (n=48). The average sensitivity, specificity, PPV and AUC after 10-iterations of the model was 0.74±0.04, 0.69 ±0.03, 0.47 ±0.01, 0.71 ±0.01.
Conclusion: This pilot study suggests machine /deep learning AI can be applied to continuous streaming data in transplant ICU to predict sepsis, and potentially other complications and ultimately aid clinical decision making and reduce adverse events for liver transplants.

0-070

IL-17A aggravates liver IR injury by mobilizing B1a cells through CXCL13

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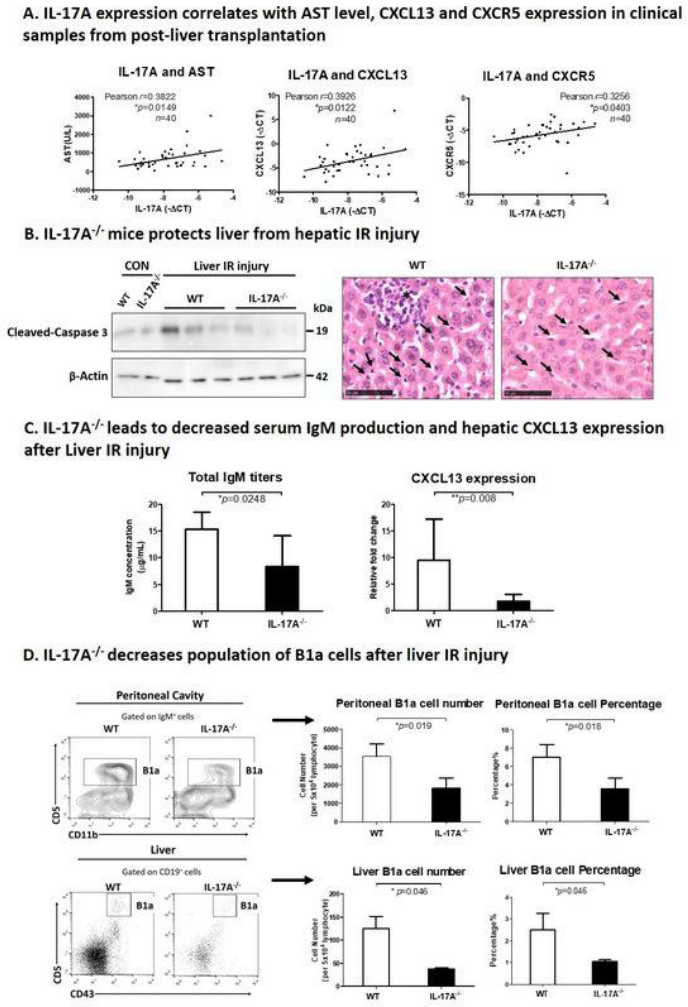
Background: IL-17A was found critical in liver ischemia-reperfusion (IR) injury. However, the mechanism remains unclear. Recently, IL-17A was reported to promote B1a cell differentiation during lung infection. B1a cells are involved in tissue ischemia reperfusion injury by producing IgM. Here we aim to explore the mechanism of IL-17A regulating hepatic ischemia reperfusion injury through clinical study and animal models.
Methods: Human liver biopsies from post-liver transplantation were used for clinical study. Hepatic ischemia reperfusion injury models were applied using IL-17A$^{-/-}$and WT C57BL/6 mice. Lymphocytes were isolated from mice peritoneal cavity, spleen and liver for *in vitro* functional study.
Results:
Firstly, IL-17A aggravates liver IR injury. In clinical study, hepatic expression of IL-17A (n=40) correlated with serum aspartate aminotransferase (AST) level post-liver transplantation (p=0.0149) (Figure 1A). Consistently, IL-17A knockout mice (IL-17A$^{-/-}$) showed decreased apoptosis from Western blot, less lymphocyte infiltration (asterisk) and less endothelial cell swelling (arrow) from H&E staining (Figure 1B).
Secondly, IL-17A induces natural IgM secretion and B1a cell mobilization after liver IR injury. In clinical study, liver expression of IL-17A (n=40) correlated with expression of CXCL13 (p=0.0122) and CXCR5 (p=0.0403) (Figure 1A). At 2 hours after hepatic IR injury, downregulation of hepatic mRNA expression of CXCL13 was found in IL-17A$^{-/-}$ mice (p=0.008). Total serum natural IgM titers were significant decreased in IL-17A$^{-/-}$ mice (p=0.0248) (Figure 1C). Consistently, decrease of peritoneal B1a cell population (p=0.019) as well as liver infiltrated B1a cell population (p=0.046) in IL-17A$^{-/-}$mice were found after liver IR injury (Figure 1D).
Conclusion: IL-17A aggravates hepatic ischemia reperfusion injury through natural IgM from B1a cells, which are mobilized by CXCL13 during the acute phase injury.



[IL-17A aggravates liver IR injury by mobilizing B1a cells through CXCL13]

0-071

Defatting steatotic rat livers during ex situ normothermic perfusion improves lactate clearance and bile quality

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Purpose: Donor livers with moderate-to-severe steatosis are not generally used for transplantation because of poor post-transplant function. Ex situ normothermic machine perfusion (ENMP) provides an opportunity to decrease fat content and assess functional improvement. We evaluated the ability of a 7-component defatting cocktail to decrease macrosteatosis (MaS) and improve perfusion parameters in rat fatty livers.

Methods: 6 each of lean Zucker rat livers (NL) and steatotic livers (SL) from obese Zucker rats underwent 6 hours of ENMP with standard perfusion medium; an additional 6 SL were perfused with the addition of a defatting cocktail (SLD) containing visfatin, hypericin, forskolin, scoparone, L-carnitine, GW7647, and GW501516. Perfusion dynamics were recorded and perfusate samples collected hourly; macrosteatosis at the end of perfusion was determined in blinded fashion by a pathologist by H & E.

Results: nAfter 6 hours ENMP, SL livers retained 41.5% MaS (range 25-58%) while SLD had only 8.5% MaS (range 1-18%); NL were < 2% MaS, as expected. At 6 hours, perfusate lactate content was significantly higher in SL (13.4 ± 4.0 mg/dL) compared to LL (6.6 ± 1.0 mg/dL, p=0.001) and SLD (8.2 ± 1.7 mg/dL, p=0.01). Perfusate ketone content was significantly higher at 4 and 6 hours in SLD compared to SL (p< 0.05 for both). Interestingly, perfusate triglyceride levels increased significantly more over 6 hours in SL (140 ng/uL) than SLD (43 ng/uL, p< 0.001). Bicarbonate content in produced bile was significantly higher in SLD (42 mmol/L) than SL (26 mmol/L), and even NL (31 mmol/L, p< 0.001), although cumulative bile volume remained higher in NL.

Conclusion: Moderate-to-severe macrosteatosis can be reversed in rat fatty livers using a 7-component defatting cocktail during 6h ENMP, resulting in significantly improved lactate clearance and bile quality. Further studies to test liver viability in a transplant model are planned.

0-072

Δ42PD1 as a new target for preventing tumor recurrence after liver transplantation

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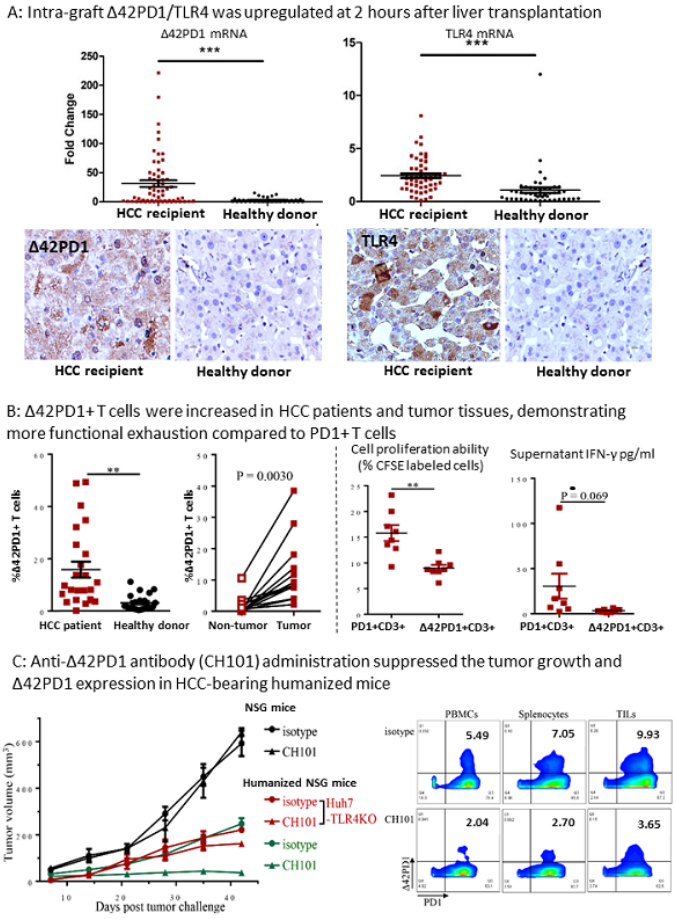
Objective: T cell functional exhaustion is one of the mechanisms that promote tumor recurrence after liver transplantation. Δ42PD1 was newly identified as an isoform of PD1 with the Toll-like receptor 4 (TLR4) as a receptor. We aimed to investigate the role of Δ42PD1 in liver transplantation and to evaluate the efficacy of Δ42PD1 blockade on HCC recurrence.

Methods: The expression of Δ42PD1/TLR4 in graft tissues after liver

transplantation was detected by RT-PCR and immunohistochemistry. Peripheral blood and tissue Δ42PD1+ T cell proportion was analyzed by flow cytometry. Proliferation of isolated T cells from HCC patients was evaluated by CFSE labeling. Supernatant IFN-γ level was detected by ELISA. Liver tumor model was established in a humanized-mouse model with human lymphocytes engrafted. Anti-Δ42PD1 antibody (CH101) or its isotype was administrated in HCC-bearing humanized mice.

Results: Intra-graft Δ42PD1/TLR4 expression was upregulated after liver transplantation (Fig1A) and was significantly higher in patients with tumor recurrence. Circulating Δ42PD1+ T cells were increased in HCC patients compared to healthy donors. Besides, there were more Δ42PD1+ T cells in tumors compared to adjacent tissues (Fig1B left). In vitro, isolated Δ42PD1+ T cells from HCC patients demonstrated more functional exhaustion with decreased low CFSE+ percentage and reduced IFN-γ secretion compared to PD1+ T cells (Fig1B right). In HCC-bearing humanized mice, CH101 exerted strong effects against tumor growth in a T cell dependent manner, involving Δ42PD1/TLR4 axis (Fig1C left). Moreover, tumor-induced Δ42PD1 expression in peripheral blood mononuclear cells, splenocytes and tumor-infiltrating lymphocytes were notably downregulated by CH101 (Fig1C right) in humanized mice, along with lower plasma IL-6, IFN-γ and IL-17a level.

Conclusion: Δ42PD1/TLR4 signaling upregulated in early phase after liver transplantation promotes HCC recurrence. Targeting Δ42PD reverses T cell exhaustion and brings restorative immune response for HCC recurrence.



[Figure 1]

0-073

Prediction of hepatocellular carcinoma (HCC) recurrence after surgical resection using clinico-pathologic and immunohistochemical (IHC) characteristics

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Background: Although surgical resection is the main therapy for HCC patients, most patients develop tumor recurrence. The different staging systems do not allow to accurately predict recurrence post-operatively. This study aims to develop a recurrent classifier (rClass) to predict the one- and three-year tumor recurrence rates after surgery.

Methods: It was a retrospective study including 677 patients (training/validation sets: 507/170, October 2010 to December 2013) and 105 patients (February 2012 to January 2013, external validation set) from two institutions, having a ≥5-year follow-up after liver resection. Several clinico-pathologic characteristics and the gene expression of 29 biomarkers using IHC on paraffin-embedded tissues (tumor and adjacent non-tumor) (Ki-67, cyclin D1, PCNA, TGF-β, S100A4, CDKN1A, CDKN1B, BAX, caspase-9, Fas, S100A9, PDCD4, survivin, VEGF, CD34, E-cadherin, β-catenin, TYSY, MMP-2, MMP-9, EMA, c-Myc, HRas, p53, PTEN, CEA, CK19 and MLH1, MSH2) were investigated. The rClass was developed using the maximum relevance minimum redundancy algorithm jointly with the multivariable logistic regression method from the training and the two, internal and external, validation cohorts.
Results: Five clinico-pathologic characteristics (age, tumor location, number and diameter, AFP level) and six immunomarkers (S100A9, PCNA, CD34, E-cadherin, HRas and p53) were integrated into a rClass and validated afterwards. Favorable discrimination was observed in all cohorts at one- and three-years respectively (AUC: the training cohort: 0.758, 95% CI: 0.718-0.794); the one-year internal and external validation cohorts: 0.751, 95% CI:0.679-0.814; 0.730, 95% CI:0.635-0.812) and the three-year cohorts (AUC: 0.734, 95% CI:0.693-0.772; 0.749, 95% CI: 0.677-0.812 and 0.730, 95% CI: 0.635-0.812). Good correlation was observed between the predicted and the actual recurrent probability for all three cohorts.
Conclusion: A tumor recurrent classifier by using both clinico-pathologic characteristics and immunomarkers is proposed. This classifier can be used to predict HCC recurrence after liver resection in order to further individualize the care of HCC patients.

0-074

Clinical features and prognosis of DIHBS (diffuse intrahepatic biliary stricture) after adult ABO-incompatible living donor liver transplantation

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Introduction: Despite the advancement in desensitization protocol, diffuse intrahepatic biliary stricture (DIHBS), an attenuated form of antibody mediated rejection (AMR), remains an unresolved problem. As a high-volume LT center, we retrospectively review clinical outcome and prognosis of recipients who developed DIHBS after ABOi LDLT.

Method: From November 2008 to December 2017, total of 497 cases of ABO incompatible LDLT were performed at Asan Medical Center. Among them, twenty-four patients (4.83%) developed DIHBS. Retrospective review of medical records of these patients was carried out.
Result: Median time of diagnosis for DIHBS after ABOi LDLT was 2.8 months. In patients with DIHBS, the 3-year patient survival rate was 69.9%. Causes of patient death in nine patients were recurrent HCC in four patients, biliary sepsis in two patients, graft failure (not associated with AMR) in one patient, post-operative bleeding after re-LT in one patient, and pneumonia in one patient. Nine patients (37.5%) received re-transplantation. Graft survival rates at 3-year was 40.6%. Both patient survival and graft survival rates were significantly lower than ABOi LDLT recipients without DIHBS (both p< 0.001). Between ABOi LDLT patients with or without DIHBS, there were no significant differences in pre-operative isoagglutinin (IA) titer, post-operative peak bilirubin, AST, ALT, IA titer, and pre- and post-operative frequency of total plasma exchange (TPE).
Among the other fifteen patients who are alive, five patients got re-LT, three patients presented mild graft dysfunction with well-functioning PTBD, three patients showed resolution of DIHBS and removed biliary drainage, and four patients demonstrate normal graft function with well-maintained biliary drainage.
Conclusion: In this study, DIHBS developed usually before 3 months after ABOi LDLT. DIHBS significantly affects short and long-term outcome in ABOi LDLT. In patients who demonstrated DIHBS, over half of the patient progress to graft failure and need re-LT.

0-075

Reevaluation of the six-month abstinence rule in liver transplant for alcoholic liver disease: a single center analysis

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Introduction: Abstinence < 6mo is considered a relative contraindication to liver transplant (LT) in alcohol-related liver disease (ALD); however, this policy potentially risks mortality in high MELD patients. Our current institutional policy waives the “6-month rule” for high acuity patients. The present study seeks to evaluate LT

outcomes in ALD with >6mo or < 6mo of pretransplant sobriety.
Methods: A single-center prospective protocol allowing LT with < 6mo sobriety (L6S) was established in 2009, and outcomes were compared to pts with >6mo sobriety (G6S) transplanted over the same period.
Results: From 2008-2017, 151 ALD pts underwent LT (69 L6S, 82 G6S). Median duration of abstinence was 49d for L6S and 300d for G6S (p< 0.001). Median listing MELD was 36 for L6S and 20 for G6S (p< 0.001). L6S tended to be younger, have higher MELD at LT, more often hospitalized, and have shorter duration from listing (all p< 0.001); whereas, G6S more likely had a secondary diagnosis in addition to ALD (p< 0.001). Despite this, overall survival was 99%, 94%, and 84% at 1-, 2-, and 4-years for L6S compared with 91%, 84%, and 81% for G6S (p=ns). Median post-transplant length of stay was greater for L6S (23d) vs. G6S (9d, p=0.02). There was no significant difference in post-LT problematic drinking (20.3%-v-11%, p=ns) or slips (26%-v-12%, p=ns) between L6S and G6S. Multivariate Cox Proportional Hazard analysis demonstrates that only presence of secondary diagnosis to ALD (HR 3.24, p=0.04) and longer pre-LT ICU stay (HR 1.07, p=0.003) significantly predict post-LT mortality.
Conclusion: Despite great medical acuity and longer recovery, survival and recidivism for L6S are similar to G6S. Given that post-LT mortality is notably affected by pre-LT ICU length of stay, earlier intervention with LT should be considered regardless of pre-LT sobriety duration in patient with proper social support.

O-076

Improvement of renal function with everolimus plus reduced tacrolimus in de novo liver transplant recipients - HEPHAISTOS study 12 month data.

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Background: The HEPHAISTOS study compared efficacy and safety of early use of everolimus [EVR] and reduced tacrolimus [rTAC] with standard tacrolimus [TAC-C] in de novo liver transplant [LTx] recipients, and demonstrated the impact of CNI minimization on renal function.
Methods: In this 12 months [M] prospective, open-label, randomized study with 15 German sites, 333 patients [pts] were randomized 1:1 between day 7 to 21 after LTx to either EVR(3-8ng/ml) + rTAC (< 5ng/ml), or TAC-C(6-10ng/ml), all with steroids until M6. Here, we report M12 outcomes on renal function from full analysis [FAS] and per protocol [PP] set.
Results: 169 and 164 pts treated with EVR+rTAC and TAC-C, respectively were analysed in this study (FAS). Mean TAC trough concentration in pts treated with EVR+rTAC exceeded target range until M3 and remained close to the upper limit of the target range thereafter. Efficacy at M12 was demonstrated with similar incidence rates with EVR+rTAC or TAC-C. Mean eGFR (MDRD4) was numerically higher with EVR+rTAC to M12 (adjusted mean difference of 4.09 mL/min/1.73m^2; p=0.0970; FAS). Among pts in the PP (n=110 EVR+rTAC, n=101 TAC-C), eGFR was significantly higher with EVR+rTAC (+7.79 mL/min/1.73m^2; p=0.0085) as compared to TAC-C, without compromising efficacy.
Conclusion: Use of EVR in combination with rTAC as early as 15 days post-LTx allowed for better renal function compared to TAC-C which was sustained up to M12. Thus, HEPHAISTOS provides evidence that an early reduction of TAC post LTx is key in improving renal function.

O-077

Results of LITMUS (NCT 02541916): the liver immune tolerance bio marker utilization study

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Background: Previously we reported a novel biomarker gene set for the identification of tolerance in murine models of rapamycin-induced cardiac tolerance and spontaneous hepatic tolerance.
Methods: In this Phase 2A single-center study, we examined whether an 8 target and 5 housekeeping gene expression panel in peripheral blood mononuclear cells (PBMC) and liver allografts could identify operationally tolerant liver transplant recipients. We first measured the panel in PBMC from 60 adult liver transplant recipients who were a minimum of 3 months post-transplant and who had no biochemical evidence of rejection. Patients with a putative tolerant gene profile in PBMC underwent a liver biopsy and were then weaned off of immunosuppression (IS). PBMC gene expression was monitored at 3, 6, and 12 months post IS withdrawal.
Results: Of the 60 patients studied, 16 had the putative tolerance gene profile in their PBMC. Twelve patients agreed to enter the withdrawal phase of the study. Prior to withdrawal, a liver biopsy was performed, and 3 patients were excluded as their biopsies showed recurrent disease and/or rejection. Of the 9 remaining patients, 5 have now been weaned off of IS and are greater than

2 years post IS withdrawal, 2 are undergoing withdrawal and 2 developed acute cellular rejection, which was easily reversed. Five of 5 patients who had the gene expression profile both in liver and PBMC were successfully weaned off immunosuppression. In patients who achieved tolerance, levels of *fgl2* remained stable over time, *foxp3* gene expression increased at 3 months and then returned to baseline, and *tigit* gene expression increased at 6 months post-IS withdrawal and remained elevated at 1 year.
Conclusion: These data suggest that a combination of gene expression monitoring in PBMC and the liver allograft may identify operationally tolerant recipients, allowing for withdrawal of immunosuppression.

O-078

Living donor liver transplantation for biliary atresia: an analysis of 2,085 cases in the Registry of the Japanese Liver Transplantation Society

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Biliary atresia (BA) is the most common indication for liver transplantation (LT) in pediatric population. This study analyzed the comprehensive factors that might influence the outcomes of patients with BA who undergo living donor LT by evaluating the largest cohort with the longest follow-up in the world.Between November 1989 and December 2015, 2,085 BA patients underwent LDLT in Japan. There were 763 male and 1,322 female recipients with a mean age of 5.9 years and body weight of 18.6 kg. The 1-, 5-, 10-, 15- and 20-year graft survival rates for the BA patients undergoing LDLT were 90.5%, 90.4%, 84.6%, 82.0% and 79.9%, respectively. The donor body mass index, ABO incompatibility, graft type, recipient age, center experience and transplant era were found to be significant predictors of the overall graft survival. Adolescent age (12 to < 18 years) was associated with a significantly worse long-term graft survival rate than younger or older ages.
We conclude that LDLT for BA is a safe and effective treatment modality that does not compromise living donors. The optimum timing for LT is crucial for a successful outcome, and early referral to transplantation center can improve the short-term outcomes of LT for BA. Further investigation of the major cause of death in liver transplanted recipients with BA in the long-term is essential, especially among adolescents.

Concurrent Oral Abstract Session: Machine Perfusion

0-079

Prevention of graft ischemia-reperfusion injury in ischemia-free liver transplantation

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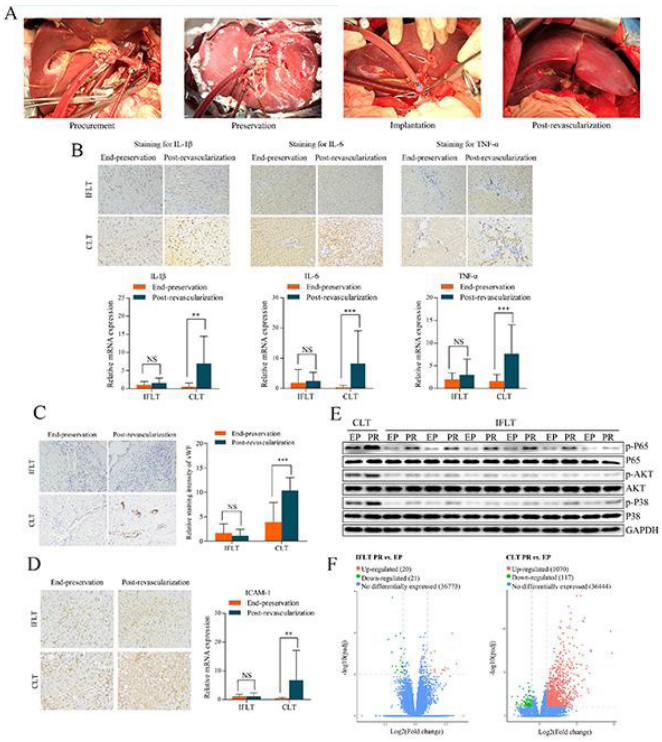
Background: Graft ischemia-reperfusion injury (IRI) is an inevitable event in organ transplantation, which leads to a number of complications and even patient deaths. We aim to prevent IRI through the innovation of ischemia-free liver transplantation (IFLT).
Methods: IFLT involves surgical techniques and the use of normothermic machine perfusion to enable a continuous blood supply to donor livers during procurement, preservation and implantation. We analyzed the perfusate and the biopsies of liver grafts of the first 14 IFLT cases to assess the severity of IRI.
Results: During the whole procedure of IFLT, the perfusion flow and pressure were stable. The liver grafts were functioning well with quick lactate clearance and continuous bile production. The metabolomic analysis showed active TCA cycling and ATP production during the procedure. The AST and ALT levels of the perfusate didn´t increase when compared to those in the serum of the donors. The Suzuki score, apoptotic hepatocyte numbers, pro-inflammatory cytokine release, endothelium injury, inflammasome and pyroptosis activity of the liver grafts after reperfusion were not elevated in IFLT. In contrast, all these IRI-related markers were substantially elevated in the standard procedure using static cold storage method. Notably, the transcriptomic analysis showed that the expression of only 20 genes were significantly up-regulated and 21 genes were down-regulated in the IFLT group, while 1070 genes were up-regulated and 117 genes were down-regulated in the control group. The single cell sequencing analysis showed profound transcription reprogramming in different cell types in the control group, while no obvious transcription reprogramming occurred in the IFLT group.
Conclusion: This study shows for the first time that IRI can be largely avoided in IFLT. A broader application of IFLT offers a brand new opportunity to optimize transplant outcomes and maximize donor organ utilization.



[Fig. 1]

0-080

Increased and safe utilization of high-risk donor livers for transplantation after ex situ resuscitation and assessment using sequential hypo- and normothermic machine perfusion

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Background: Despite persistent donor organ shortage, a high number of donor livers is currently not used for transplantation. We aimed to increase the number of transplantable livers by resuscitating and assessing hepatobiliary viability of initially declined high-risk livers using a protocol of end-ischemic sequential ex situ hypothermic and normothermic machine perfusion.
Method: In this prospective clinical trial, all nationwide declined livers were eligible for inclusion (Netherlands Trial Registry NTR5972). The protocol consisted of one hour hypothermic oxygenated perfusion (10°C) for resuscitation, one hour of controlled oxygenated rewarming, and subsequent normothermic machine perfusion (NMP) for viability testing. A perfusion fluid containing a hemoglobin-based oxygen carrier was used for all temperature phases. During the first 150 min of NMP, hepatobiliary viability was assessed, using the following criteria: perfusate lactate < 1.7mmol/L, pH 7.35-7.45, cumulative bile production >10mL and biliary pH>7.45. Livers meeting these criteria were secondary accepted for transplantation. All recipients gave written informed consent. Primary endpoint was safety and feasibility, as reflected by a 3-months graft survival rate of at least 80%.
Results: Between August 2017 and October 2018, 16 livers underwent machine perfusion after an average of 288 (241-480) min of static cold preservation. All livers were derived from donation after circulatory death donors, with a median age of 63 (range 42-82) years. During NMP, all livers cleared lactate and produced sufficient bile volume, but in 5 cases biliary pH remained < 7.45. The 11 (69%) livers that met all viability criteria were successfully transplanted, increasing the number of deceased donor liver transplants by 20%. Patient and graft survival at 3 months was 100%.
Conclusion: Sequential hypo- and normothermic machine perfusion enabled resuscitation and selection of initially declined high-risk donor livers. This method offered a valuable tool to safely increase the number of transplantable livers by 20%.

0-081

Assessment of clinical perfusates for normothermic ex-situ liver perfusion in a pig transplant model with DCD grafts

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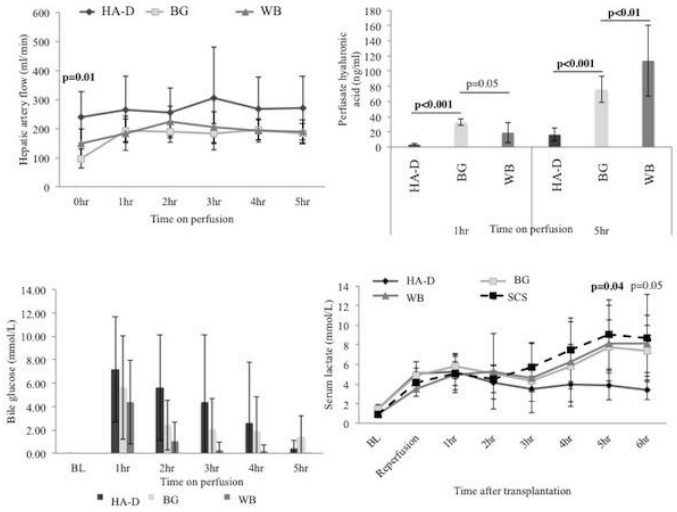
Background: Human-albumin/Dextran(HA-D), Bovine-gelatin(BG) and plasma plus packed red blood cells have been used in European and North-American clinical trials of normothermic ex-situ liver perfusion(NEsLP). We compared the effects of these perfusates in a porcine model during NEsLP and after transplantation.
Methods: Porcine livers were retrieved 30mins following circulatory death. After 5hrs of NEsLP, grafts were transplanted. Three groups(n=6) were assessed[HA-D vs BG vs whole blood(WB)]. One group of static cold storage(SCS) was evaluated for comparison with the perfusion groups. Hemodynamic variables, liver and endothelial injury and function were assessed during NEsLP and post-transplantation.
Results: Hepatic artery flow was higher since the beginning of NEsLP in the HA-D group (HA-D:238±90ml/min vs BG:97±33ml/min vs WB:148±49ml/min;p=0.01). Hyaluronic-acid was found lower in the HA-D group by the end of perfusion(HA-D:16.28±7.59ng/ul vs BG:76.05±15.30ng/ul vs WB:114±46ng/ul;p< 0.001). After transplant, AST was lower in the HA-D group when compared to the other groups(HA-D:444±226IU/L vs BG:1033±694IU/L vs WB:616±444IU/L vs SCS:2235±1878IU/L). At 5hr after transplant, lactate was decreased in the HA-D group(HA-D:3.88±1.49mmol/L vs BG:7.79±2.68mmol/L vs WB:8.16±3.86mmol/L vs SCS:9.06±3.54mmol/L;p=0.04). INR was improved in HA-D grafts compared to the other groups(HA-D:1.23±0.30 vs BG:1.63±0.20 vs WB:1.50±0.31 vs SCS:1.97±1.55;p=0.03) after transplantation. In contrast, the BG group displayed lower AST during NEsLP(BG:142±52IU/L vs HA-D:183±53IU/L vs WB:285±74IU/L;p=0.01) and less cleaved-caspase-3 staining(BG:0.95±1.14% vs HA-D:2.05±0.73% vs WB:1.74±0.54%) after transplantation. The bile from the WB group showed more physiologic pH(WB:7.59±0.18 vs HA-D:7.54±0.11 vs BG:7.34±0.37) and glucose(WB:0±0mmol/L vs HA-D:0.38±0.75mmol/L vs BG:1.42±1.75mmol/L) at the end of NEsLP.
Conclusion: HA-D, BG and WB perfusates have different effects on graft function and hepatocyte, biliary and endothelial injury. Optimization of the perfusates based on the characteristics of these solutions will potentially improve the outcomes with the use of NEsLP in marginal grafts.



[Comparison of clinical perfusates during NEsLP and after transplantation]

between 2013 and 2016 were compared in terms of intra-operative thromboelastography (TEG) characteristics (R-time, K-time, α-angle, maximum amplitude [MA], G-value and LY30) to a propensity matched control group, where the grafts were preserved by traditional static cold storage (SCS).

Results: After propensity matching, none of the TEG characteristics were found to differ significantly between the 72 pairs of SCS and NMP organs when measured pre-implantation. However, post-implantation, NMP organs had significantly shorter K-time (median: 2.8 vs. 3.6 mins, p=0.010) and R+K-time (11.4 vs. 13.7 mins, p=0.016), as well as significantly larger α-Angle (55.9 vs. 44.8 deg, p=0.002), MA (53.5 vs. 49.6 mm, p=0.044) and G-values (5.8 vs. 4.9k dynes/cm^2, p=0.043) than SCS organs. Hyperfibrinolysis after implantation was also mitigated by NMP, with fewer patients requiring aggressive factor correction during surgery [LY30=0, NMP vs. SCS: 83% vs. 60%, p=0.004]. As a result, NMP organs required significantly fewer units of platelets to be transfused during the transplant procedure (median: 5 vs. 0, p=0.001).

Conclusion: In this large study, we have shown that NMP liver grafts return better coagulation profiles intraoperatively, which could be attributed to the preservation of liver grafts under physiological conditions.

0-082

Normothermic machine perfusion enhances intraoperative hepatocellular synthetic capacity: a propensity-score matched analysis

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Background: Normothermic machine perfusion (NMP) of liver grafts is increasingly being incorporated in clinical practice and evidence so far has also shown that NMP plays a role in reconditioning the synthetic and energy capabilities of grafts. Intraoperative coagulation profile is a surrogate of graft quality and preservation status; however, to date this aspect has not been documented.

Method: The LT recipients who received NMP liver grafts in the QEHB

0-083

Novel real time prediction of liver graft function during hypothermic oxygenated machine perfusion prior to liver transplantation

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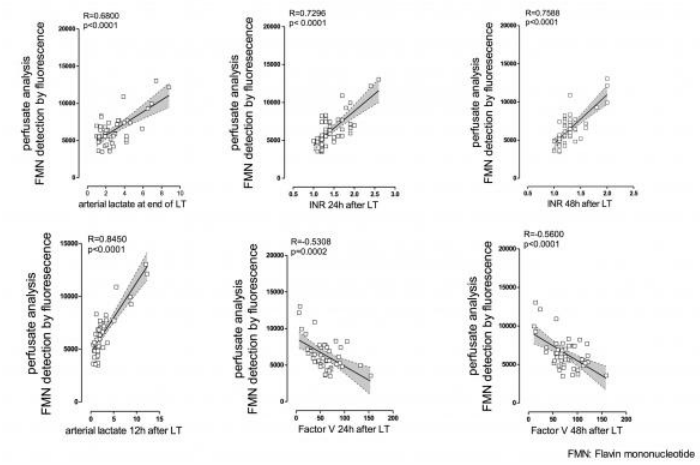
Background: *Ex-situ* machine perfusion is a new method to potentially repair injured organs and assess organ function. We have developed a simple machine perfusion technique, hypothermic oxygenated perfusion (HOPE), which is applied after cold storage for 1-2 hours through the portal vein. Here we analyse, whether liver function can be predicted during HOPE, besides optimization of outcomes.

Methodology: Endischemic HOPE-treatment was used to improve and assess all livers from donation after circulatory death (DCD) and marginal brain death donors at our centre in the past 5-years. The overall tumour censored 5y-graft survival was 89%. Recent reports, suggest a significant injury of mitochondrial complex I during

re-oxygenation after ischemia. Here we quantified the released mitochondrial flavoproteins (flavin-mononucleotide, FMN) in the perfusate of 50 human livers during HOPE (fluormetric analysis). Monochrome light (wavelength 450nm) was introduced into the perfusate, and a spectroscopic detector quantified the proportion of fluorescent light. The peaks detected at a wavelength of 500-600nm, corresponded to the emission spectrum of FMN, and were validated by NMR-analysis. Perfusate measurements were correlated to liver graft function after transplantation.
Results: Real time optical measurement of mitochondrial FMN release in machine perfusates of fifty livers correlated strongly with lactate clearance and coagulation factors (INR, Factor V) at day 1 and 2 after transplantation (Figure 1). ROC-analysis revealed an area under the curve of 0.80 (95%-CI:0.67-0.93) for allograft dysfunction.
Conclusion: We demonstrate for the first time an accurate and fast prediction of liver graft function during *ex-situ* machine perfusion before implantation, which base on determining the level of complex-I-injury in liver cell mitochondria. We expect a high clinical relevance of our results, as on-line estimation of outcome before liver implantation will substantially increase the safe utilization of high-risk livers previously deemed unsuitable for transplantation.



[Prediction of graft function by machine perfusate analysis during HOPE]

0-084

Benefit of hypothermic oxygenated machine perfusion in liver transplantation with grafts from extended criteria Donors after Brain Death (DBD)

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Background: Hypothermic oxygenated machine perfusion (HOPE) was introduced to decrease ischemia-reperfusion injury and reduce biliary complications in liver transplantation (LT). Available clinical data are mainly focused on LT with grafts from donors after cardiocirculatory death, whereas data on extended-criteria DBD LT are lacking. We aimed at evaluating HOPE impact on early LT outcomes and biliary complications.
Methods: Data on primary adult DBD LTs performed in the period March 2016 to June 2018 were prospectively collected and retrospectively analyzed. Minimum follow-up was 6 months. HOPE was used in case of donor age > 80, donor body mass index > 30, severe graft steatosis at macroscopic evaluation or expected long ischemia time. Outcomes of recipients of grafts treated with HOPE were compared to those after static cold storage (SCS). Propensity score matching (1:2) and Bayesian model averaging were used to overcome selection bias. Associations between first-hour perfusion values and post-LT transaminases peak and early allograft dysfunction (EAD) onset were analyzed.
Results: 269 grafts preserved by SCS were compared to 25 treated with HOPE. Propensity score matching analysis showed a significant reduction of the incidence of stage 2-3 acute kidney injury (AKI) (16% versus 42%, p=0.046) and a trend towards a reduction of severe post-reperfusion syndrome (PRS) (4% versus 20%, p=0.13). Bayesian model averaging confirmed these findings and showed a reduction of post-LT transaminases peak and EAD rate in HOPE group. HOPE treatment had no effect on biliary complications (overall and graft cholangiopathy). There was no difference in patient and graft survival. First-hour flow and resistance values during HOPE did not correlate with transaminases peak or EAD rate.
Conclusions: HOPE was associated with reduced severe PRS, stage 2-3 AKI and EAD rate and lower transaminases peak. HOPE potential in reducing biliary complications and as a tool to assess graft viability requires further investigation.

0-085

Real-time metabolic function assessment of extended criteria donor liver grafts during normothermic machine perfusion

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Background: The persistent organ shortage has resulted in a higher utilization of extended criteria donor (ECD) livers to reduce mortality on the waiting list. Nonetheless many of these livers are declined

for safety reasons, especially in donation after circulatory death. To effectively increase the donor pool, an objective assessment of ECD livers, focusing on residual graft function rather than graft injury, should be implemented. So far no reliable liver function test is available for normothermic machine perfusion (NMP) of the liver. The maximum liver function capacity (LiMAx) test is a clinical cytochromal breath test, based on metabolism of 13C-methacetin, with LiMAx-values >315 µg/kg/h indicating normal liver function. We adapted the LiMAx-test to measure liver metabolism during ex vivo machine perfusion.
Method: Seven donor livers, declined from transplantation, were perfused for 4 hours, using NMP. After one hour of stabilization, LiMAx-testing was performed. LiMAx-signal was obtained from the membrane oxygenator of the NMP device. In addition, lactate, ALT and AST were measured to study a relation with LiMAx-outcome.
Results: During NMP, CO_2 concentrations could be measured form the air outlet of the membrane oxygenator. However, the 13C-methacetin dose needed to be adjusted to liver weight, i.e. 25% of the clinical dose.
All dose and CO_2-adjusted LiMAx-values were between 28 and 409 µg/kg/h. We found that livers with LiMAx-values >315 µg/kg/h had lower ALT (260-691 U/L) and AST levels (292-761 U/L) after two hours compared to livers with LiMAx-values < 315 µg/kg/h (1630-18602; 2870-14532 U/L; both p=0.05). Also, the livers with high LiMAx-values had shorter clearance time of lactate (< 90 vs. 120 min; p=0.08).
Conclusion: In conclusion, the LiMAx-test is feasible to assess liver metabolism during NMP after adjusting the 13C-methacin dose to liver weight. LiMAx-testing could quickly identify fully functional ECD livers on NMP, that are currently rejected for transplantation.

0-086

Viability testing and transplantation of marginal donor livers (VITTAL) trial: NMP-L perfusate proteomics reveals biomarkers predictive of graft viability and post transplant complications.

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Background. The VITTAL clinical trial proves that normothermic machine perfusion of the liver (NMP-L) can increase utilisation of extended criteria donor organs (ECD). In addition NMP-L may improve transplant logistics, reduce warm ischaemic time, and permit donor liver functional assessment. The present study was undertaken to seek potential biomarkers predictive of liver transplantability and post transplant complications in VITTAL trial perfusate samples.
Methods. Of the 31 livers perfused, 22 were transplanted and 9 failed to achieve our established viability criteria at the point of decision to transplant. Untargetted MS proteomic analysis of the perfusates was then undertaken.
Results. A higher number of liver derived target proteins were detected in the non transplanted group compared with the transplanted group (931 +/- SEM 73 vs 520 +/-SEM 40 respectively p >0.0005) with no significant difference between DCD vs DBD livers. A group of 10 unique proteins were detected in 22/22 of the transplanted livers. No proteins were common to all 9 of the non transplanted group. However when combined with data from livers which went on to develop PT complications, a series of 7 proteins were uniquely detected. Of the cohort of 22 livers transplanted, perfusates from those that developed ITBL contained 2 unique proteins; EAD combined with non transplant also contained two unique proteins; no unique protein targets were detected in PRS; Samples of perfusates from transplanted livers which developed acute kidney injury contained 19 unique proteins.
Conclusion. These data show that untargeted proteomics was able to identify clusters of proteins which discriminate between transplantable and non transplantable livers. It was also possible to identify markers predictive of the most common types of post transplant complications. This suggests that objective point of use tests could be developed to augment subjective transplantability criteria, and prospectively identify those livers which may develop PT complications.

0-087

Improved transplant outcomes in ischemia-free liver transplantation: a report of the first 30 cases

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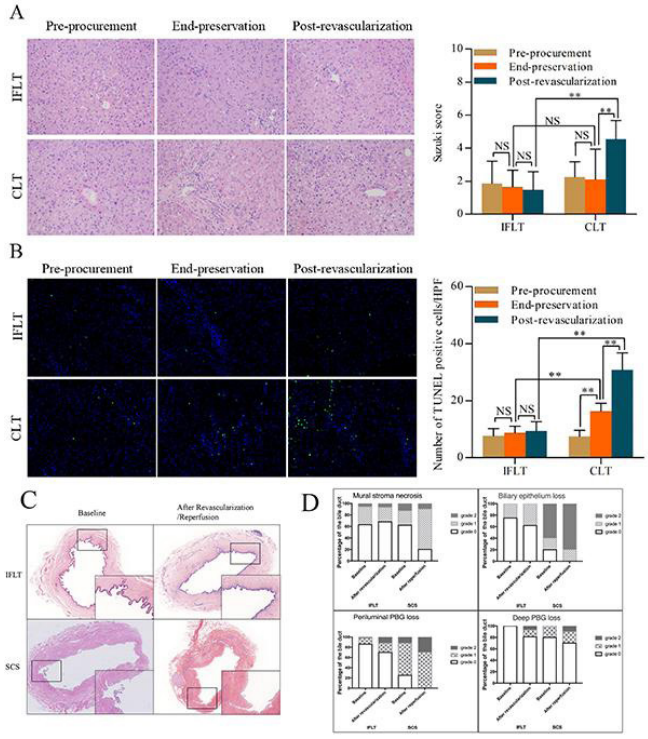
Background: We developed a novel procedure called ischemia-free liver transplantation (IFLT) to bridge liver grafts from donors to recipients without cessation of blood supply. Herein, we report the clinical outcomes of the first 30 cases of IFLT in human.
Methods: IFLT involves innovative surgical techniques and the use of normothermic machine perfusion to enable a continuous oxygenated blood supply to donor livers during procurement, preservation and implantation. In this prospective, non-randomized controlled study, 30 donor livers were transplanted in the IFLT group. Livers that were transplanted using a conventional procedure

during the same period were treated as controls.
Results: During the operation, the mean arterial pressure were more stable and the incidence of post-reperfusion syndrome was much lower in IFLT. Of the 30 patients in the IFLT group, 1 (3%) had EAD, compared with 47 of 89 (53%) patients in the control group (p< 0.001). The AST (365 versus 1551 U/L, P< 0.001) and ALT (169 versus 660 U/L, P< 0.001) serum levels were much lower in the IFLT group. The Tbil level on day 7 post-transplantation was lower in the IFLT group than in the control group (2.3 versus 5.7 mg/dL, p< 0.001). No PNF occurred in the IFLT group, while there were 5 cases of PNF (6%) in the control group. The pathological studies revealed minimal injury of hepatocytes and biliary epithelium during IFLT. The bile with good quality was continually produced throughout procurement, preservation and implantation in IFLT. There was no non-anastomosis biliary stricture in the IFLT group. Histological analysis of IFLT allograft biopsies and TUNEL showed a minimal injury to the liver tissues and bile duct.



[Fig.1]

Conclusion: IFLT provides an approach to avoid graft ischemia-reperfusion injury and can therefore optimize post-transplant outcomes and maximize organ utilization.

Concurrent Oral Abstract Session: Malignancies

0-088

Increased need of locoregional therapies is a surrogate of tumor biology in patients undergoing liver transplantation for hepatocellular carcinoma

Gorgen A.[1], McCluskey S.[1], McCluskey S.[1], Zhu M.[1], Abreu P.[1], Hansen B.E.[2], Ghanekar A.[1], Lilly L.[3], Cattral M.[1], Galvin Z.[3], Selzner M.[1], Bhat M.[3], Selzner N.[3], McGilvray I.[1], Greig P.D.[1], Grant D.R.[1], Sapisochin G.[1]

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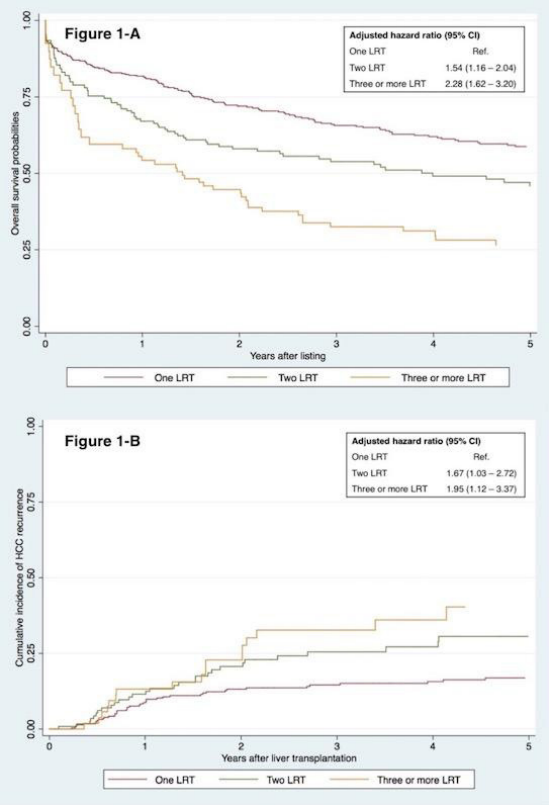
Background: We hypothesized that an increased need for locoregional therapies (LRT) during the waiting time would be an independent predictor of hepatocellular carcinoma (HCC) recurrence and poor survival after liver transplantation (LT).
Methods: Patients with HCC listed for LT between 2000-2016 were included in an intention-to-treat analysis (ITT). Patients were divided according to the number of LRT prior to LT: 1, 2 or ≥3. Patients who did not receive LRT were excluded. Overall survival (OS) and the cumulative recurrence incidence (CRI) were assessed by the Kaplan-Meier method and compared with the log-rank test. Multivariable regression with competing-risks was applied to identify predictors of HCC recurrence. The number of LRT was included in validated prediction scores and compared by c-statistics. The median follow-up was 3.2 (IQR 1.6-7.1) years.
Results: 1,005 patients with HCC were listed during the study period of which 621 (61.5%) were treated with LRT. The three groups had similar profiles. OS was higher for patients who underwent 1-LRT (Figure 1-A). In a multivariable regression, undergoing 2-LRT [HR=1.54 (95%CI:1.16-2.04) and ≥3-LRT [HR=2.28 (95%CI:1.62-3.20)] was predictive of death. Among the 481 patients who underwent LT, the actuarial 5-year CRI was 13.8%, 24.2% and 29.8% for patients with 1, 2 and ≥3-LRT, respectively (p=0.003) (Figure 1-B). The risk of recurrence was higher for patients who underwent 2-LRT [HR=1.67 (95%CI:1.03-2.72) or ≥3-LRT [HR=1.95 (95%CI:1.12-3.37)]. Other predictors of recurrence were AFP>100ng/mL and pre-transplant tumor size. The AFP score's accuracy was 0.66 (95%CI:0.60-0.72) and the accuracy of Metroticket 2.0 was 0.65 (95%CI:0.58-0.72). The accuracy of both scores increased [0.69 (95%CI:0.63-0.75), p=0.03, and 0.67 (95%CI:0.61-0.74), p=0.004, respectively] after including the number of LRTs.
Conclusion: The increased need of LRT prior to LT is correlated with a poorer prognosis after LT independently from size and number of tumors.



[Figure 1]

0-089

Effect of everolimus on hepatocellular carcinoma recurrence after liver transplantation

Joo D.J.[1], Lee J.J.[2], Kim D.G.[1], Lee J.G.[1], Lee J.[1], Kim S.H.[3], Han D.H.[1], Lee H.S.[4], Ju M.K.[1], Choi G.H.[1], Choi J.S.[1], Kim M.S.[1], Kim S.I.[1]

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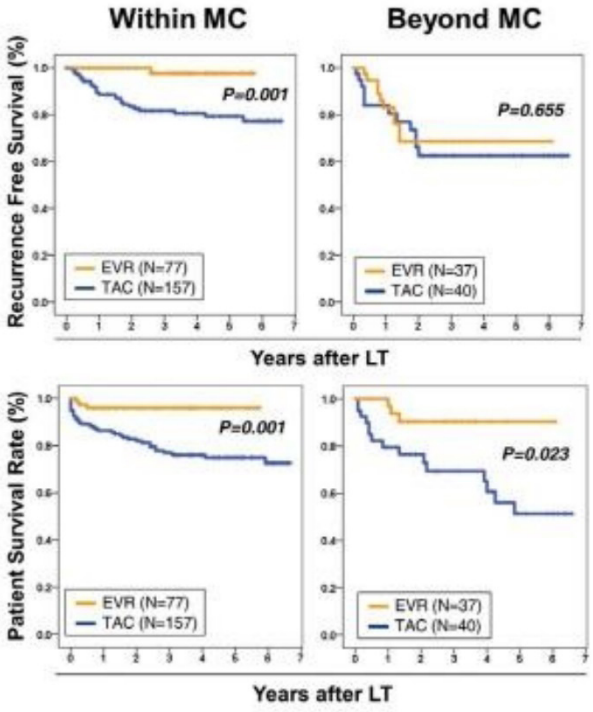
Introduction: This study was retrospectively conducted to reveal the effect of everolimus (EVR) particularly in the HCC patients who underwent liver transplantation (LT).
Patients and methods: Total 311 HCC patients underwent LT during the study period. We divided the patients into two groups according

to the immune suppressive agents; tacrolimus (TAC) group and EVR group. TAC group maintained their TAC blood level around 5-8 ng/mL. EVR blood level was around 3-5 ng/mL with low dose TAC < 5 ng/mL. We compared the oncologic outcomes.
Results: Seventy-seven recipients (24.8%) had tumors above Milan criteria (MC) before LT. Of 311 recipients, 49 patients (15.8%) had HCC recurrence after LT. The number of EVR group was 114 (36.7%), TAC group was 197 (63.3%). The patients beyond MC took more EVR than within MC (48.1% vs 32.9%). More LDLTs were performed in EVR group (78.1%) than TAC group (65.0%; *p*=0.015). EVR group included more patients with above MC tumors than TAC group (32.5% vs 10.3%, *p*=0.020). However, HCC recurrence happened more in TAC group than in EVR group (19.3% vs 9.6%, *p*=0.025). Regarding the survival rates, EVR group showed better outcomes both in recurrence-free survival and overall patient survival rates (*p*=0.029 and *p*< 0.001, respectively). EVR group within MC showed better recurrence-free survival than TAC group, but there was no significant difference between two groups who had tumors beyond MC. However, in the overall patient survival rates, EVR group showed better outcomes than TAC group regardless of their tumor status. In the Cox regression analysis, EVR was an independent factor decreasing risk of HCC recurrence after LT (HR: 0.352, *p*=0.003).
Conclusions: EVR-based immune suppression showed better oncologic outcomes after LT for HCC patients and was an independent factor decreasing the risk of HCC recurrence.



[Recurrence-free survival and overall patient survival rates]

0-090

Predicting recurrence of hepatocellular carcinoma after liver transplantation using a novel model that incorporates tumor- and donor-related factors: the DARLICA score

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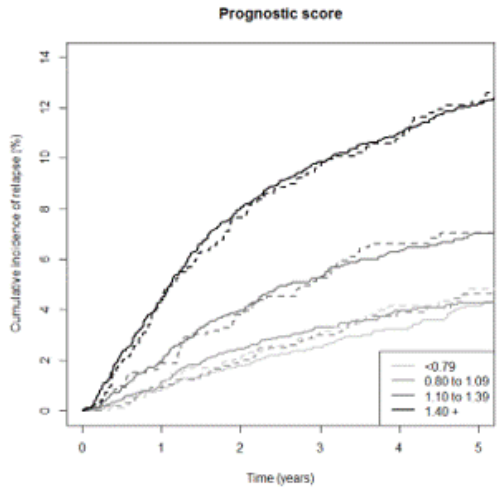
Background: Evidence indicates that liver graft quality has a clinically-relevant impact on the risk of hepatocellular carcinoma (HCC) recurrence after liver transplantation. The aim of this study was to develop a prognostic score that combines tumor and donor characteristics, to predict post-transplant HCC recurrence.
Method: Within the Scientific Registry of Transplant Recipients, we identified patients with HCC who received a liver transplantation between 2004 and 2014 (training set, n=10,887), and we calculated post-transplant HCC recurrence rates. We fitted a multivariable competing-risk regression including recipient-, tumor- and donor-related factors, from which a prognostic score (the Donor And Recipient score for Liver Cancer, DARLICA) was developed. The score was validated in a distinct subset of the population (n=3,627).
Results: Baseline characteristics were similar between patients in the training (n=10,887) and validation (n=3,627) sets. In the training set, after allowing for competing events, we found that total tumor diameter (hazard ratio [HR] 1.52 (95%CI 1.28 to 1.81) p< 0.001), alpha-feto protein (HR 1.27 (95%CI 1.23 to 1.32) p< 0.0001), recipient male gender (HR 1.43 (95%CI 1.18 to 1.74) p< 0.001), donor body mass index (HR 1.26 (95%CI 1.01 to 1.58) p=0.037), and liver graft allocation policy (HR 1.22 (95%CI 1.03 to 1.44) p=0.020) were significantly and independently associated with post-transplant HCC recurrence. Based on the coefficients of that model, we developed the DARLICA score, and applied it in the validation set (n=3627).
Conclusion: The DARLICA score is the first score predicting post-transplant HCC recurrence that incorporates both donor and tumor characteristics. It is based on readily available variables, and it could help transplant teams identifying, at the time of waitlist inscription, beneficial (or hazardous) combinations between the recipient and the donor.



[Cumulative rate of liver cancer recurrence according to quartiles of the DARLICA score.]

0-091

An explant correlation study of 377 cirrhotic patients transplanted for hepatocellular carcinoma: a continuous assessment of each National MELD-Exceptions Experts Committee performance is needed

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Introduction: In 2009, we performed our first national explant correlation study of cirrhotic patients who underwent liver transplantation (LT) for hepatocellular carcinoma (HCC) revealing that diagnosis and staging accuracy with preoperative imaging was very poor. Our aim is to evaluate current National MELD-Exception Experts Committee (NMEEC) performance.
Methods: Between 2010 and 2016, we identified patients listed for LT in our national waiting list. Regulation provides extra-MELD points for T_2HCC and other conditions. Using a prospective database, we identified patients in whom priority points were requested for T_2HCC. We analyzed NMEEC judgment, access to LT and death. Pathology reports of explanted livers were correlated with preoperative imaging.
Results: From a cohort of 4095 listed patients, 795 (19.4%) obtained extra-MELD points. Overall positive judgment for T_2HCC requests was 96.4% (482/500) and, consequently, they had higher LT access (76.7% vs. 45%; p< 0.05) and lower mortality (8.1% vs. 35%; p< 0.05) when compared with patients without extra-MELD points. Of 18 with denied priority, 7 were transplanted and included in explant study. Overall mortality rate of unprioritized patients increased when compared with period 2005-2009 (14% vs 35%, p< 0.05).
For the explant correlation study, 30 livers were excluded due to complete necrosis. Positive judgment for T_2HCC was correct in only 175/340 (51.4%). Incorrect diagnosis was present in 30/340 (8.8%) being: 1 lymphoma, 1 biliary cist, 1 hamartoma, 2 cholangiocarcinomas, 3 hemangiomas, and 22 regenerative nodules. For staging analysis we excluded 15 livers receiving downstaging therapy. Incorrect staging was confirmed in 120/295 (40.6%) being reported as T_1 HCC (n=41) and T_{3-4} HCC (n=79). Finally, positive and negative predictive values for T_2HCC judgment were 51.5% and 57.1%, respectively.
Conclusions: Most requests of extra-MELD points for T_2 HCC are approved in Argentina. However, pre-transplant imaging needs to be urgently revised to provide justice on liver allocation.

0-092

Stratifying post-transplant HCC recurrence risk: a two-centre externally validated predictive model

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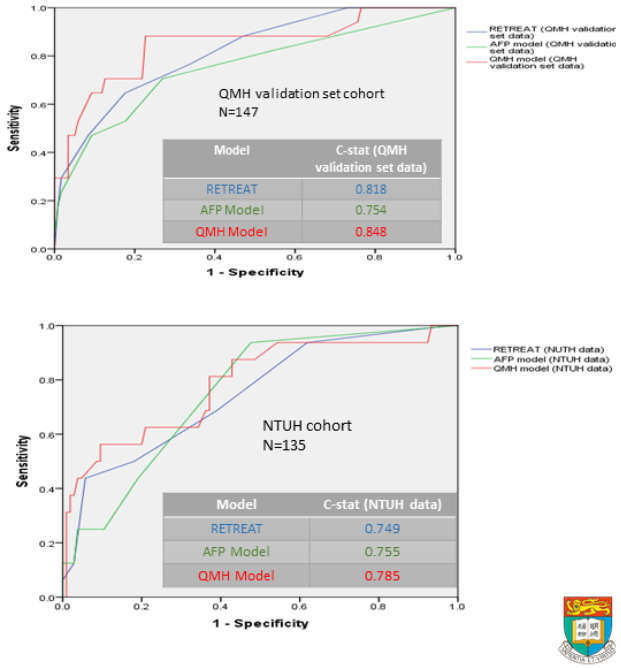
Objective: HCC recurrence after liver transplantation (LT) happens in about 10-30% of the patients. A user-friendly, accurate predictive model allows individualized surveillance in high risk population for early detection of recurrence.
Method: Retrospective cohort of consecutive HCC patients undergoing LT in Queen Mary Hospital (QMH) were recruited. Data randomization to training and validation set was performed. Independent factors identified by multivariate analysis in training were used to derive a predictive formula, which was subsequently validated internally using QMH validated set and externally by National Taiwan University Hospital (NTUH) with concordance statistics
Results: There were 465 patients from QMH and NUTH recruited. Multivariate analysis in the QMH training set (183 patients) identified three independent factors associated with post-LT HCC recurrence,

namely, alpha-fetoprotein (AFP) over 400 ng/ml (P=0.012, HR 2.92); sum of maximum tumour size and number (P=0.013, HR 1.15) and 3. salvage LT (P=0.033, HR 2.08). The derived scoring model showed good predictability to post-LT recurrence (c-stat: 0.75). Internal validation using 147 separate patient dataset demonstrated high discrimination ability (c-stat: 0.85). Validation set patients were classified into low (0 to 9), moderate (10 to 14) and high-risk groups (over 14) accordingly, and the risk of HCC was respectively 4%, 22%, 62% (c-stat 0.811). The total risk score continued to demonstrate satisfactory performance with the use of NTUH patient dataset (external validation) with c-stat of 0.75. Using the same stratification model, the recurrence risk in each NTUH group was 7%,31% and 75% respectively (c-stat: 0.70). The Chi-square goodness-of-fit test showed no significant discrepancy between the expected and observed recurrence risk with the stratification model (P=0.55). **Conclusion:** A reliable and user-friendly scoring model for the prediction of post-LT HCC recurrence was derived, internally and externally validated.

QMH risk score model:
AFP>400(0 or 7) + Salvage LT (0 or 5) + Tumour size(cm) + Tumour number



[Accuracy of different models in predicting post-LT HCC recurrence using QMH and NTUH data]

0-093

An intention-to-treat competing-risk model for candidates with hepatocellular cancer waiting for liver transplantation

Lai Q.[1,2], Cucchetti A.[3], Halazun K.[4], Cillo U.[5], Iesari S.[2], Finkenstedt A.[6], Soin A.S.[7], Rossi M.[1], Uemoto S.[8], Chen C.-L.[9], Hoppe-Lotichius M.[10], Soejima Y.[11], Xie Q.-F.[12], Zheng S.-S.[12,13], Lo C.M.[14], Lerut J.[2]

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Background: Since the introduction of Milan Criteria (MC), all transplant prognostic scoring systems for patients with hepatocellular cancer (HCC) were almost exclusively based on features available at surgery, failing to consider the intention-to-treat (ITT) point of view. This study aims to develop comprehensive ITT models able to predict the risk of de-listing and HCC-specific death after liver transplantation (LT), exclusively using characteristics available at first referral.
Methods: A derivation (n=2,318) and an external validation data-set (n=773) of HCC patients listed for LT between January 2000 and March 2017 were obtained from an International cohort composed by twelve centres coming from the United States, Europe and Asia. The study was registered at http://www.ClinicalTrials.gov (ID: NCT03595345).
Results: In the derivation data-set, after performing a competing-risk analysis, three independent covariates predicting de-listing (Model#1) were identified: age at first referral (sub-hazard ratio, SHR=1.049; p=0.001), MELD at first referral (SHR=1.033; p=0.002) and living donor LT (SHR=0.422; p-value=0.001). The risk of post-LT HCC-specific death (Model#2) was predicted by the combination of the Metroticket 2.0 calculated at first referral (SHR=1.724; p=0.001), and MELD at first referral (SHR=0.970; p=0.045). In the external validation, both Model#1 and #2 showed the highest diagnostic performances among the tested scores (c-statistic=63.3% and 67.7%, respectively). The upper acceptable limit of post-LT HCC-specific death identified for the Model#2 was 13%, corresponding to the combination of alpha-fetoprotein (AFP) and morphological values: AFP≤20 ng/mL and up-to-twelve; AFP=21-200 ng/mL and up-to-ten; AFP=201-500 ng/mL and up-to-seven; and, AFP=501-1,000 ng/mL and up-to-five.
Results: Our study presents a scoring system based on a large International HCC patient population listed for LT. A freely accessible web-calculator has been created to estimate the individual risks of drop-out and HCC-specific death after LT. A “recalculation” of the

risks after neo-adjuvant treatments should improve the quality of patient selection and indications.

0-094

Inclusion of serum interleukin 6 and α-fetoprotein into traditional criteria improves prognostic accuracy for hepatocellular carcinoma after liver transplantation

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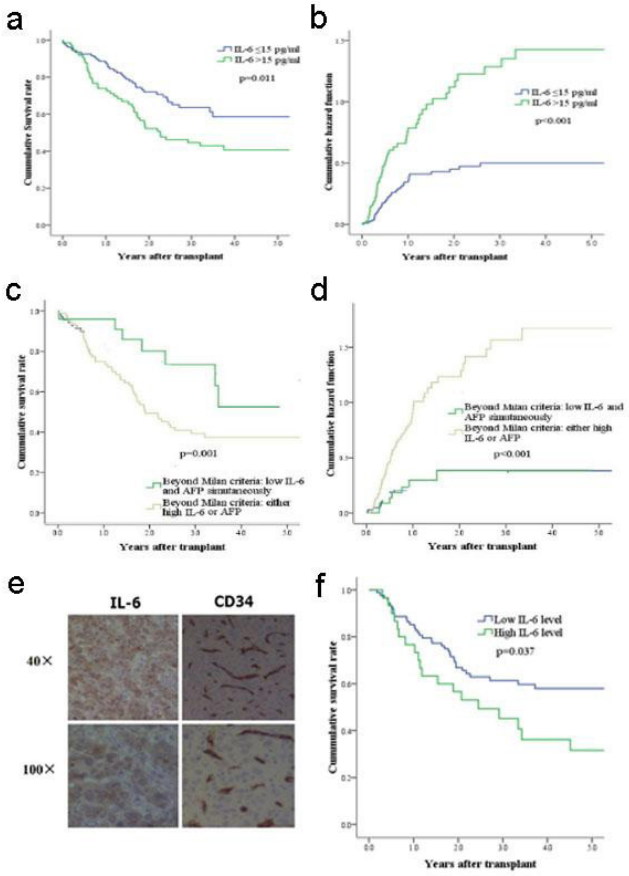
Background: Patient selection is critically important to ensure the outcomes of liver transplantation for hepatocellular carcinoma (HCC). The traditional criteria, Milan criteria, have been challenged for being too restrictive and not precise enough.
Methods: This study retrospectively enrolled 179 HCC patients undergoing liver transplantation for HCC, and serum Interleukin 6 (IL-6) level is acquired to assess its prognostic value based on Milan criteria. Another cohort of 118 patients was enrolled to assess the role of tissue IL-6 level as well.
Results: Elevated serum IL-6 level (>15pg/ml) was associated with increased tumor recurrence rate and decreased overall survival after liver transplantation (p< 0.01, n=179). Serum IL-6, alpha-fetoprotein (AFP), and Milan criteria were independent risk factors predicting post-transplant tumor recurrence. In patients fulfilling Milan criteria (n=70), serum IL-6, but not AFP, can successfully predict post-transplant tumor recurrence (p=0.002). In patients exceeding Milan criteria (n=109), IL-6 and AFP were independent risk factor for tumor recurrence (p< 0.05), and patients of low IL-6 and AFP simultaneously can achieve acceptable outcomes almost identical to those within Milan criteria. Elevated serum IL-6 level correlated with tumor tissue IL6 level (p=0.049). Elevated tumor tissue IL-6 level also correlated increased micro-vascular density and decreased overall survival after liver transplantation (p< 0.05, n=118).
Conclusions: Serum and tissue IL-6 correlates with post-transplant outcomes for patients with HCC. The new stratification system combining serum IL-6 and AFP with Milan criteria is more precise guiding candidate selection, and is able to define an extra subset of eligible candidates without any sacrifice in survival.



[a. Elevated serum IL-6 level was associated with decreased post-transplant survival (p=0.011). b. El]

0-095

Outcomes of liver transplantation for mixed hepatocholangiocarcinoma

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Background: Mixed hepatocholangiocarcinomas (HCC-CCA) are rare tumors with both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA) differentiations. They are usually associated with a worse prognosis than pure HCC tumors

however only a few series describing outcomes following liver transplantation (LT) have been reported. We sought to compare post-OLT outcomes of HCC-CCA and HCC in the largest series from the Western hemisphere to date.

Methods: This is a single-center retrospective cohort study of all consecutive patients with HCC treated with between 1998 and 2018. Patient and tumor characteristics as well as post-LT survival and oncologic outcomes were compared among patients with pure HCC and those with mixed HCC-CCA identified on liver explant.

Results: A total of 18 HCC-CCA cases were identified and their outcomes compared to 615 pure HCC patients. The median follow-up duration for the cohort was 54 months (IQR 23-103). Both groups were comparable in terms of preoperative findings. Notable differences however were seen on liver explant pathology, HCC-CCA tumors were significantly more aggressive: 41% were Grade 3 and 41% Grade 4 vs 28 and 16% (p=0.033) of HCC tumors; 60% exhibited microvascular (vs 26%, p=0.006) and 36% lymphatic invasion (vs 5%, p< 0.001). Patients with mixed HCC-CCA tumors had a significantly lower 5-year survival rate of 39 vs 75% (p< 0.001) as well as a lower 5-year recurrence-free survival rate of 42 vs 87% (p< 0.001). Moreover, the time to recurrence was significantly shorter for HCC-CCA patients with a median of 7 (IQR 3 - 8) vs 15 months (IQR 8 - 33) (p=0.004).

Conclusion: These findings from the largest Western series to date further confirm that mixed HCC-CCA are more aggressive than pure HCC tumors and confer a worse prognosis following liver transplantation.

Table: Comparison of baseline and tumor characteristics in HCC and HCC-CCA patients.

	Mixed HCC-CCA (n=18)	HCC (n=615)	*P* value
Baseline characteristics			
Age, years	61.8 (57.3 – 63.9)	60.2 (54.2 – 64.7)	0.300
Gender, male	89%	78%	0.388
BMI, kg/m²	28 (26 – 32)	27 (25 – 31)	0.571
ESLD etiology			0.654
HCV	66%	63%	
HBV	11%	12%	
NASH	0%	8%	
Alcohol	17%	9%	
Other	6%	8%	
Lab MELD at LT	10 (7 -14)	13 (9 – 18)	0.078
Match MELD at LT	25 (22 – 31)	25 (22 – 29)	0.495
AFP at LT	8 (6 – 33)	11 (5 – 32)	0.673
Max preLT AFP	35 (12 – 51)	21 (8 – 114)	0.906
Radiologic tumor characteristics			
Number of tumors preLT			0.129
0	0%	8%	
1	33%	50%	
2	45%	21%	
3	11%	8%	
≥4	11%	13%	
Largest tumor size, cm	3.5 (1.9 – 5)	2.5 (1.6 – 3.8)	0.059
Total tumor size, cm	5 (2.5 – 5.9)	3.2 (2 – 5.5)	0.111
Bilobar tumor	13%	7%	0.334
Within Milan Criteria	79%	86%	0.323
Pathologic tumor characteristics			
Tumor Grade			**0.033**
Unknown	6%	15%	
1	0%	7%	
2	12%	34%	
3	41%	28%	
4	41%	16%	
Macrovascular invasion	0%	3%	0.936
Microvascular invasion	60%	26%	**0.006**
Lymphatic invasion	36%	5%	**<0.001**
Bilobar	39%	19%	0.062

Data reported as % or Median (IQR)

Figure 1: Kaplan-Meier Survival Analysis of OS in HCC and HCC-CCA patients

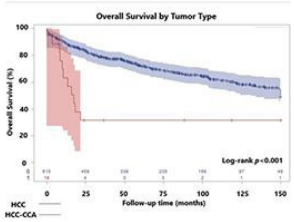
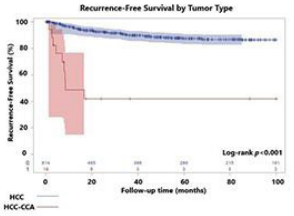


Figure 2: Kaplan-Meier Survival Analysis of RFS in HCC and HCC-CCA patients



[Images]

0-096

Incidental/misdiagnosed intrahepatic cholangiocarcinoma in patients undergoing liver transplantation: nationwide study in Japan

Hara T.[1], Eguchi S.[1], Yoshizumi T.[2], Hasegawa K.[2], Kaido T.[2], Hamada T.[1], Takamura H.[2], Shimamura T.[2], Umeda Y.[2], Shinoda M.[2], Ogura Y.[2], Fukumoto T.[2], Kasahara M.[2], Furukawa H.[2], Ohdan H.[2]

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Background: Intrahepatic cholangiocarcinoma (ICC) had been thought to be contraindication for liver transplantation (LT) due to poorer outcome. In the meanwhile, incidental/misdiagnosed ICC (iICC) are infrequently reported. Although, the favorable outcome of patients with early ICC undergoing LT have been reported recently, the incidence of iICC and the outcome after LT is still unclear in eastern Asia.

Method: We conducted nationwide survey to analyze the incidence of iICC and outcome after LT in Japan.

Results: Between January 2001 and December 2015, a total of 6997 LT was performed in Japan. Among them, 18 cases (0.26%) of iICC were reported from 11 transplant centers. Five cases were misdiagnosed as HCC preoperatively. The median tumor size in explanted liver was 2.8 [1.5-4.5] cm and the number of tumor was 1 [1-7]. Well differentiated tumors were found in 7 cases. Recurrence after LT was found in 10 patients (56%). The most common site for recurrence was extrahepatic (90%). The recurrence-free survival rates at 1, 3, 5 years were 83.3%, 65.5%, 45.8%, respectively. The overall survival rates at 1, 3, and 5 years were 77.8%, 61.1%, and 42.8%, respectively. Comparing with the national data in Japan, the results were inferior to that of patients with HCC who underwent LT (84.8%, 70.5%, and 54.7%, respectively). Unlike with previous reports from western countries, single tumors 2 cm or smaller, well differentiated lesions, and lack of microvascular invasions were not associated with better OS and RFS.

Conclusion: Though the outcome of LT in patients with iICC was poorer than that of patients with HCC in Japan, 3-year OS was still higher than 60%. The results of the present study will provide encouraging information to patients who were diagnosed as iICC after LT.

Concurrent Oral Abstract Session: Pathology / Radiology / Interventional Radiology / Molecular Imaging

0-097

Transcriptome-based molecular subtypes for hepatocellular carcinoma in liver transplantation

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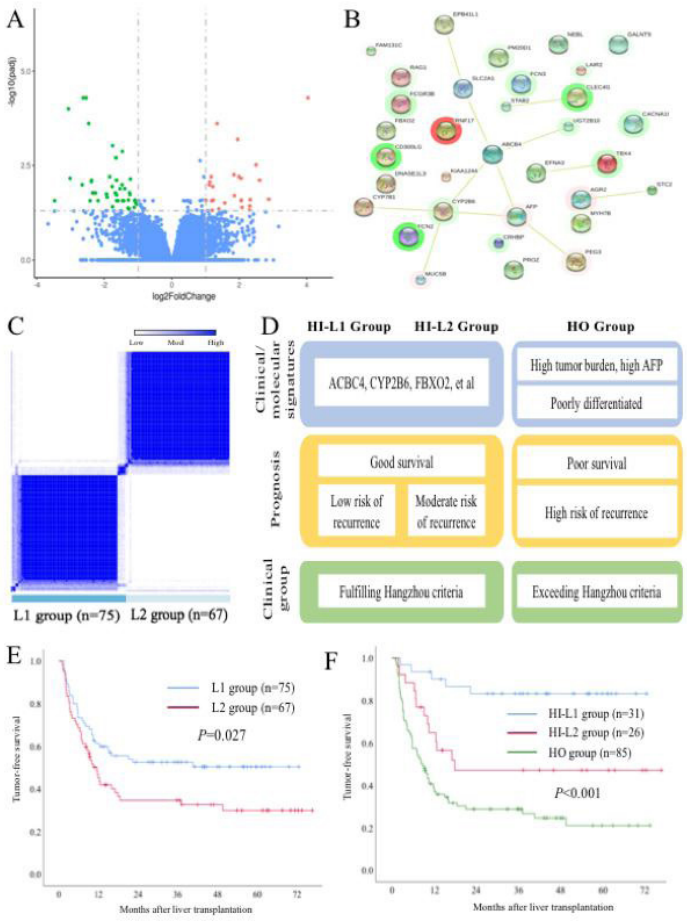
Background: Heterogeneity of hepatocellular carcinoma (HCC) causes difficulty preventing tumor recurrence after liver transplantation, and finally leads to poor outcomes. This study aims to develop a pathology assay for molecular subtyping, and to establish a grading system for HCC patients undergoing liver transplantation.
Methods: Tumor tissue RNA sequencing was performed on 142 HCC patients undergoing liver transplantation in our hospital. The resultant omics data and matched clinical manifestations were integrated for molecular subtyping of these patients.
Results: Transcriptome profiling identifies 50 genes and a network responsible for the regulation of tumor recurrence after liver transplantation (Figure A and B). According to overall clustering matched with clinical manifestations, 2 distinct subtypes of HCC (termed as L1and L2) were identified (Figure C). An analysis of gene signatures identified ACBC4, CYP2B6 and FBXO2 as differential molecular between groups. The L2 group (n=67) had significantly decreased tumor-free survival compared with the L1 group (n=75, p=0.027, Figure D). However, the other clinical features (tumor size, number, et al.) were comparable between the 2 subtypes (p>0.05). We further combined our molecular subtyping results with Hangzhou criteria, an effective selecting criteria for transplantable HCC patients, and we finally established a novel grading system (Figure E). According to the system, the patients fulfilling Hangzhou criteria were further stratified into HI-L1 (n=31) and HI-L2 (n=26) group. HI-L2 group showed significantly higher risk of tumor recurrence compared with the HI-L1 group (p=0.003, Figure F).
Conclusion: RNA sequencing profiling achieved acceptable molecular subtyping results for HCC patients undergoing liver transplantation. The grading system combining Hangzhou criteria and our molecular subtyping assay is more precise in predicting tumor recurrence after liver transplantation.



[Molecular subtyping for hepatocelluar carcinoma in liver transplantation based on RNA sequencing]

0-098

Cytomegalovirus (CMV) infection induces an angiogenic response through hepatic stellate cells (HSCs) and leads to early post-transplant liver fibrosis (LF) and poor graft survival

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Background: The ability of the CMV to infect the endothelial cells (ECs) is critical. CMV can increase EC adhesion, permeability, and create a pro-inflammatory environment that can promote angiogenesis. This study aimed to show both the direct and indirect effects of CMV on the development of LF.
Methods: CMV positive 24 patients (Group 1) and CMV negative 45 patients (Group 2) were included in the study. Number of AR episodes were recorded. All biopsies were scored and immunostained with α-SMA, TNF-α, TGF-β, and CD31. Activated HSCs determined by the expression of α-SMA and angiogenes was highlighted with CD31. The development of LF during 18 months was evaluated in follow-up biopsies.
Results: The mean number of AR episodes were higher in Group 1 (1.45±1.2) compared to Group 2 (0.55±0.7) (p=0.001). The degree of HSC activation, angiogenesis, liver TGF-β and TNF-α expression were higher in Group 1 compared to Group 2 (p< 0.001).The degree of angiogenesis showed a positive correlation with the degree of leukocyte infiltration, HSC activation, liver TGF-β and TNF-α expression (p< 0.001). LF was found to be higher in Group 1 (87.5%) compared to Group 2 (33.1%) (p< 0.001). Also, a significant relationship was found between the groups in regards to the fibrosis score (p< 0.01). LF showed a positive correlation with the degree of leukocyte infiltration, angiogenesis, HSC activation, liver TGF-β and TNF-α expression (P< 0.001).Overall 10-year graft survival was 91% and 67% for CMV negative and positive patients, respectively (p=0.008).
Conclusion: We showed that CMV infection plays multiple roles on the induction of angiogenesis and therefore the development of LF. CMV increases the incidence of AR episodes characterized by inflammation, and EC activation which in turn leads to both the development of HSC activation and progressive cytokine and growth factor expression with proangiogenic action that stimulates angiogenesis.

0-099

The spectrum of histopathology of living donor livers and their impact on short and long-term outcomes in pediatric liver transplantation (LT): Beijing experience

Zhao X.[1,2,3], He Y.[2,3,4], Liu J.[5], Zhang Q.[3,6], Liu L.[1,2,3], Wei L.[2,3,4], Qu W.[2,3,4], Zeng Z.[2,3,4], Zhang H.[2,3,4], Liu Y.[2,3,4], Jia J.[1,3], Sun L.[2,3,7], Zhu Z.[2,3,4]

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Background: The prevalence of non-alcoholic fatty liver diseases is increasing in general population, affecting thereby the donor pool for LT. This study aims to evaluate the histopathologic spectrum of living donor grafts and investigate the impact of different histological findings, particularly hepatic steatosis on recipients' short and long-term clinical outcomes.
Methods: Histological features of 298 liver tissues collected during the LT from July 2013 to September 2018 were systematically assessed by two pathologists. Clinical characteristics including recipients' clinical outcomes were retrieved. The graft survival, overall survival and degree of histological findings were assessed by Kaplan-Meier analysis using SPSS 25.0.
Result: Donors: average age: 31.9±5.5-year-old, male/female ratio: 3:4, BMI 22.3±3.0 kg/m^2. Recipients: average age: 2.9±3.3-year-old, male/female ratio: 1:1. Indications for LDLT: biliary atresia 209/298(70.1%) and genetic/metabolic liver diseases 89/298(29.9%).
Macrovesicular steatosis up to 30% was identified in 138(46.3%) donors: 0-< 5% 99/298(33.2%), 5-< 10% 32/298(10.7%), 10-< 20% 2/298(0.7%) and 20-< 30% 5/298(1.7%). Portal inflammation was present in 83/284(29.2%): mild in 79/284(27.8%), mild-moderate in 4/284(1.4%). Other histological findings were megamitochondria73/298(24.5%),glycogen nuclei36/298(12.1%), mild ductular reaction 28/298(9.4%), apoptotic bodies 18/298(6.0%), incidental hepatocanalicular cholestasis 7/298(2.3%), ceroid macrophages 4/298(1.3%) and hemosiderin 2/298(0.7%).
The graft survival at 1-year, 3-year and 5-year was 96.4%, 94.3%, 94.3% and overall survival was 98.8%, 97.0% and 96.1% respectively in patients receiving grafts with < 5% steatosis. The graft survival at 1-year, 3-years and 5-year was 97.4%, 90.9%, 90.9% and overall survival was 100.0%, 97.3% and 97.3% in patients receiving grafts with ≥5% steatosis. No significance of steatosis on graft survival and overall survival(p=0.883 and p=0.701).
Conclusion: A spectrum of liver histopathology was identified incidentally in this healthy donor cohort. Hepatic steatosis ≤30% and mild-to-moderate portal inflammation had no significant impact on graft survival and overall survival. This study will further enhance patient care in pediatric LDLT.

0-100

Recurrent primary sclerosing cholangitis after liver transplantation: histological factors

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Background: Recurrence of primary sclerosing cholangitis (rPSC) after liver transplantation (LT) occurs in 15 to 25% and affects long-term graft survival. While various clinical risk factors for recurrence have been identified, potential pre-transplantation liver histological features have not been evaluated. The aim of this study was to identify clinical and histological factors associated with rPSC.
Method: We retrospectively studied a cohort of 57 patients transplanted for PSC between 1989 and 2016, and only patients who survived at least 6 months after LT were studied. Recurrent PSC was defined by the Mayo clinic classification. Pre, post-LT biopsies and explanted livers were reviewed and morphological features defining PSC were scored according to Nakanuma system.
Results: A total of 22 patients (39%) developed rPSC in a median time of 48 months (23-129 months). 4 patients were retransplanted for rPSC. Age at diagnosis, presence of IBD, type of graft and donor characteristics were not associated with rPSC. In contrast, episodes of cholangitis before transplantation were more frequent in the rPSC group, as compared to no rPSC (64% vs 36%, p=0.047). Similarly, the use of ciclosporine, as compared to tacrolimus, was significantly associated with rPSC, 27% vs 6%, p=0.047. The histologic scoring system, validated for the prognosis of PSC, was not able to predict rPSC when assessed on pre-LT biopsies and explanted livers. In contrast, the presence of onion skin scar on explanted livers was significantly associated with rPSC, as compared to no rPSC group (71% vs 42%, p=0.03).
Conclusion: Our results suggest that episodes of cholangitis before LT, use of ciclosporine and onion skin scar present on explanted livers were significantly associated with rPSC. In contrast, no histological factor on preLT biopsy seems to be associated with the risk of rPSC. Further studies are required to better assess the risk for developing rPSC.

O-101

Expression of Keratin 19 in advanced hepatocellular carcinoma and resistance to sorafenib treatment

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Background: Keratin 19 (CK19), a biliary/hepatic progenitor cell marker, is expressed in a subset of hepatocellular carcinomas (HCC) with poor prognosis. Our aim is to identify the prediction of the therapeutic response of Keratin 19 in patients with advanced-stage hepatocellular carcinoma (HCC) treated with sorafenib, especially for those who are treated with sorafenib after transarterial chemoembolization (TACE) treatment.
Patients and methods: We retrospectively evaluated 71 patients with advanced-stage HCC who had received sorafenib at the First Affiliated Hospital of Zhejiang University School of Medicine in China from January 2010 to December 2016, and for whom tumor specimens were available for CK19 immunohistochemical analysis (IHC), including 25 residual/recurrent tumors adjacent to the TACE treatment site.
Results: CK19 expression was significantly correlated with pathological features including tumor burden, AFP, age, TACE treatment. CK19 were expressed in Twenty-five of 71 (35%) and in ten of 25 CK19-positive TACE-treated HCCs. CK19 expression was an independent prognostic factor of hepatocarcinoma Survival, The median overall survival (m OS) of CK19-positive HCCs was 47months while that of CK19-negative HCCs was 12 months (P=0.044), and the median time to progress were 3 and 7months with the range from1.7 to 4.2 and 4-10 months (P=0.008), respectively. Importantly, HCC patients with high expression of CK19 and preoperative TACE showed poor prognosis.
Conclusion: The CK19 immunophenotype of tumoral tissue may predict improved response to sorafenib in HCC patients, and that decreasing CK19 expression may be beneficial for the combination treatment of sorafenib and TACE in hepatocarcinoma. TACE treatments may trigger the expression of CK19 proteins that are normally associated with poor prognosis of hepatocarcinoma patients.

O-102

Radiomics analysis allows for predicting recurrence of hepatocellular carcinoma after liver transplantation

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Background: Hepatocellular carcinoma is the most common primary liver cancer and ranks third as a causation of cancer death worldwide.Liver transplantation,as the most efficient treatment for end-stage liver disease, is recommended in patients with clinical-proved portal hypertension and early stage HCC meeting the Milan criteria.However,Recurrence have always been the main factors that affect the curative effect of HCC after liver transplantation. Therefore, there is an urgent need for a tool that can accurately evaluate the biological characteristics of HCC before operation so as

to predict the risk of relapse after liver transplantation.
Methods: Our study consisted of 133 patients with clinical pathologically confirmed HCC after liver transplantation from October 2011 to December 2016. Radiomic features were extracted from hepatic artery phase computed tomography (CT) images and a radiomics signature was generated by using the least absolute shrinkage and selection operator, or LASSO, Cox regression model. Association between the radiomics signature and recurrence-free survival (RFS) was explored. Preoperative clinical factors potentially associated with RFS were evaluated to develop a clinical model. A combined model was also built.
Results: Nine robust radiomic features were chosen from 84 candidate features in arterial phase to build a radiomics signature eventually that was significantly associated with RFS ($P < 0.001$).A radiomics nomogram consisting of the radiomics signature and clinical factors shows good predictive performance for RFS with a C-index of 0.785 (95% confidence interval [CI]:0.674-0.895) in training dataset and 0.789 (95%CI:0.620-0.957) in validation dataset. The radiomics nomogram calibration curves showed satisfied agreement in both training ($p = 0.121$) and validation cohort ($p = 0.164$).
Conclusions: Radiomics analysis allows for accurately predicting recurrence of hepatocellular carcinoma after liver transplantation.

0-103

EUS guided fine needle aspiration helps accurately characterize FDG-18 PET avid lymph nodes in prospective recipients with hepatocellular carcinoma

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Background: Accurate diagnosis of metastatic disease is important to prevent futile liver transplantation (LT) in hepatocellular carcinoma (HCC) patients. Imaging (contrast CT) characteristics of suspicious lymph nodes (LN) are not always conclusive, percutaneous image guided fine needle aspiration (FNA) is difficult owing to deep location and presence of collaterals. We studied utility of FDG-18 positron emission tomography (PET) (which is used to exclude extrahepatic disease prior to LT), and endoscopic ultrasound (EUS) guided FNA in definitive characterization of these suspicious LN's.
Methods: From October 2013-July 2016, 73 HCC patients with suspicious LN metastases (abdominal or mediastinal) on whole body FDG-18 PET CT scan (avid LN's and/or ≥1 cm) underwent EUS guided FNA.
Results: EUS FNA provided a definitive diagnosis in 89% (65/73), 8 samples were suboptimal for comment. Of 65 EUS guided FNA, 19 (29%) were positive for metastases, 41 showed reactive lymphadenitis (63%), 5 showed chronic granulomatous lymphadenopathy (8%). Most metastatic LN's were portocaval in location (14), rest were celiac (2), subcarinal (2), and para aortic (1). 79% (15) of metastatic LN's were FDG-18 PET avid, 53% (10) had SUV max ≥5. 68% (13/19) were >1cm, while the remaining were less. Sensitivity, positive predictive value, and accuracy of PET-avidity and SUV max values (79%/35%/51%, and 67%/53%/67%, respectively) were low. In 16/19 patients with LN metastases, tumours were beyond UCSF criteria, and tumour FDG-18 PET avidity correlated with that of the LN's. Absence of LN metastases on EUS FNA allowed us to proceed directly with LT in 41 patients, and in 5 patients LT was performed after initial anti tubercular treatment.
Conclusion: All suspicious FDG-18 PET avid or ≥1 cm LN's in prospective LT recipients with HCC are not necessarily metastatic. EUS guided FNA further helps in decision making, and avoids unnecessary exclusion of curative LT in these patients.

0-104

Outcome of liver transplant for HCC after high intensity focused ultrasound as bridging therapy

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Introduction: High intensity focused ultrasound (HIFU) ablation has several advantages over radiofrequecy ablation and transarterial chemoemobilzation including no needle tract seeding and absence of adhesion in subsequence operations. In this study, we aim to analyze whether high intensive focused ultrasound is an effective bridging therapy for patient with HCC.
Patients and methods: From January 2007 to December 2018, 265 consecutive HCC patients were listed for liver transplant (UCSF criteria). The median waiting time for liver transplantation was 6.21 months. 24 patients received HIFU-TACE as a bringing therapy, 11 patients received HIFU as bridging therapy. 36 patients received TACE as bridging therapy and 99 patients received no treatment before liver transplantation.
Patients were comparable for Child-Pugh and Model for End-Stage Liver Disease scores, tumor size and number and cause of cirrhosis.
Results: 7 patients receiving HIFU-TACE (29.2%) had complete tumour response, 5 patients (20.8%) had partial response, 6 (25.0%) patients are no change and 6 (25.0%) patients are progressive disease.

4 patients receiving HIFU (36.4%) had complete tumour response, 1 patient (9.1%) had partial response, 5 (45.5%) patients are no change and 1 (9.1%) patients are progressive disease.
For patient who had HIFU-TACE bridging therapy, the overall 1year, 3 year and 5 year survival was 95.8%, 91.7% and 85.9%. The disease free survival was 91.7%, 87.3% and 82.2%.
For patient who had HIFU bridging therapy, the overall 1year, 3 year and 5 year survival was 100%, 100% and 100%. The disease free survival was 100%, 90.9% and 90.9%.
For patient who has TACE bridging therapy, the overall 1year, 3 year and 5 year survival was 91.7%, 77.0% and 77.0%. The disease free survival was 88.6%, 76.4% and 76.4%.
Conclusions: High intensive focused ultrasound ablation is a safe and effective method in the treatment of HCC for patient with advanced cirrhosis.

O-105

The association of number and type of liver directed therapies (LDT) on portal vein thrombosis (PVT) in waitlisted patients with hepatocellular cancer (HCC)

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Background: Patients with HCC receive LDT to prevent tumor progression and as a bridge to liver transplant (LT). The influence of waiting time after HCC diagnosis and LDTs, on PVT in HCC patients is unknown.
Methods: This is a retrospective case-control study to examine the association between number of LDT and PVT in HCC patients who underwent LT. Data between 2011-2018 for HCC patients undergoing LT were collected. Unpaired t-tests and chi-squared tests compared patients transplanted with and without PVT. Odds of PVT (odds ratios and 95% confidence intervals) were estimated using logistic regression.
Results: 289 patients were included, 45 patients (15.6%) had PVT prior to LT. The most common etiology of ESLD was HCV (50.9%). The median MELD at LT was significantly higher in the PVT group than controls (15 vs 11 $p < 0.01$). In the case group, median time from HCC diagnosis to PVT diagnosis was 1 year (IQR: 0.4-1.7 years). Patients most frequently underwent one (32.5%) or two (26.3%) LDTs prior to PVT or LT. On univariate analysis, patients with PVT prior to LT had longer median waitlist time (1.4 vs. 1.2 yrs, p=0.02), more EBL during LT (2.5L vs. 1.2L, $p< 0.001$), but no difference in the LDT number prior to PVT diagnosis (p=0.78). Using logistic regression, odds of PVT were not associated with receiving any LDT before PVT (OR=0.41, 95% CI 0.10-1.66, p=0.22), type of LDT (TACE/TAE OR=0.87, 95% CI 0.28-2.68, p=0.80; RFA/MWA OR=0.88, 95% CI 0.44-1.77, p=0.72; EtOH or cryoablation OR=1.09, 95% CI 0.30-3.93, p=0.90), or number of LDT (OR=1.01 per 1 LDT increase, 95% CI 0.83-1.22, p=0.94; 2+ LDTs vs 1 OR=1.32, 95% CI 0.64-2.72, p=0.45).
Conclusions: Number or type of LDT were not independently associated with PVT in adult HCC patients who underwent LT.

Concurrent Oral Abstract Session: Short and Long-Term Patient and Allograft Outcomes

0-106

Long term outcomes for patients transplanted with hepatopulmonary syndrome and portopulmonary hypertension, 1985-2017

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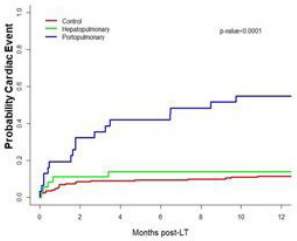
	Control N=201	HPS N=36	PoPH N=31	P
Baseline MAP	73.0	81.0	69.0	0.022
Baseline MPAP	20.0	21.0	30.0	<0.001
Post Reperfusion MPAP	20.0	19.0	31.5	<0.001
Baseline Pulm Sys Pres	28.0	29.0	41.5	<0.001
Post Reperfusion Pulm Sys Pres	29.0	28.0	47.0	<0.001
Baseline Pulm Diast Pres	14.0	14.5	22.0	<0.001
Post Reperfusion Pulm Diast Pres	13.0	13.0	18.5	<0.001
Baseline PVR	81.0	53.0	154	<0.001
Post Reperfusion PVR	65.0	51.0	175	<0.001
Baseline CVP	11.0	12.0	9.00	0.021
Post Reperfusion CVP	10.0	10.0	7.00	0.009
Baseline CO	7.30	8.10	7.20	0.653
Post Reperfusion CO	10.2	11.9	10.1	0.096



[Table: Intraoperative hemodynamics Figure: Probability of cardiac event]

Background: Hepatopulmonary syndrome (HPS) and portopulmonary hypertension (PoPH) are accepted indications for LT; data regarding the natural history and outcomes after LT is variable.
Methods: We examined all LT at Baylor University Medical Center (1985-2017). Patients with HPS (n=36) and PoPH (n=31) were matched (3:1) to controls. We examined morbidity (LOS, readmissions), cardiac events (arrhythmias, new onset heart failure, myocardial infarction, and catheterizations), mortality and causes of death. Cumulative incidence of cardiac events was assessed.
Results: Cases: median age 52 (IQR 48-56), 53.7% female, HCV (44.8%). **HPS:** mean PaO2 was 55 mmHg (severe HPS) prior to LT. **PoPH:** mean pulmonary artery mean pressure (mPAP) was 42 mmHg prior to LT. Intraoperatively, cases had a shorter cold ischemia time (5.3 vs 7.1 hrs, P = 0.01) and OR time (5.5 vs. 6 hrs, P = 0.02). Despite this, cases had longer ICU stay (4 vs. 2, p< 0.01) and overall LOS (12 vs. 9, p< 0.01). The cumulative incidence of cardiac events within 1 year was highest in PoPH (55%) as compared to HPS (14%) and controls (11.1%) (p< 0.01). (**Figure**)
We examined intraoperative hemodynamics. PoPH had higher MPAP and PVR at baseline and post reperfusion (**Table**). Patients that had cardiac events had higher mPAP (23mmHg, IQR 19-30 vs. 20mmHg (IQR 17-25), p=0.02). Overall survival rate at 36-months was 69.4% for HPS, 80.6% for PoPH, and 76.6% for controls (p=NS). Causes of death were similar.
Conclusion: Patients with PoPH have 3-5 times higher incidence of cardiac events within the first year with differences in intraoperative hemodynamics. Despite higher morbidity, patients with HPS and PoPH have similar overall and graft survival rates compared to controls. Deaths in this group of patients are not cardiac and similar to controls.

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The effect of performance status at the time of transplantation on outcomes following liver transplantation: a national cohort study in the United Kingdom and Ireland

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Introduction: In the setting of liver transplantation (LT) the impact of frailty and compromised performance status (PS) on post-transplant outcomes are not well characterised in patients with chronic liver disease (CLD). In a national cohort of patients with CLD we examined the association of pre-LT PS on post-LT patient survival.
Methods: 7285 patients with cirrhotic CLD who received a first LT between 1997 and 2016 were studied. Pre-LT PS was assessed using the 5-level modified Eastern Cooperative Oncology Group (ECOG) score. We used stratified cox-regression methods to estimate hazard ratios (HR) that compared post-transplantation mortality for ECOG status in three post-transplantation time-periods (epochs): 0 to 90 days, 90 days to 1-year and 1 year to 5-years, and across different eras of transplantation (1995 to 2005 and 2006 to 2016).
Results: 5-year post-LT patient survival was 84.6% in patients able to carry out normal activity without restriction (ECOG PS1) decreasing to 71.0% in those completely reliant on nursing and medical care (ECOG PS5; p < 0.001). With adjustment for donor and recipient characteristics, the impact of ECOG PS5 on mortality was

significantly poorer in the first 90-days (HR: 2.14 95%CI: 1.43-3.20), but not significantly worse thereafter (90 days to 1-year: HR 1.59, 0.84-3.01; 1-year to 5-years: HR 0.82, 0.46-1.47). Over era, survival improved for patients in each ECOG status (PS1: 0.65, 0.31-1.37; PS2: 0.54, 0.41-0.70, PS3: 0.57, 0.48-0.68, PS4: 0.67, 0.50-0.90 and PS5 0.51, 0.30-0.89), however the effect of era did not differ significantly between ECOG status (p for interaction 0.81).
Conclusions: LT recipient PS is independently predictive of post-transplant mortality with the strongest association in those with greatest compromise. In these patients, its impact is most marked in the first 3-months after surgery. Over era, mortality has decreased by at least one third for patients in each ECOG category.

0-108

The impact of transarterial chemoembolization on complications and survival after liver transplantation: a national study using linked healthcare data.

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Introduction: The impact of transarterial chemoembolization (TACE) on early and late post-transplantation outcomes has not been identified in a representative cohort of recipients with hepatocellular carcinoma (HCC). To address this evidence gap, we linked the Standard National Liver Transplant registry to patient level data from an administrative dataset that captures all hospital admissions in the English National Health Service. We then used this fully representative cohort with highly complete follow-up to examine the impact of TACE on graft failure, mortality, tumour recurrence and post-operative complications.
Methods: We identified a population-based cohort of HCC recipients of a liver transplant (aged ≥ 16 years) between 2006 and 2016. We partitioned our cohort according to HCC recipients who had received TACE on the transplant waitlist and used stratified Cox regression methods to compare mortality and estimate hazard ratios (HR).
Results: 385 TACE and 583 non-TACE recipients were included. 5-year post-transplant survival was 75.2% (95%CI: 68.8% to 80.5%) in patients who received TACE and 75.0% (95%CI: 70.5% to 78.8%) in those who did not. With adjustment for donor and recipient characteristics, no significant differences in graft survival (HR: 1.01, 95%CI: 0.73-1.40, p=0.96) or mortality (HR 0.96, 95%CI: 0.67-1.38, p=0.82) were identified. Also, the impact of TACE on mortality did not differ according to the number of TACE treatments (≥2 TACE treatments HR: 0.97, 95%CI: 0.61-1.55, p=0.90), the time-period after transplantation (p for interaction = 0.29) or the use of circulatory death donors (p for interaction = 0.97). The incidence of hepatic artery thrombosis was lower in those who received TACE (1.3% vs 2.5%, respectively, p=0.09).
Conclusion: The use of TACE on HCC patients on the liver transplant waitlist does not increase the risk of early post-operative complications or graft failure nor does it improve long-term patient survival or rates of tumour recurrence.

0-109

Long-term outcome after liver transplantation for autoimmune hepatitis: a French national study on 344 patients over 30 years

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Introduction: Autoimmune hepatitis (AIH) is a rare indication (< 5%) for liver transplantation (LT). The aims of this study were: to evaluate disease recurrence, patient and graft survival after LT for AIH and to identify prognostic factors.
Methods: A multicenter retrospective nationwide study including 20 centers was conducted. All patients aged ≥16, transplanted for AIH in France were identified from the French Agence de la Biomédecine databases.
Results: 344 patients (271 women) transplanted from 1987 to 2018 were included. Median age at LT was 43.6 years (IQR, 30.3-54.8). Median time of follow-up was 74.4 months (IQR, 27.7-152.4). The indication for LT was fulminant liver failure in 58 cases and liver cirrhosis for 283 patients. AIH recurrence rate was 5.6%, 35.9% and 51.5% at 1, 10 and 20 years respectively. In multivariate analysis, only HLA A1B8DR3 haplotype was significantly associated with recurrence (OR=2.766; 95% CI, 1.129-6.772; p=0.026). Forty-six patients underwent retransplantation (9 for disease recurrence) after a median time of 15.4 months (IQR, 1.2-68.3). Graft survival was 84.2%, 69.3%, 56.4% at 1, 10, and 20 years respectively. Patient survival was 88.0%, 75.7% and 66.5% at 1, 10 and 20 years respectively. The main causes of death were sepsis (n=26), malignancies (n=12) and liver failure (n=16, including 4 recurrent AIH). In multivariate analysis risk factors significantly associated with poorer survival were: age at LT (OR=1.041; 95% CI, 1.013-1.069; p=0.004), HLA A1B8DR3 haplotype (OR=2.743; 95% CI, 1.426-5.276; p=0.003), LT in the context of acute-on-chronic liver failure (OR=2.494; 95% CI, 1.130-5.525; p=0.024), retransplantation (OR=4.391; 95% CI, 1.868-10.318; p=0.001) and long-term maintenance of corticosteroids (OR=2.551; 95% CI, 1.082-6.019; p=0.032).
Conclusion: Our results confirm that survival after LT for AIH is excellent. Disease recurrence is frequent and can lead to graft loss, but does not seem to strongly affect patient survival.

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Late acute rejection increases risk of graft failure in LDLT recipients: data from the A2ALL cohort

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Introduction: Late acute rejection (LAR) is defined as an initial episode of acute rejection occurring >6 months after transplantation. LAR in liver transplantation (LT) is associated with an increased risk of graft failure and death. The purpose of this study was to examine LAR in recipients of living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT) using data from the Adult-to-Adult Living Donor Liver Transplantation Study (A2ALL) cohort to identify predictors and determine the impact of LAR on graft and patient survival.
Methods: A2ALL recipients who underwent LDLT or DDLT between April 1998 and January 2014 were included. We compared recipients with early acute rejection (EAR), LAR, and no acute rejection using Kruskal-Wallis and Chi-squared tests; graft and patient survival were estimated using Kaplan-Meier methods.
Results: 1752 patients were included, 1187 were LDLT recipients and 565 were DDLT recipients. A total of 346 (19.7%) had EAR and 109 (6.2%) experienced LAR. Demographic data is summarized in Table 1. Compared with EAR, patients with LAR had fewer biliary strictures (35.9% vs. 39.8%, p< 0.001) and fewer median number of complications (3.5 vs. 3, p< 0.001). In univariate logistic regression, no factors were identified that predicted late versus acute rejection. In Kaplan Meier analysis, there was no difference in graft or patient survival among recipients with early acute rejection versus late acute rejection. This did not differ when DDLT and LDLT were analyzed separately. However, when assessing via Cox regression as a time-varying covariate, graft loss was significantly higher for patients with late acute rejection.
Conclusion: Approximately 6.2% of patients in the A2ALL cohort developed LAR. LAR was associated with increased graft loss.

	Total	Early Acute Rejection	Late Acute Rejection	No Rejection	P-value
N (%)	1752	346 (19.7%)	109 (6.2%)	1297 (74%)	--
Sex (%female)	39.1%	40.8%	49.5%	37.8%	0.043
Age	53.2	51.7	52.7	53.6	<0.001
Race (%Caucasian)	87.4%	85.6%	86.1%	88%	0.913
LDLT (%)	67.8%	64.2%	68.8%	68.6%	0.282
Related	41.4%	37.5%	34.9%	43%	0.298
Left lobe	4.2%	2.3%	3.7%	4.7%	0.127
DDLT	36.5%	39.1%	39.5%	35.5%	0.298
Primary Dx					
HCV	34.9%	37.9%	31.2%	34.5%	0.360
ALD	14.3%	13%	15.6%	14.6%	0.689
PBC	4.7%	6.6%	3.7%	4.2%	0.166
PSC	13%	11.6%	11%	13.5%	0.559
AIH	4.7%	7.5%	5.5%	3.9%	0.018

[Table 1]

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Risk stratification of patients undergoing simultaneous liver transplantation and cardiac surgery

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Background: Evaluate risk factors and outcomes of combined liver transplantation (OLT) and cardiac surgery, including coronary artery grafting and valve replacement.
Methods: Between 1/2005 and 8/2018, 1362 patients underwent OLT at our institution. 19 of them underwent combined liver transplantation and cardiac surgery. Retrospective analysis using logistic regression was conducted to assess the impact of demographics, pre-operative, intraoperative and post-operative variables on morbidity and mortality. Odds ratio and 95% confidence intervals were calculated. A predictive model of morbidity and mortality was established and statistically validated.
Results: At the time of liver transplant, eight patients underwent CABG, eight underwent valve replacement and three underwent CABG + valve replacement. Mean age was 59 ± 9, mean cardiac Euroscore was 5.3± 3.3 and mean MELD score was 20 ± 6. Statistically significant association was found between baseline eGFR and mortality (OR= 0.953, P= 0.05) and morbidity (OR= 0.95, P= 0.048). Predictive plots demonstrated solid correlation between pre-operative renal function and morbidity and mortality (Figure 1). Other correlations were found between dialysis post-OLT (OR= 27.5, P= 0.01)/ surgical re-exploration (OR= 11, P= 0.03) and mortality, and between dialysis post-OLT (OR= 12.5, P= 0.02)/surgical re-exploration (OR= 6.6 P= 0.04) and morbidity. Overall survival rate at 1, 3 and 5 years was 91%, 85% and 77% respectively.
Conclusions: Pre transplant renal function is the strongest predictor of mortality and morbidity for simultaneous liver transplantation and cardiac surgery independently of patient MELD score and cardiac Euroscore at the time of transplant. Predictive model was built based on our data.

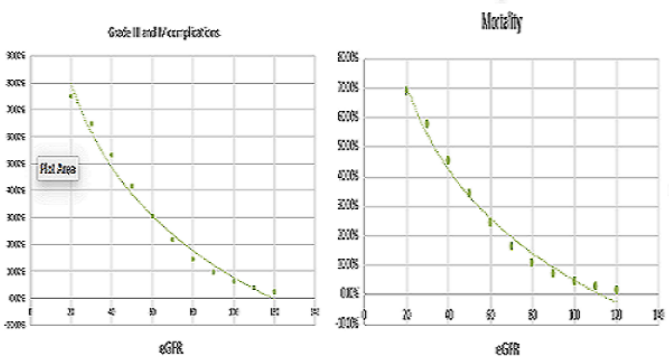

Fig 1. Predictive plots of eGFR on A) morbidity, B) mortality in simultaneous combined liver-heart surgery.

[Predictive plots]

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Establishment of a novel integrated model for prediction of hepatocellular carcinoma recurrence after liver transplantation

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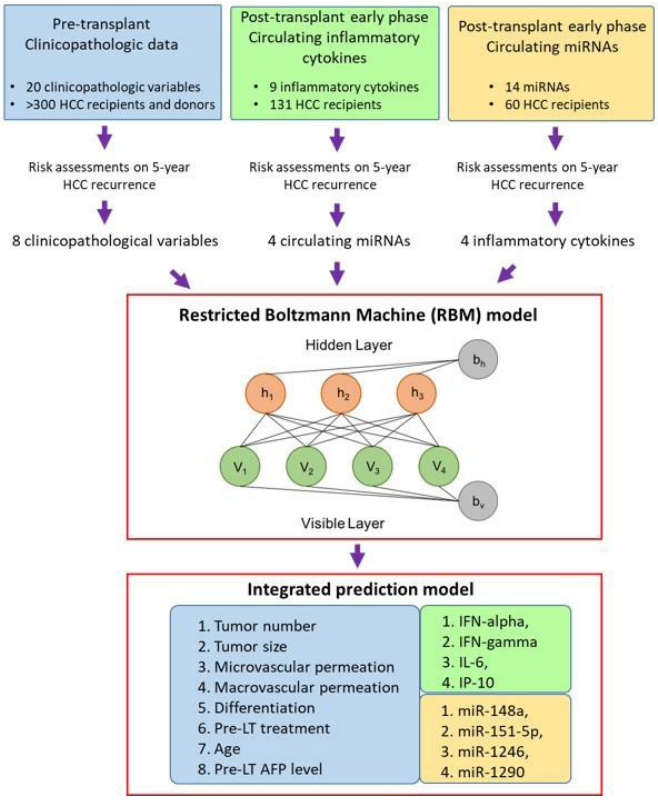
Background and aim: Hepatocellular carcinoma (HCC) recurrence after liver transplantation remains a significant challenge under current pre-transplant selection criteria. We have demonstrated that elevated post-transplant graft injury-related factors such as inflammatory cytokines and microRNAs rise risks of late phase HCC recurrence, suggesting that both pre-transplant and post-transplant factors are essential components in building an accurate risk-assessing model on HCC recurrence. Conventional prediction models have limitations in integrating different clinicopathological and experimental data sets which are always non-proportionate.
Method: Univariate risk regression analyses were used for clinicopathological factors and experimental variables (9 circulating inflammatory cytokines and 14 miRNAs) to identify risk variables on HCC recurrence in HCC patients undergone liver transplantation in Hong Kong Liver Transplantation Centre. A Restricted Boltzman Machine (RBM) model was employed to integrate the clinicopathological and experimental variables to generate an integrated prediction model for assessing the risk of post-transplant HCC recurrence (Fig.1).
Result: We identified 8 pre-transplant clinicopathological factors (AFP level, tumor number, tumor size, differentiation, microvascular invasion, macrovascular permeation and pre-transplant treatment), 4 post-transplant circulating inflammatory cytokines (IFN-alpha, IFN-gamma, IL-6 and IP-10) and 4 post-transplant circulating miRNAs (miR-148a, miR-151-5p, miR-1246 and miR-1290) showing significant risks on 5-year post-transplant HCC recurrence. The RBM model overcome the limitation of non-proportionate data imputation between clinicopathological and experimental data. The prediction model consisting of 8-clinicopathological variables achieved a c-statistic of 0.8 on prediction of a 5-year risk of HCC recurrence, while the prediction model consisting of 8-clinicopathological variables, 4-inflammatory cytokines and 4-miRNAs could achieve a c-statistic of 0.9. This integrated prediction model showed more accurate prediction than the Milan criteria and UCSF criteria.
Conclusion: We have established a novel prediction model which integrates the post-transplant inflammation responding factors with pre-transplant clinicopathological factors increases the prediction accuracy on post-transplantation HCC recurrence.



[Figure 1. A novel integrated model for prediction of HCC recurrence after liver transplantation]

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Utilization of LDLT *vs.* DDLT for patients with high medical acuity (MELD ≥ 35)

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Background: Patients(pts) w/MELD≥35 are at significant risk for immediate waitlist mortality. With scarcity of deceased donors, LDLT may shorten time to liver transplant(LT); however, utilization of LDLT for high MELD is controversial due to the increase in donor/recipient risk-to-benefit ratio and the concern for the insufficient size of the partial graft. The current collaboration compares the outcomes following DDLT and LDLT for pts w/MELD≥35 to assess if LDLT is an acceptable alternative for pts with very high medical acuity.
Methods: Between 2005-2015, 412 pts, MELD≥35 underwent LT (Korea DDLT(132)/LDLT(133)/ US DDLT(147)). Patient survival(PS), graft survival(GS), recipient and donor characteristics, pre-LT medical acuity (dialysis, ventilator, ascites, infection(Ifx)), causes of death(COD) and graft loss(COGL), post-LT complications, ICU/hospital length of stay were studied. Relative risk(RR) of mortality by pre-LT risk factors were analyzed.
Results: For Korean DDLT/LDLT/US DDLT: 1-yr-PS 74%/81%/90%, 5-yr-PS 65%/78%/71%(P< 0.02); 1-yr-GS 74%/81%/90%, 5-yr-GS 61%/75%/71%(P< 0.05). Korean DDLT group had highest pre-LT medical acuity *vs.* Korean LDLT/US DDLT groups(Table 1). Most common COD were Ifx, CVA, graft failure for Korean groups; Ifx, malignancy, graft failure for US group. Most common COGL were death with function and rejection for all groups(Table 2). For Korean DDLT/LDLT and US DDLT: RR of mortality by pre-LT dialysis (1.7/3.5/1.5), ventilatory support (5.5/2.6/0.9), ifx (1/2/1), ascites (2.1/3.2/2.9), encephalopathy (3.5/3.6/0.75). Post-LT Ifx rates for Korean DDLT/LDLT were lower than for US DDLT: 23%/17% *vs.* 64%(P< 0.01)(Table 3). LDLT group had 2 pts w/ primary non-function (one GRWR< 0.8) and 15 pts w/ small-for-size grafts (all GRWR< 0.8).
Conclusion: Outcomes of LDLT recipients w/MELD≥35 are comparable to DDLT recipients w/MELD≥35 at centers with substantial experience. With pre-LT medical optimization of recipients and judicious graft selection, LDLT provides an acceptable LT option for pts with very high waitlist mortality.

Table 1	Korea Deceased Donor (n=132) Median or %	Korea Living Donor (n=133) Median or %	US Deceased Donor (n=147) Median or %	p-value
Median Age (Years) (IQR)	48 yrs (43, 57)	48 yrs (42, 54)	55 yrs (46, 61)	<0.0001
Male Sex	74%	68%	61%	NA
Ethnicity				<0.0001
Asian	100%	100%	9%	
Caucasian	0	0	69%	
African American	0	0	11%	
Hispanic	0	0	5%	
Other	0	0	7%	
Liver Disease				<0.0001
HBV	54%	51%	10%	
HCV	0%	2%	28%	
Etoh(ALC)	19%	13%	15%	
NASH	0%	0%	9%	
Autoimmune	2%	4%	18%	
Other	26%	30%	21%	
HCC Diagnosis	9%*	5%	2%*	<0.01*
BMI (kg/m2) (IQR)	24.4 (22.1, 26.7)	24.2 (21.8, 26.8)	28.2 (24.1, 33.5)	<0.0001
MELD (IQR)	41 (38, 44)	39 (36, 42)	40 (38, 40)	<0.0001
Pre-Tx Ventilator	53%	38%	8%	<0.0001
Pre-Tx Dialysis	58%	38%	45%	0.004
Pre-Tx Ascites	96%	91%	82%	<0.0001
Pre-Tx Bacteremia	12%	7%	1%	<0.001
Donor Age (Years) (IQR)	44 yrs (34, 53)	26 yrs (21, 32)	43 yrs (27, 55)	<0.0001
Donor Male Sex	68%	71%	43%	<0.0001
Donor BMI (kg/m2) (IQR)	23.1 (21.3, 25.5)	22.1 (20.4, 23.8)	26.6 (23, 31.1)	<0.0001
GRWR (median, range)		1.02 (0.71-1.7)		
Donor Type				
Living	0	100%	0	
DBD	100%	0	94%	
DCD	0	0	6%	

Table 2: Causes of Death	Korea DDLT (n=46)	Korea LDLT (n=31)	US DDLT (n=42)	p-value
Infection	54%	48%	36%	NA
Cerebrovascular	11%	20%*	5%*	<0.05*
Primary malignancy	7%	3%	14%	NA
Graft failure	9%	16%	10%	NA
Cardiovascular diases	2%	3%	7%	NA
HCC recurrence	4%	7%	2%	NA
Respiratory failure	0*	0	10%*	<0.03*
Other	9%	3%	12%	NA
Unknown	4%	0	5%	NA
Causes of Graft Loss	**Korea DDLT (n=53)**	**Korea LDLT (n=35)**	**US DDLT (n=43)**	
Death with function	77%	63%	74%	
Rejection	11%	14%	15%	
Biliary complications	0	0	5%	
Ischemia	2%	9%	0	
Thrombosis	0	0	2%	
PNF	2%	3%	0	
CMV Hepatitis	2%	0	0	
Tylenol tyoxicity	0	0	2%	
HCV recurrence	0	0	2%	
Unknown	6%	11%	0	

Table 3	Korea DDLT (n=132)	Korea LDLT (n=133)	US DDLT (n=147)	
Post-LT ICU stay (median, IQR)	10 (6, 24)	10 (5, 18)	15 (10, 24)	<0.0001
Post-LT hospital stay (median, IQR)	29 (9, 81)	40 (25, 88)	23 (15, 39)	<0.0001
Within 3 months:				
Infection	23%	17%	64%	<0.0001
Rejection	5%	3%	5%	NA
Bile leak	2%	5%	5%	NA
Hepatic artery thrombosis	0	0	3%	NA
Portal vein stenosis	2%	2%	0	NA
Hepatic vein stenosis	0	3%	1%	NA

[Demographics and Outcomes]

O-114

Improvement in long-term survival outcome in adult-to-adult living donor liver transplantation - a 20-year experience in Hong Kong

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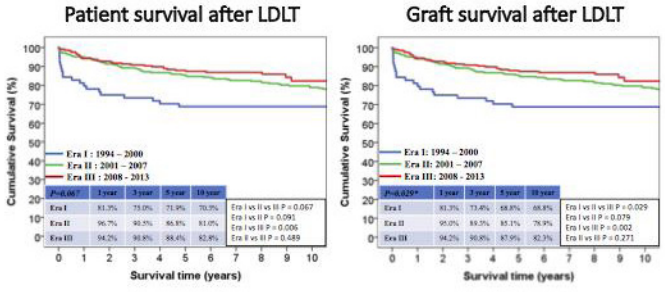
Background: There is limited data in the literature on the analysis of long-term survival outcome with respect to the different time frames of LDLT.
Methods: From 1994 to 2013, 513 LDLT performed were retrospectively reviewed. This retrospective study aims to compare long-term recipient and donor outcome after LDLT in a tertiary referral center over 20 years (Era I: 1994 - 2000, n = 64; Era II: 2001 - 2007, n = 242; Era III: 2006 - 2013, n = 207).
Results: Era III had significantly older patients, less patients with hepatitis B infection and fulminant liver failure, more patients with HCC and Child grade A or B, lower MELD score, and less patients with critical condition nursed in intensive care unit. Regarding donor outcome, Era III had significantly less operating time, less intraoperative blood loss and less patients with blood transfusion than Era I and II. Era II had significantly less donor morbidity than Era I. Short-term outcomes of recipients were significantly better in Era III than Era I and II, in terms of less intensive care unit stay, lower hospital mortality, lower postoperative complication rate and less hospital stay. With median follow-up of 123 months, the 5 and 10-year graft survival rate of Era III were also significantly better than Era I (87.9% vs. 67.8% and 82.3% vs. 68.8%) (P = 0.002). (Figure 1) By multivariable analysis, Child grade C (HR 0.390, 95%CI 0.203 - 0.749), hospital stay (HR 1.007, 95% CI 1.000 - 1.015) and Era I vs. III (HR 0.413, 95% CI 0.214 - 0.796) were poor independent prognostic factors affecting graft survival.
Conclusion: There is continuous improvements in recipient and donor outcome over 20 years, in terms of decreased complication rate and prolonged long-term survival.



[Figure 1]

Concurrent Oral Abstract Session: Anesthesia / Critical Care Medicine

O-115

Feasibility and safety of the mild hypothermia and acute kidney injury in liver transplantation (MHALT) trial

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Background: Patients undergoing liver transplantation (LT) are at high risk of postoperative acute kidney injury (AKI). In LT patients, AKI predicts negative outcomes such as progression to chronic kidney disease, graft loss, and mortality. Mild hypothermia (MHT, 34-35 °C) has been shown to protect against AKI in rodent models of renal ischemia, and to reduce delayed graft function after kidney transplant from deceased donors. Based on these results, we are performing a single-blinded randomized controlled trial of MHT during LT (NCT03534141), with the hypothesis that MHT will reduce the incidence of AKI after LT.
Method: The study was approved by the local institutional review board and is overseen by a data safety monitoring board. After informed consent, patients were randomized to MHT or normothermia at the time of LT. Temperature was maintained by an esophageal cooling device plus standard measures. In the MHT arm, systemic cooling was initiated after induction of anesthesia and maintained through portal vein reperfusion. To enhance local cooling, ice was placed over the right kidney during the anhepatic phase. In the control arm, normothermia was maintained.
Results: 17 patients have been randomized (MHT, n=9; normothermia, n=8). Patients in the MHT arm had significantly lower core temperatures compared with controls at the beginning (34.5±0.3 vs. 36.5±0.6 °C) and end of the anhepatic phase (34.0±0.5 vs. 35.9±0.7 °C, mean ± SD, both p< 0.0001). There was no significant difference in median [IQR] estimated blood loss (1800mL [1275,3700] vs. 1375mL [625,3750]), units of FFP transfused (6 [3,9] vs. 7 [2,9.5], both *p*>0.9), RBC, or platelet transfusions between arms. *P*-values are from unpaired t-tests. No severe adverse events have been observed.
Conclusion: Preliminary data indicate that the MHALT trial is safe and feasible. The primary outcome for a larger cohort will be incidence of AKI within 72 hours after LT.

O-116

Liver transplantation for patients with grade 3 acute-on-chronic liver failure: pre-transplant factors of post-transplant mortality in a multicenter study

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Background: Liver transplantation (LT) for patients with cirrhosis and multiple organ failure (MOF) is a controversial procedure given the ongoing organ shortage, especially since diverging post-LT outcomes have been reported. We report the post-LT results of a multicenter cohort and identify pre-LT criteria to help predict post-LT outcome.
Method: Patients who received LT with grade 3 acute-on-chronic liver failure between 2007 and 2017 in 5 transplant centers were retrospectively included and divided into a determination cohort (Strasbourg) and a validation cohort (Beaujon, Mondor, Tours and King's College in London). One-year post-LT mortality risk factors were screened in the determination cohort and a multivariate logistic regression analysis was conducted. A predictive model was derived and evaluated in both cohorts by using the area under the receiver operating characteristic (AUROC) curve.
Results: 152 patients met the inclusion criteria (76 in the determination cohort and 76 in the validation cohort). The overall one-year survival rate was 67.1%. In multivariate analysis, older age (OR = 1.092, 95% CI = 1.003 - 1.19, p = 0.0416), respiratory failure (not intubated vs. intubated vs. intubated with PaO_2/FiO_2< 200mmHg: OR = 4.34, 95% CI = 1.02 - 18.49, p = 0.047), lactate levels > 4 mmol/l (OR = 8.04, 95% CI = 1.56 - 41.51, p = 0.0128) and lower leukocyte count prior to LT (OR = 0.86, CI 95% = 0.76 - 0.97, p = 0.014) were independent risk factors of one-year mortality. A predictive model derived from these factors was tested by comparing the AUROC curves of both cohorts (0.87 vs. 0.80 respectively, p = 0.296).
Conclusion: We have identified four simple and clinically relevant factors that can be used to estimate the post-transplant outcome of cirrhotic patients with MOF and assist in the decision-making process with regards to the organ allocation to such patients.

O-117

An individualized, in-hospital prehabilitation programme for patients with cirrhotic liver disease awaiting transplantation surgery: a single-centre feasibility study

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Background: Physical deconditioning, sarcopenia and frailty are all associated with increased mortality in end-stage liver disease. The period of time spent on the waiting list prior to liver transplantation (LT) provides an opportunity to optimise fitness and reduce the physiological impact of major surgery. We assessed the feasibility and effectiveness of a six-week prehabilitation programme in patients with cirrhotic liver disease awaiting transplantation.
Methods: Cirrhotic patients awaiting LT were recruited to take part in a 6 week, in-hospital exercise training programme, over 18 months from June 2016. The intervention arm consisted of 3x 40min sessions per week of individualized, interval training formulated from baseline cardiopulmonary exercise testing (CPET) measures on a bicycle ergometer. CPET data and anthropometric measures were compared to a group of matched control participants also awaiting LT, who had not undergone the exercise intervention. Both groups received structured nutritional advice.
Results: Thirty-three patients were recruited with twenty (9 in the intervention group, 11 controls) completing the 6-week study period. VO_2 at peak in the intervention group rose from a mean (SD) of 16.2 (± 3.4) ml/kg/min at baseline to 18.5 (±4.6) ml/kg/min at week 6 (p=0.02). VO_2at peak in the control group decreased from a mean (SD) of 19.0 (± 6.1) ml/kg/min to 17.1 (±6.0) at week 6 (p=0.03). A significant increase in hand grip strength was demonstrated in the intervention group (all anthropometric measures are presented in table 1).
There were no adverse events associated with exercise training.
Conclusion: We have demonstrated the feasibility and safety of an in-hospital exercise training programme for patients awaiting LT. We observed signals of improvement in physiological fitness and muscle strength/mass in the intervention group. Further research should focus on determining the optimal prehabilitation programme design involving multidisciplinary input.

	Exercise (n=9)		Usual care (n=11)	
	Wk 0	Wk 6	Wk 0	Wk 6
BMI (dry weight) Mean (SD)	30.9 (5.6)	31.1 (5.5)	27 (4.6)	26.9 (3.8)
Handgrip (kg) Mean (SD)	26.4 (7.5)	29.4 (6.4)**	29.1 (10.7)	30.5 (13)
MAC (cm) Mean (SD)	35.4 (7)	35.7 (6.9)	30.2 (3.7)	30 (3.5)
MAMC (cm) Mean (SD)	28.6 (4.6)	29.9 (5.7)	24.2 (3.3)	23.5 (3.7)

[Anthropometric measures at baseline and week 6 in both the intervention and control groups]

O-118

Pre-transplant metabolic syndrome associated with major adverse cardiovascular events after liver transplantation

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Purpose: Metabolic syndrome (MS) is an important risk factor for cardiovascular disease, but the prevalence of pre-transplant MS and its effect on early major adverse cardiovascular events (MACE) and mortality after liver transplantation has not been well described.
Methods: After institutional review board approval, adult primary LT recipients between January 2009 and December 2015 were retrospectively reviewed. MS was defined according to the 2009 harmonized definition. MACE was defined as new-onset myocardial infarction, heart failure, atrial fibrillation, cardiac arrest, pulmonary embolism, and/or stroke. Patients were divided into two groups: MS and non-MS. Propensity score matching was used to control differences between the two groups. Multivariate logistic regression was used to identify risk factors.
Results: Among 858 recipients included in the study, 243 (28.3%) recipients met diagnostic criteria of pre-transplant MS. After matching, the two groups (241 pairs) were well balanced. The MS group had a significantly higher incidence of MACE than non-MS group (25.7% versus 17.8%, P= 0.035). Pre-transplant MS remained as an independent risk factor for early MACE in a model including intraoperative factors (odds ratio, 1.77; 95% confidence interval, 1.13-2.78; P=0.014). Pre-transplant MS was not associated with the 30-day mortality.
Conclusions: Pre-transplant MS in LT recipients is associated with a significantly higher incidence of MACE within 30 days in LT recipients. Early recognition and aggressive management of pre-transplant MS may be needed.

0-119

Live donor liver transplantation in recipients with left ventricular dysfunction

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Introduction: Data on feasibility, management, and outcomes of liver transplantation (LT) in patients with pre-existing severe coronary artery disease (CAD),previous angioplasty (PTCA) or bypass (CABG),or left ventricular dysfunction (LVD) is scarce.
Methods: We reviewed epidemiology, disease characteristics, and outcomes of living donor liver transplantation (LDLT) in recipients with LVD (EF< 50%) from our series of 1946 LDLT's performed between June 2010 to July 2018. All patients underwent a detailed cardiac evaluation during LDLT work-up including CT calcium score, dobutamine stress ECHO. CT coronary angiogram, stress thallium or conventional angiography were performed as indicated.
Results: Twelve male patients had LVD during work up; EF improved in 3 of them to >50% at the time of LT. Mean age, BMI were 56±7 years, and 25±5 kg/m^2, respectively. Underlying cirrhosis was due to ethanol (6), Hepatitis C (2), nonalcoholic steatohepatitis (2) and cryptogenic (2). Two recipients were post CABG, 1 was post PTCA, 5 had a history of myocardial infarction (including 2 post CABG and 1 PTCA), 2 had dilated cardiomyopathy (one of them also had left bundle branch block with ICD with non-critical CAD), and 4 had cirrhotic cardiomyopathy. EF ranged from 25%-45%. Mean LDLT anesthetic duration was 11 hours. Intraoperative course was uneventful in all except 2 patients, who developed ventricular ectopics, managed successfully with intravenous lidocaine. All recipients, except one who required IABP, were extubated on POD1. Three patients developed stress cardiomyopathy with decreased EF post operatively, 2 improved, while 1 needed IABP support (EF was 25%), and died of multi-organ failure on POD20. Another patient died on POD30 due to septic shock. Mean hospital stay was 22 days. There were no long term cardiac deaths.
Conclusion: LT in patients with LVD although challenging, can result in successful outcomes with careful preoperative work up, risk evaluation, and meticulous and vigilant intraoperative monitoring.

0-120

The cardiac output optimisation following liver transplant (COLT) trial: a feasibility randomised controlled trial

Martin D.[1,2], Morkane C.[2], Strachan A.[2], Schofield N.[2], Filipe H.[2], Froghi F.[1,3], Eastgate C.[2], McNeil M.[2], Anastasiou Z.[4], Soggiu F.[1], Selves L.[3], Singh J.[5,6], Longworth L.[6], Gurusamy K.[1], Koti R.[1,3], Thorburn D.[7], Mallett S.[2], Davidson B.[1,3]

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Background: Goal directed fluid therapy (GDFT) has been shown to reduce morbidity following major surgery but has not been robustly assessed in the setting of liver transplantation. We therefore conducted a prospective trial to assess feasibility of delivering GDFT following liver transplantation.
Methods: Patients with liver cirrhosis were recruited to either 12 hours of GDFT using a non-invasive cardiac output monitor or standard care (SC) guided by attending clinicians. The primary outcome measure of the study was feasibility. Postoperative complications were scored on the Clavien-Dindo (CD) scale, quality of life was measured using EQ-5D-5L and an assessment of resource use was conducted. Follow up occurred at 90 and 180 days after surgery.
Results: During the 16 month recruitment period 224 patients were identified as eligible for the trial; of these, 122 were formally approached of whom 114 (93.4%) consented to participate. 60 patients were enrolled into the trial, stratification by organ donor characteristics occurred prior to randomisation. No patients were removed from the study by the clinical teams involved. Median crystalloid administered during the 12 hour intervention period was 3500 ml in the GDFT group versus 2225 ml in the SC group. There were an increased number of CD grade 3 complications in the GDFT group at discharge from hospital (63.3%) versus the SC group (20.0%). No other differences between groups in the number or severity of postoperative complications were detected. There was no statistically significant difference in quality of life scores and resource use between the groups.
Conclusions: This feasibility study has demonstrated that it is possible to recruit patients to a study of GDFT following liver transplantation and deliver the intervention in an ICU setting. The study was not powered to show differences in outcomes but has shown higher rates of grade 3 complications in the GDFT group.

O-121

Perioperative fluid management strategies and postoperative outcomes in liver transplantation: a systematic review

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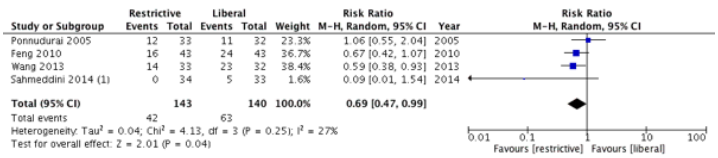
Background: Liver transplant (LTX) recipients suffer many complications and fluid management is an important aspect of perioperative care. Restrictive fluid management strategies have been described but their impact on outcomes are unclear. We conducted a systematic review to evaluate the effects of restrictive perioperative fluid management strategies compared to liberal ones on postoperative outcomes.
Method: We searched CINAHL, EMB Reviews, EMBASE, MEDLINE and the grey literature from inception to July 10th 2018. We included randomized controlled trials (RCTs) and observational cohort studies that compared two fluid management strategies in adult LTX recipients. Our primary outcome was the incidence of acute kidney injury (AKI). Our secondary outcomes were bleeding, mortality and other postoperative complications. Four authors selected the studies and two abstracted data independently. We used the RoB 2.0 and ROBINS-I tools to evaluate the risk of bias (ROB). When appropriate, data from RCTs were pooled using relative risks and mean differences with random-effect models.
Results: We included 7 RCTs (5 at high ROB) and 29 observational studies (27 at high or critical ROB). Data from RCTs and cohort studies suggested that the use of restrictive fluid management strategies did not affect the incidence of AKI or mortality. Fewer pulmonary complications (figure), reduced duration of mechanical ventilation (mean difference = -13.04 hours [-22.2, -3.08], N=130, I^2=0%) and reduced blood loss (-1.29 liter [-1.92, 0.66], N=151, I^2=0%) were observed from RCTs with a low or very low level of certainty. No effect on graft or non-pulmonary infectious complications was observed.



[Postoperative pulmonary complications]

Discussion: We did not observe any effect of a restrictive fluid management strategy on the risk of AKI but, based on a low quality of evidence, we observed possible effects on other outcomes. This review will help design future clinical trials.

O-122

Thromboelastography demonstrates significant hypercoagulability in patients undergoing Right Donor Hepatectomy - a prospective single center analysis

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Background: Un availability of deceased donors in the east has led to a rise in popularity in living donor liver transplantation (LDLT). Preventing post-operative complications is a major concern in LDLT's. There are reports of fatal pulmonary embolism which has happened in Living Donors. More over a study examining TEG patterns by Cerutti et al in 10 liver donors in 2004 showed a significant development of hypercoagulability in 6 patients. We attempted to the same on a larger sample size of patients.
Methods: 80 patients who underwent right donor hepatectomies were enrolled in the study. In addition to the baseline investigations and demographics, **TEG analysis was done a day prior to surgery and POD1,3,5 & 7 respectively**. Post - operative blood counts, liver function tests & PT-INR were also recorded & statistically analyzed.
Results: The evolution of TEG variables are summarized in **image 1**. All patients were hypercoagulable at post - operative day (POD) 1 & 3. 98.8 % of patients were hypercoagulable in POD5 & 67.5 % of patients in POD 7. None of the patients were hypo coagulable in spite of an **increased PT INR & decreased platelet counts**. **r time & k- time had significantly shortened throughout the post-operative period whereas alpha angle and MA had significantly increased. The Coagulation Index (CI) demonstrated maximum hypercoagulability in POD1 (5.17±.75), gradually decreasing towards POD7 maintaining hypercoagulability throughout.**
Conclusion: In spite of the routine laboratory investigations

suggesting hypocoagulability, **TEG monitoring showed significant hypercoagulability in all the patients who underwent right donor hepatectomies**. This result of ours has far-reaching impact on donor safety post living donor liver transplantation. We strongly recommend early post-operative mobilization and anti - thrombotic prophylaxis on all patients undergoing donor hepatectomies.

TEG Parameters	Day 0	Day 1	Day 3	Day 5	Day 7
r-time (minutes)	4.32±.68	4.06±.61*	3.74±.48*	3.225±.35*	3.225±.35*
k-time (minutes)	2.76±.60	2.59±.51	1.84±.43*	1.601±.30*	1.623±.30*
Alpha angle (degrees)	58.33±5.9	69.04±5.8*	72.41±4.8*	71.63±5.1*	71.63±5.1*
MA (mm)	50.48±2.2	68.5±4.5*	67.81±4.6*	67.76±5.02*	67.75±6.9*
LY 30 (%)	0.437±.72	1.54±.52*	0.99±.45*	0.32±.22	0.12±.18*
CI	2.48±.40	5.17±.75*	4.94±.78*	4.87±.83*	4.11±1.1*

*Table 1:Perioperartive Evolution of TEG Variables (r-time,k-time, alpha angle,MA,LY 30 &CI) in 80 adult living liver donors. Data expressed as mean±sd. *P<.05 from Day 0*

[Perioperative Evolution of TEG Parameters]

O-123

Predicting acute kidney injury after orthotopic liver transplantation using machine learning

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Background: In patients undergoing orthotopic liver transplantation (OLT), the incidence of acute kidney injury (AKI) is up to 60%. Renal injury after OLT can lead to dialysis and is known to increase post-transplant mortality. A Gradient Boosting Machine (GBM) is a form of machine learning that typically uses ensemble decision trees and builds a model in a stage-wise fashion. The aim of this project was to evaluate the use of GBMs to accurately predict AKI after OLT.
Methods: We retrospectively studied 745 adult patients' records who underwent OLT at UCSF between June 2012 and August 2018. Patients requiring pre-operative dialysis were excluded. For each transplant, we included 904 variables, including demographics, vital signs, ventilator settings, medications, diagnoses, and all available laboratory results. Data was included until the end of surgery defined as "anesthesia stop." AKI was defined as either stage 2 or 3 kidney injury according to the International Club of Ascites 2015 criteria modified to 48 hours postoperative. The data were normalized and separated into training (64%), validation (16%), and test sets (20%). A gradient boosting machine (GBM) model was trained using the python package XGBoost with the default package parameters for binary classification. The GBM performed better than logistic regression, random forest, and fully connected deep neural network on the validation set.
Results: The incidence of AKI ≥ Stage 2 was 33.7%. We achieved a test accuracy of 75.84% of predicting AKI ≥ Stage 2 and a ROC-AUC of 0.800 on the test set.
Conclusion: Machine learning can be used on perioperative data to predict postoperative outcomes. Our results suggest that additional data and further model optimization will improve predictability. Such models could be updated real-time to guide patient management. A better understanding of the individual patient's risk for AKI can guide postoperative management and improve postoperative outcomes.

Concurrent Oral Abstract Session: Surgical Videos for Technical Innovation

O-124

Living donor liver transplantation using left trisection graft with caudate lobe

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Background: Due to small remnant volume or anatomical variation, a right liver graft may be precluded in adult living donor liver transplantation (LDLT). Right posterior section, right anterior section graft, or dual donor grafts have been proposed as alternative grafts of right and left liver grafts. Here, we report a case of LDLT using left trisection graft with caudate lobe.
Methods: The recipient was a 55-years old female with hepatitis B virus associated liver cirrhosis. The donor had a type III portal vein (PV) anomaly. Donor's right hepatic artery (HA) was extrahepatically divided into right anterior and posterior HA and left HA was originated from left gastric artery. Preoperative cholangiography showed trifurcation of bile duct. Left trisection graft with caudate lobe was measured 620 gram that was 0.88% of graft to recipient weight ratio.
Results: With J shaped incision, hilar dissection of the donor was performed to isolate the left and right anterior and posterior branches of the HA and PV. Then, the liver was transected in a plane that was demarcated on the liver surface, temporarily occluding the right posterior branch of the HA and PV. We encountered 1 PV opening, 1 hepatic vein opening, 3 HAs, and 3 bile duct openings in the left trisection graft with caudate lobe that were safely anastomosed in the recipient. There was no complication in donor and recipient side after operation.
Conclusions: Although it was a complex operation, left trisection graft with caudate lobe might be a feasible option for special situations involving donors unsuitable for right liver donation.

O-125

Pure laparoscopic living donor right hepatectomy with hanging maneuver repositioning and rubber band retraction technique

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Most important concern in living donor liver transplantation is donor safety. At the same time, laparoscopic approach has become widely performed in major hepatectomy. Nowadays, pure laparoscopic donor hepatectomy has been increased with development of surgical technique. hanging maneuver and rubber band retraction technique is very useful technique for donor safety.
Donor is 37 years old male. His liver is good condition. There is no anomaly in liver anatomy. Mid hepatic vein has two branches from right liver. MRCP show normal confluence of bile duct. According this finding, we planned pure laparoscopic living donor right hepatectomy.
After the pathologist confirmed that there was no fatty liver in the liver biopsy, a cholecystectomy was performed. Firstly, full right lobe mobilization was performed, and hilar dissection was done. right hepatic artery was isolated carefully. Right portal vein was completely exposed and isolated under retracting right hepatic artery laterally. Liver parenchymal transection line was drawn after transient clamping of the right hepatic artery and right portal vein using bulldog clamp. Transection plane was straightly exposed using rubber band retraction technique. After liver parenchymal resection was performed in half, silastic drain was inserted between the right hepatic vein and mid hepatic vein for hanging maneuver. After hilar plate was isolated carefully, silastic drain for hanging maneuver was pulled up behind the hepatic hilum. The caudate lobe parenchyma was divided, and parenchyma transaction was completed. After suprapubic transverse incision was made for liver delivery, right bile duct, right hepatic artery, right portal vein was divided. Right hepatic vein also ligated and divided using endo GIA. The donor was discharged on the 7th postoperative day after confirming that there was no complication on postoperative CT scan. After follow-up of more than one year, donor and recipient live well without complication.

0-126

Surgical tips of pure laparoscopic donor right hemihepatectomy for donors with portal vein anatomical variations

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Introduction: Several reports from centers highly specialized in living-donor liver transplantation and laparoscopic liver surgery addressed good outcomes of total laparoscopic living donor hepatectomy for adults. However, donors with anatomical variations of the right portal vein or hepatic ducts or with marginal liver grafts are considered unsuitable for this procedure by most centers.
Method: From March 2017 to November 2018, 15 cases of pure laparoscopic right hemihepatectomy in a donor with portal vein variation were performed by the single experienced surgeon. We describe in this report about the standardized procedure for safe totally laparoscopic adult living donor hepatectomy for donors with variations of the right portal vein.
Results: Right hepatic artery should be temporary clamped for making demarcation line. We usually do not dissect around artery for preventing hidden injury of the hepatic artery. Instead, we clamped right side of Glissonian tissue bluntly after isolating right portal vein. Bile duct division was performed using ICG cholangiography. We usually used bulldog clamp during the first bile duct division for preventing bile spillage that disturbing ICG cholangiography during the division of the other bile duct. There are different methods to control the right portal vein branches including 1)Hem-o-lock clips supported with metal clips.2)Laparoscopic vascular staplers.3)Hem-o-lock clips to temporary control the portal vein branches stumps which are then replaced with sutures (continuous prolene 5/0 sutures). Then hem-o-lock clips could be removed from the portal vein stumps.
Conclusion: Portal vein anatomic variations can be overcome by appropriate surgical procedures.

0-127

Robotic living donor left lateral sectionectomy

Kim J., Cheah Y.L., Simon C.J., Akoad M.E.

Lahey Hospital & Medical Center, Transplantation, Burlington, United States

Robotic living donor hepatectomies are technically challenging operations. The accepted benefits of this minimally-invasive surgery include less postoperative pain, enhanced postoperative recovery with faster return to pre-donation status, and may further reduce postoperative morbidity. In 2018, our transplantation institute started performing totally robotic living donor hepatectomies in well-selected donors. Here we present a case of a totally robotic donor left lateral sectionectomy in a healthy adult male. There were no intraoperative and/or postoperative issues or complications.
The patient is a 31-year-old healthy male who had completed our robust living donor evaluation process and wished to donate a portion of his liver to his son who had decompensated end-stage liver disease secondary to alpha-1-antitrypsin deficiency. The calculated volume of the donor's left lateral section was 244 ml; his liver remnant was calculated to be 83%. The estimated graft to body weight ratio was 1.26.
This totally robotic left lateral sectionectomy was performed without intraoperative issues or complications. The estimated blood loss was 100 mL. His postoperative course was uneventful and he was discharged home in excellent condition on postoperative day 3. Both donor and recipient are doing well.

0-128

Robotic living donor right hepatectomy

Kim J., Cheah Y.L., Simon C.J., Akoad M.E.

Lahey Hospital & Medical Center, Transplantation, Burlington, United States

Robotic living donor hepatectomies are technically challenging operations. Accepted benefits of this minimally-invasive surgery include less postoperative pain, enhanced postoperative recovery with faster return to pre-donation status, and reduced postoperative morbidity. In 2018, our transplantation institute started performing totally robotic living donor hepatectomies in well-selected donors.
Here we present a video of one representative robotic donor right hepatectomy. The patient is a 26-year-old healthy nurse who successfully completed our living donor evaluation process. She underwent a robust informed consent process and went on to donate her right liver to her father who had decompensated end-stage liver disease secondary to primary sclerosing cholangitis. Her right liver volume was 760 ml leaving her with a calculated liver remnant of 38%. The estimated graft to body weight ratio was 0.98. This totally robotic right donor hepatectomy was performed without intraoperative issues or complications. The estimated blood loss was 100 mL. The patient's postoperative course was uneventful and she was discharged home in excellent condition on postoperative day 6. She participated in a 5-mile run at 2 weeks post liver donation. Eight weeks post liver donation, she returned to full-time obstetric nursing. Her father has recovered well and enjoys excellent liver graft function with no postoperative issues from his liver transplantation.

0-129

Simultaneous living donor liver transplantation with reconstruction of neo atrium and IVC for inflammatory myofibroblastic tumor of the liver

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Inflammatory myofibroblastic tumors (IMTs) of the liver are rare neoplasms. We report a rare case of a 3 year old girl with right liver lobe IMT with contiguous spread to IVC and right atrium presenting as Budd Chiari syndrome with liver failure. Pre operative biopsy from the lesion confirmed the diagnosis and the cells showed expression of ALK-1. Child was initially managed with crizotinib and other supportive treatment. Six months after presentation to our centre following clinical improvement she underwent en-block excision of the tumour (hepatectomy with right atrial extension) and underwent living donor liver transplantation (left lateral segment) with right atrial reconstruction and suprarenal IVC replacement with PTFE graft. Child was discharged 3 weeks following operation and 12 months follow up showed disease free response. To our best knowledge, no such case has ever been reported in literature. We have attached a video presentation of the surgical aspects in this case. The child was subjected to circulatory arrest and put on Heart-lung machine during reconstruction of right atrium done with pericardium, followed by reconstruction of IVC with PTFE and implantation of left lateral segment liver graft.

Concurrent Oral Abstract Session: Pediatrics

0-130

Quantitative immunophenotyping of liver biopsies predicts successful immunosuppression withdrawal (ISW) in pediatric liver transplant (LT) recipients

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We aimed to identify predictors of operational tolerance (OT) among clinical, histological, serological, immunohistochemical (IHC) and/or tissue transcriptional variables in highly selected pediatric LT recipients undergoing ISW.

Methods: 88 recipients (39M; 31 living grafts) at 12 centers met clinical, biochemical, and histological eligibility criteria for closely monitored ISW. OT, the primary endpoint, was defined as normal ALT, GGT and stable liver histology 1yr after last IS dose. Quantitative immunophenotyping of liver biopsies was done using multiplex IHC and Nearcyte software to examine expression of CD3/CD4/CD8 (T cells), CD34 (endothelial cells), CD45 (leukocytes), MHC class II expression [antigen-presenting cells (APCs)], and MAC387 (infiltrating macrophages). APC within 5 microns of a leukocyte, was defined as an APC:leukocyte pairing and quantified. Tissue gene expression using Affymetrix microarrays was analyzed. Uni- and multi-variable logistic regression with forward selection and ROC analysis with bootstrapped estimates of AUC and its confidence interval were used to identify variables that predicted OT.

Results: 33/88 (38%; 95%CI 27-49%) subjects were OT. ISW outcome was not predicted by clinical, biochemical, serological, or tissue transcriptional profile. Compared to non-OT (NOT), more OT subjects exhibited no portal or no peri-venular inflammation (FigA). Among quantitative IHC features, the number of APC:leukocyte pairings, infiltrating macrophages, and CD8+ T cells/mm^2 differed between OT and NOT subjects. The multi-variable model (FigB) showed that lobular APC:leukocyte pairings (OR 0.74; 95%CI 0.61-0.91) and infiltrating macrophages (OR 0.90; 95%CI 0.83-0.98) predicted OT with bootstrapped AUC=0.86 (95%CI 0.75-0.96)(FigC).

Conclusion: Despite limiting ISW to subjects with mild inflammation and/or fibrosis by screening biopsy, the absence of portal and peri-venular inflammation still correlated with OT. Quantitative assessment of APC:leukocyte pairings and infiltrating macrophages suggesting an allo-immune response and/or tissue injury was, however, more potent than standard histology at predicting OT.

Biopsy features associated with tolerance

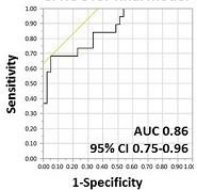
A: Comparison of tolerant and non-tolerant subjects for H&E and IHC features

H & E features		Tolerant	Non-Tolerant	P value
No inflammation (vs mild)	Portal	23 (70%)	25 (46%)	0.030
	Peri-venular	33 (100%)	48 (87%)	0.042
Multiplex IHC features (#/mm^2 of tissue)				
APC:leukocyte pairings	Portal	3.1 (2.20)	5.4 (3.85)	0.002
	Lobule	6.6 (2.69)	10.8 (4.54)	<0.001
Infiltrating macrophages		13.8 (7.74)	25.6 (16.8)	<0.001
CD8+ T cells		36.3 (29.6)	58.5 (53.0)	0.026

B: Final Multivariable Model to Predict Tolerance

Multiplex IHC features	Odds Ratio	95% CI	P value
APC:leukocyte pairings in the lobule	0.74	0.61-0.91	0.003
Infiltrating macrophages	0.90	0.83-0.98	0.013

C: ROC for final model



[FIGURE]

0-131

Next-gen sequencing reveals a role for MMP7 in the liver in biliary atresia

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Background: The disease phenotype in biliary atresia (BA) is caused by a fibro-inflammatory process. The first line of management is a Kasai Porto-enterostomy (KPE). Several factors have been postulated to affect the outcome of KPE and/or the subsequent progression of liver disease. However, no such biomarkers have been identified in the liver. We aimed to address this deficit by using Next-gen Sequencing (NGS) to identify candidate genes that can predict the prognosis of KPE.

Methods: Liver biopsies were obtained from 22 consecutive patients who underwent KPE and at the time of liver transplantation (LT) from 3 children in this group who developed End Stage Liver Disease

(ESLD). Control liver biopsies were obtained from 4 age matched subjects with idiopathic giant cell hepatitis, primary hyperoxaluria and propionic acidemia. Whole transcriptome mRNA sequencing was performed on all samples. The results were confirmed with quantitative real time PCR (q-RT-PCR). Outcome of KPE was defined as jaundice clearance, measured as serum direct bilirubin level < 2 mg/dL six months after KPE.
Results: Seven of 22 children cleared jaundice. There was a significant increase in Matrix Metalloproteinase 7 (MMP7) mRNA levels in the liver of children with BA compared to controls. Moreover, MMP7 expression was significantly increased in children who failed KPE compared to those who cleared jaundice. MMP7 gene expression levels were the highest at the time of LT compared to the time of diagnosis.
Conclusion: MMP7 expression in the liver is diagnostic of BA and increased expression indicates a poor prognosis for KPE. Increased MMP expression at the time of LT also implies a role for this gene in the relentless progression of fibrosis that leads to ESLD. Viable therapies that target this pathway may halt the progression of liver disease and maximize the success of KPE.

0-132

Silent allograft fibrosis in 10-year post-transplantation histology of pediatric liver transplantation: is it really silent?

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Background: This study is designed to analyze factors related to long-term allograft fibrosis in clinically stable pediatric liver transplantation patients.
Methods: Pediatric patients who underwent liver transplantation at Samsung Medical Center from January 1997 to January 2008 were reviewed. Ten-year protocol biopsies were reviewed by expert pathologist specialized in liver transplantation. The degree of inflammation and fibrosis were classified based on Banff criteria and METAVIR system, respectively. Analysis of risk factors related to allograft fibrosis was performed using multivariable logistic regression.
Results: Sixty-six clinically silent pediatric patients who underwent 10-year post-transplantation biopsy were included. Protocol biopsy revealed 9 cases (13.6%) with rejection activity index≥3 based on Banff classification and 31 cases (47.0%) with METAVIR fibrosis stage ≥F1. All the characteristics were similar except for previous experience of rejection when classified by Banff criteria (29.4% in normal, 60.9% in indeterminant, and 55.6% in mild rejection, P=0.039) and METAVIR fibrosis (34.3% in F0, 36.8% in F1, and 83.3% in F2, P=0.009) More than 3 events with aminotransferases elevated above 50 U/L was the only significant factor for METAVIR F1-F2. (OR=3.351, CI=1.160-9.643, P=0.026) Mean total bilirubin≥1.0 mg/dL during the entire period (OR=10.388, CI=1.414-76.322, P=0.021) and experience of rejection (OR=10.403, CI=1.788-60.531, P=0.009) were significant risk factors for METAVIR F2.
Conclusion: Even in clinically silent pediatric liver transplantation patients, long-term fibrosis occurs frequently and repeated elevation of aminotransferases were related to METAVIR F1-F2 while experience of rejection and elevated mean total bilirubin ≥1.0 mg/dL were related to METAVIR F2.

0-133

Liver allograft fibrosis after pediatric liver transplantation: risk factors and tools for early detection

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Introduction: Progressive allograft fibrosis(AF) after pediatric liver transplantation(pLT) has high prevalence in post-transplant liver biopsies and influences long-term outcomes. Our aim was to define the incidence and risk factors for AF after pLT.
Methods: A retrospective single-center analysis of clinical and histological data was performed, including all pLT with at least 5-years of follow-up and undergoing protocol liver biopsy at 6 months, 1-2-5 years. Fibrosis was reviewed using the METAVIR and Ishak systems, and the novel Liver Allograft Fibrosis score(LAFs), which specifies the portal/sinusoidal/centrilobular fibrosis.
Results: Out of 200 pLT performed between 2008-2018, 50(25%)LT [age:2.5(1-19)years, male 33(66%)]were included and 200 biopsies reviewed. Type of grafts comprised 14(28%) whole, 26(52%)

split, 6(12%)reduced, 4(8%)living-donor grafts. Tacrolimus-based immunosuppression regimen was used. After LT, 9(18%)biliary and 7(14%)vascular complications, 12(32%)acute rejections were observed; 34(68%)recipients had at least one episode of deranged liver function tests (LFTs). At 5-years, the 3 scoring systems showed similar incidence of fibrosis (n=41,82%) and fibrosis grading [Metavir:1.1±0.5; Ishak:1.3±0.8; LAFs:1.5±1.2;(p=0.345)]. No differences were found in fibrosis progression rate (progression: 62% vs. 58% vs. 70%; stable: 38% vs. 42% vs. 30%;p=n.s.) between the 3 scoring systems. In the LAFs, fibrosis involved the portal tract (82%), sinusoidal (14%) and centrolobular (12%)areas. Other histological findings included chronic hepatitis(n=13,26%), chronic rejection(n=1,2%) and steatosis(n=3,6%). Children with fibrosis progression had higher incidence of biliary complications(p=0.043) and prolonged ischemic times(p=0.038), thus 34% had normal LFTs. At Cox-analysis only biliary complications (HR:0.128,CI:0.017-0.972,p=0.037) were associated with fibrosis progression, which was found mainly in sinusoidal area.
Conclusion: Our series confirms that AF has high prevalence after pLT, however we found low fibrosis grading compared with other series. Fibrosis progression was associated with post-LT biliary complications and detected in sinusoidal area. The novel LAFs histological system, which defines the areas of fibrosis, is a useful tool to early detect the causes of AF.

O-134

Paediatric domino liver transplant from paediatric multi visceral transplant recipient

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Background: Domino liver transplantation, where a patient being transplanted himself donates his/her liver to another patient, has been done for many years. But it is very rare in paediatric population. Usually, livers come from donors with metabolic disorders. However, in this case the donor liver was retrieved from a patient with intestinal neuropathic dysmotility with normal liver appearance, histopathology and function.
Method: The recipient was a 3-year-old patient with cholestatic disease with unknown cause of cholangiopathy. He received a whole domino, caval replacement liver transplant from an 8-year-old patient with severe intestinal failure due to neuropathic dysmotility, who underwent multivisceral transplant (liver, stomach, duodenum, pancreas, small and large bowel) with macroscopically healthy liver and normal histopathology.
Results: In patient who received domino liver postoperative outcome was favourable, with no immediate complications following his transplant. The 17-days allograft liver biopsy showed no evidence of rejection. One month after the transplant, the patient underwent MRCP which showed biliary anastomotic stricture. ERCP with biliary stent insertion was unsuccessful therefore he will require biliary reconstruction in the immediate future.
Conclusion: Given the fact that there is a long-term shortage of liver donors, domino transplants are a safe and promising alternative and indications may further be expanded to the usage of livers from patients receiving multivisceral transplants where the recipient's liver is healthy.

O-135

Pediatric liver transplantation in mainland China

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Background: In 1963, Starzl et al's first attempt of liver transplantation (LT) in a child with biliary atresia opened up a new era of transplant surgery in human history. LT has been the best treatment option for pediatric end-stage liver diseases. In mainland China, the development of pediatric liver transplantation (PLT) started late, but it has been developing rapidly in recent years.
Methods: Patients younger than 18 years who underwent LT before Dec 2017 were investigated using data from China Liver Transplant Registry (CLTR; available at http://www.cltr.org/).
Results: The first successful PLT in mainland China was performed in 1996. However, in the next 10 years after that, PLT has not been carried out extensively in the whole country. In the early stage, recipients were mostly older children such as those with Wilson's diseases, and the graft type was simplex with only grafts from living donors. In recent years, transplant centers which carried out PLT have been extended from only several large centers to numerous medium-scale centers, and the government has vigorously promoted the policy of donation after cardiac death (DCD), which led to a remarkable increase of annual PLT caseloads in the past 5 years. Until 2017, a total of 2766 PLTs have been performed in mainland China, and annual PLT caseloads have reached 722 in 2017. Biliary atresia was the most common indication, and more than 75% of PLT recipients were younger than 3 years. The survival outcomes have been greatly improved with accumulation of technical experience.
Conclusions: Enhancement of multidisciplinary cooperations has greatly improved outcomes after PLT. Long term posttransplant follow-up and management are still challenging tasks.

0-136

Pediatric liver retransplantation: prognostic scoring tool

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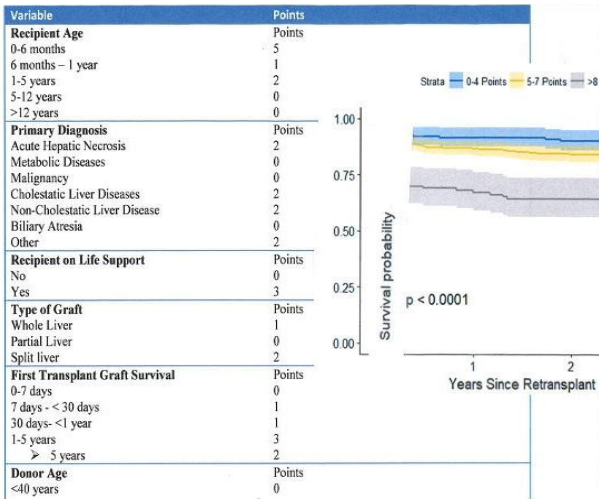
Introduction: Liver Re-transplantation is the only option for survival when a transplanted liver fails. Outcomes of retransplanted livers are inferior compared-to primary-transplants. In this study, we evaluate the outcomes of pediatric liver Re-transplantation and propose a prognostic-scoring-system.
Methods: Of the 8,188, children in SRTRdatabase who received liver-transplants (2002-2018), 731 were Re-transplants. Proportional-hazards-models using backward-variable selection were used to identify recipient, donor, and surgical-characteristics associated with survival. A prognostic-scoring system was constructed based on the fitted-model. Survival-curves based on risk groups of the prognostic-score were estimated using the Kaplan-Meier methods.
Results: Recipient age ($p < 0.001$), Primary Diagnosis ($p = 0.04$), Recipient on life-support at time of retransplant ($p < 0.001$) Survival time of the first graft ($p = 0.006$) Graft type ($p = 0.033$); and donor age > 40 ($p = 0.008$) predicted survival. Survival was significantly different ($p < 0.001$) for those at low risk (0-4 points), medium risk (5-7 points), and high risk (8+ points) (Figure 1). Survival was equivalent between low risk pediatric re-transplant recipients and pediatric primary liver transplant recipients ($p = 0.46$) but significantly worse for medium ($p < 0.001$) and high risk ($p < 0.001$) re-transplant recipients
Conclusion: With simple clinical characteristics, this scoring tool can modestly discriminate between those children at high risk and those children at low risk of poor outcomes after liver Re-transplantation. If validated by future studies, this scoring system could provide prognostic guidance to the family and patient.



Variable	Points
Recipient Age	Points
0-6 months	5
6 months – 1 year	1
1-5 years	2
5-12 years	0
>12 years	0
Primary Diagnosis	Points
Acute Hepatic Necrosis	2
Metabolic Diseases	0
Malignancy	0
Cholestatic Liver Diseases	2
Non-Cholestatic Liver Disease	2
Biliary Atresia	0
Other	2
Recipient on Life Support	Points
No	0
Yes	3
Type of Graft	Points
Whole Liver	1
Partial Liver	0
Split liver	2
First Transplant Graft Survival	Points
0-7 days	0
7 days - < 30 days	1
30 days- <1 year	1
1-5 years	3
➢ 5 years	2
Donor Age	Points
<40 years	0

[Figure 1]

0-137

Long-term neurodevelopmental outcomes in children with biliary atresia

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Background: Biliary atresia (BA) is a cholestatic liver disease in infants. Kasai porto-enterostomy (KPE) and liver transplantation (LTx) strongly improved long-term survival of BA patients. Little is known, however, about the long-term neurodevelopment of BA patients. We aimed to assess neurodevelopmental outcomes in school-aged BA patients.
Method: All Dutch school-aged children (6-12 years), diagnosed with BA, were invited to participate in this cross-sectional study. We used validated tests and questionnaires to assess motor skills, cognition, and behavior. Scores were compared to Dutch norms. Results are given in percentages or means±SD.
Results: We included 46 children (78% participation), with a median age of 11 years (range 6-13 years). Thirty-six children received LTx (78%). Twelve children (26%) received special education (*vs* 2.4% of the norm population; $p< 0.01$). Motor outcome was significantly lower compared to the norm population ($n=41$; $p< 0.01$), with 25% normal (*vs* 85%), 25% borderline (*vs* 10%) and 50% low scores (*vs* 5%). Total and performance IQ were significantly lower in BA patients compared to the norm population (91±18 and 88±18, respectively, *vs* norm 100±15; both $p< 0.01$), while verbal IQ was not (96±17; $p=0.09$). Children scored significantly lower on planning, visuomotor integration, attention and perceptual ability (Z-scores of respectively -0.42±0.97; -0.59±0.93; -0.64±1.03 and -0.40±1.13; all $p< 0.01$). Scores on memory and strategy formation were not significantly different from the norm population. Parents reported problems in behavior (23% *vs* 2%) and attention/hyperactivity (10%/18% *vs* 5%; both $p< 0.01$), not in executive functioning. There were no significant differences in scores between children who had undergone LTx and those who had not.
Conclusion: A higher fraction of school-aged children with BA have neurodevelopmental impairments compared to the norm population, especially regarding motor skills. Our data strongly warrant evaluation of neurodevelopmental intervention programs to assess whether long-term outcomes could be improved.

O-138

Study on the risk factors of portal vein stenosis after pediatric liver transplantation

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Objective: To analyze the incidence and possible risk factors of portal vein stenosis after pediatric liver transplantation.
Methods: Retrospective analysis of 396 cases of pediatric liver transplantation (age ≤14 years old) at the liver transplantation center of Beijing friendship hospital from June 2013 to December 2017. collecting relevant data, calculating the incidence, as well as the children with portal vein stenosis may be related to preoperative, intraoperative, and postoperative, a total of 23 factors for statistical analysis.
Results: The incidence of portal venous stenosis after pediatric liver transplantation was 6.6%, Weight (≤7 kg), of portal vein diameter of recipients (≤0.4 cm), GRWR (≥3.5%), the use of cold storage portal vein grafts, recipients of superior mesenteric vein and splenic vein anastomosis end rendezvous, preoperative portal vein reverse blood flow are risk factors of portal vein stenosis after pediatric liver transplantation, recipients of portal vein diameter (≤0.4 cm) and the use cold preservation grafts are independent risk factors of portal vein stenosis after pediatric liver transplantation.
Conclusion: The incidence of portal vein stenosis after pediatric liver transplantation agrees with the other reports. The child Combined with portal hypertension, Weight (≤7 kg), of portal vein diameter of recipients (≤0.4 cm), GRWR (≥3.5%), the use of cold storage portal vein grafts, recipients of superior mesenteric vein and splenic vein anastomosis end rendezvous, preoperative portal vein reverse blood flow are more likely to develop portal vein stenosis after liver transplantation.

Concurrent Oral Abstract Session: Viral Hepatitis / Alcoholic Liver Diseases / NASH / NAFLD

0-139

Favorable waitlist outcomes in patients with alcoholic liver disease in the MELD-Na era

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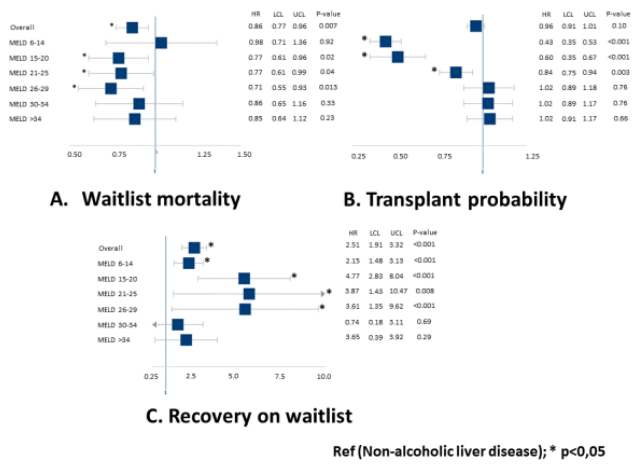
Purpose: Patients with Alcoholic liver disease (ALD) are required to be abstinent prior to listing. This may reduce disease progression while on waitlist and therefore alter waitlist outcomes compared to other disease etiologies. We aimed to evaluate discrepancy of waitlist outcomes between those with ALD and non-alcoholic liver disease (NALD).
Methods: Data on adults listed liver or liver-kidney transplant after introduction of MELD-Na score (Jan 2016-June 2018) obtained from OPTN/UNOS. Following selected as major liver disease etiologies: ALD, hepatitis C, non-alcoholic steatohepatitis, primary biliary cholangitis, and primary sclerosing cholangitis. Patients with overlapping diseases and those with exception scores excluded. Patients categorized into different listing MELD-Na score groups to identify variations in waitlist outcomes after adjusting for risk factors.
Results: Patients with ALD showed lowest waitlist mortality and highest recovery among disease groups, thereby ALD (n=6472) were compared to NALD patients (n=7283). ALD patients showed lower mortality (HR 0.82, p< 0.001), higher transplant probability (HR 1.12, p< 0.001), and higher recovery rate on waitlist (HR 2.23 P< 0.001). Overall waitlist mortality stratified by listing MELD-Na was lower in ALD patients in mid-score groups (score of 15-29) (Figure 1, p< 0.05), whereas no difference in lowest (6-14) and higher-score groups (30 or higher). Overall transplant probability similar in ALD and NALD patients in score groups of 26 or higher, whereas ALD had lower probability in lower score groups (< 26). ALD also showed higher chance of recovery in lower to mid score groups (6-29).
Conclusions: ALD cirrhosis patients have lower waitlist mortality and better recovery while on waitlist compared to patients with other etiologies. This was prominent in mid score groups. These results suggest that risk stratification and prioritization of liver allocation may need to be altered according to liver disease etiologies.



[Figure 1]

0-140

The evolution of living donor liver transplantation for alcoholic liver cirrhosis in a high volume center: the Eastern perspective

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Background: Alcoholic liver disease (ALD) has been a growing indication for living donor liver transplantation (LDLT) in Asia but certain medical, ethical and psycho-social issues question its appropriateness. Reports on long-term outcomes of LDLT for ALD are also scarce and so our aim was to report our center's experience for the past 15 years and how LDLT has evolved to be the treatment of choice for end-stage liver disease secondary to ALD in a high volume center.
Methodology: A total of 1,384 consecutive LDLT was performed from January 2003 to August 2016 at Kaohsiung Chang Gung Memorial Hospital, and 87 patients had a pre-operative diagnosis of alcoholic liver disease (ALD) with or without hepatocellular carcinoma (HCC). This group was systematically matched with non-ALD (NALD) patients in a ratio of 1:2 using equiprobability method. Overall patient survival was compared using Kaplan-Meier analysis, and incidences of post-transplant De novo malignancy and alcohol relapse were described.
Results: Patient demographics were comparable, as well as

preoperative and intra-operative data. Of the 87 patients in the ALD group, 26 (30%) had concomitant HCC. Median follow-up for this study was 50 months. Overall patient survival at 1, 3 and 5 years for ALD were 98%, 97% and 92% respectively, while the NALD group had similar survival rates (P=0.282). The rate for De novo malignancy was 6% while that for recidivism was 7% despite only 76% of the patients meeting the 6 months abstinence rule.
Conclusion: Results from our center show that LDLT for ALD has comparable short and long term outcomes when compared to NALD, and the close relationship between donor and recipient seems to positively affect alcohol relapse rate and patient compliance to medication.

O-141

Effects of preexisting-diabetes mellitus on post-transplant outcomes for patients with NASH: a 10-year UNOS experience

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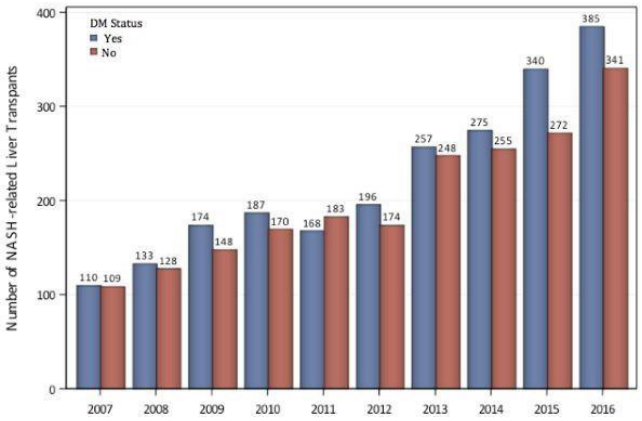
Background: Nonalcoholic steatohepatitis (NASH) related cirrhosis has become leading indication for liver transplantation (LT) in the United States due to the growing epidemic of obesity and diabetes mellitus (DM).We aimed to examine effects of preexisting DM on post-LT outcomes for patients with NASH.
Method: A retrospective analysis was performed among 4,253 adult patients from the United Network for Organ Sharing (UNOS) database who received deceased donor LT from 2007 to 2016 due to primary diagnosis of NASH. Recipients had preexisting diabetes mellitus prior to LT (n=2225) were compared to those who had not (n=2028).T-tests and Chi-square tests were used to compare the baseline characteristics between DM and non-DM patients. Cox regressions were used to model the effect of DM status on post-LT graft and patient survivals for a 10-year follow up period.
Results: The number of NASH patients with DM underwent LT has been increasing between 2007 and 2016 with a total of 2,225 (52.3%) transplanted (Figure 1). NASH patients with DM were older (59.8±7.3 vs 56.8±9.4, p< .0001), more likely to be Hispanic (283±12.7 vs 223±11.0) and Asian race (p< .0001). Portal vein thrombosis, dialysis, and longer waiting time on the waitlist were found significantly associated with worse graft survival (all p-values < .04), while older ages, Asian or Hispanic, having a MELD score > 35, portal vein thrombosis and dialysis were significant risk factors for lower patient survival rates (all p-values < .03). After adjusting for significant risk factors, NASH patients with DM experienced both decreased graft survival and patient survival after LT throughout the 10-year follow-up period.
Conclusion: Post-transplant survival is significantly impacted by preexisting DM. Glycemic control may be necessary to improve survival in NASH patients having DM undergoing LT.



[Figure 1: NASH-related liver transplants rates for NASH patients by DM status, 2007-2016]

O-142

Development of a model to predict survival in recipients of liver transplant (LT) for non-alcoholic steatohepatitis (NASH)

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Background: The aim of our study was to develop a model to predict survival in recipients of LT for NASH.
Method: LT recipients for NASH were identified from the Scientific Registry of Transplant Recipients (SRTR) database (n = 11326, from 1987-2017). We excluded patients with HCC or those less than 18 years of age. Only recipient-specific factors were analysed using univariate and multivariate Cox Proportional Hazard models.
Results: Survival post LT for patients with NASH at 7 days, 30 days, 1 year, 3 year and at 5 years were 98 %, 95 %, 86 %, 80 % and 74 % respectively. Table 1 shows the recipient factors associated with the patient survival. Age and Serum Creatinine are analysed as continuous variables. The model was internally validated and calibrated, giving Bootstrap-corrected errors of 0.0036, 0.0008, 0.0151, 0.0097 and 0.0048, for the survival probabilities for 7, 30 days,

1, 3 and 5 years respectively.
Conclusion: We have developed and validated a Cox model that is able to accurately predict patient survival post LT using recipient factors. Derivation of a practically useable risk calculator, along with validation in a local cohort at the University Health Network will further help in delineating risk assessment in an individual candidate for transplant.

Survival Predictors	p-value	Hazard Ratio (95% CI)
History of Diabetes	<0.001	1.17 (1.08, 1.27)
History of Angina	0.051	1.17 (1, 1.36)
Recipient Age (at transplant)	<0.001	1.02 (1.02, 1.02)
Portal vein thrombosis	0.034	1.12 (1.01, 1.24)
Mechanical ventilation at time of transplant	<0.001	1.37 (1.19, 1.57)
Non hospitalised recipients	<0.001	0.77 (0.71, 0.83)
Serum Creatinine before transplant	0.038	1.04 (1, 1.07)
TIPS procedure prior to transplant	0.028	1.13 (1.01, 1.26)

[Table-1 Independent Predictors of Patient survival]

O-143

Post-transplant hepatic steatosis in patients receiving liver transplantation for HBV-related diseases: a metabonomic-based strategy for risk factors analysis

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Background: High prevalence of post-transplant hepatic steatosis (PTHS) was reported in patients receiving LT for alcoholic/non-alcoholic fatty liver disease and cryptogenic cirrhosis. However, the incidence and risk factors of PTHS in patients with hepatitis B virus (HBV)-related liver diseases, a major indication for LT in China, remains unknown.
Methods: A total of 267 adult patients who underwent primary LT for HBV-related liver diseases between January 2015 and December 2017 were included. Liver-to-spleen density ratio (LSR) in computed tomography was calculated dynamically after LT. PTHS was diagnosed as a LSR < 1.0 and also partially verified by biopsy. An UPLC-MS global metabolite profile was performed to detect the metabolite-related features of PTHS.
Results: PTHS occurred in only 7.5% of all liver recipients at 3-month post-LT. However, the incidence dramatically increased to 23.4%, 47.9%, and 57.4%, at 6-, 12- and 24-month post-LT, respectively. Although no significant difference in overall survival was found, PTHS group showed higher incidence of post-transplant metabolic disorders (e.g., hyperlipidemia, overweight and sarcopenia) and tumor recurrence as compared to non-PTHS group. Recipient overweight and high tacrolimus concentration were independent clinical risk factors of PTHS. Using recipient peripheral blood, we identified 168 significantly differentially expressed metabolites (DEM) including Docosahexaenoic acid, Eicosenoic acid, Oleic acid, and Palmitoleic acid, which were significantly enriched in fatty acid biosynthesis. In predicting PTHS, 8 DEMs had area under ROC curves of > 0.9. Incorporating recipient's DEMs into the clinical model significantly increased the predictive accuracy. In contrast, the DEMs from donor graft samples did not improve the predictive ability of clinical model.
Conclusions: PTHS is a common and fast-progressive disease with adverse outcome after LT in HBV-related liver disorder patients. The metabolic status of recipient but not donor graft determines the development of PTHS.

O-144

Renal safety of entecavir and tenofovir with hepatitis B immunoglobulin in liver transplant patients

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Combination of potent nucleos(t)ide analougues (NAs) and hepatitis B immunoglobulin is recommended after liver transplantation for the prevention of hepatitis B virus (HBV) recurrence. Despite its proven efficacy, renal safety of NAs in liver transplant recipients has not been well defined. We aimed to assess the impact of entecavir and tenofovir on glomerular and tubular function. We analyzed 201 liver transplant patients treated with entecavir (n=122) or tenofovir (n=79) with hepatitis B immunoglobulin between 2012 and 2016. Serum creatinine, phosphorus, and uric acid were measured, and

estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. Proximal tubular dysfunction was defined as the combination of hypophosphatemia (< 2 mg/dL) and hypouricemia (< 2 mg/dL). Mean eGFR at start of NAs after liver transplant was 100.8 for entecavir, 102.7 mL/min/1.73 m² for tenofovir group (*P*=0.554). Mean eGFR at the last on-treatment visit was 80.0 for entecavir and 82.5 mL/min/1.73 m² for tenofovir group (*P*=0.491). During the 28 months of median follow-up, 30 patients experienced decrease of eGFR < 30 mL/min/1.73 m² (20 [16.4%] of entecavir and 10 [12.7%] of tenofovir group, *P*=0.468). Serum phosphorus and uric acid in both groups were statistically not significant at start of NAs. A total of 37 patients developed renal tubular dysfunction (11 [9.0%] of entecavir and 26 [32.9%] of tenofovir group, P< 0.001). Tenofovir (HR, 5.24; 95% CI, 2.25-12.19; *P*< 0.001), decrease of eGFR < 30 mL/min/1.73 m² (HR, 4.44; 95% CI, 1.67-11.85; *P*=0.003), and use of mTOR inhibitor (HR, 2.31; 95% CI, 1.04-5.11; *P*=0.04) were independent risk factors for proximal tubular dysfunction. The effect of tenofovir on glomerular function was comparable to that of entecavir in liver transplant patients. However, tenofovir increased the risk of proximal tubular dysfunction. Longitudinal studies are needed to assess the long-term outcomes.

O-145

Patients treated for HCV and listed for LT in a French multicenter study: what happens at 3 years

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Background: Combinations of DAA have shown excellent results to treat HCV-infection in cirrhotic patient but some issues remain unresolved regarding efficacy in patients awaiting liver transplantation (LT).
Method and aims: This is an observational, multicenter, and retrospective analysis from 18 LT centers in France, of patients treated for HCV and listed for LT. Complete clinical and biological response (CBR) to HCV treatment was defined by Child score A. The aim of this study was the evaluation of impact of HCV treatment, delisting and outcomes of patients listed for HCC or decompensated cirrhosis.
Results: 183 HCV-positive patients treated by DAA while awaiting LT between November 2013 and June 2015 were enrolled. SVR rate was 83%. The mean follow-up after treatment was 39.6 months (± 1.5). LT indication was HCC (106 (58%)) or decompensated cirrhosis (77 (42%)). Patients were mostly male (145, (79%)) median age of 59 years-old (± 2.2) and comorbidities: diabetes (49, (27%)), alcohol consumption (39, 21%), arterial hypertension (45, (25%)) and dyslipidemia (8, (4%)). At baseline for decompensated cirrhosis, mean MELD was 12 (6-32) and Child B9. Among these patients, 10 (16%), 22 (35%) and 31 (49%) had respectively a CBR complete, partial and no response. 40 patients (52%) were transplanted, 36 are alive. 37 patients (48%) were not transplanted: 6 are inactive and 26 were delisted (21 for improvement) and 4 developed HCC during the follow up. Among patients listed for HCC, 80 (75%) were transplanted, 73 are alive. Only 8 patients (7.5%) have been delisted for HCC progression. Predictive factors of delisting will be presented at the meeting.
Conclusion: HCV-treatment in patients awaiting LT allows delisting for improvement in 27% (21/77) of cases. After treatment only 7.5% (8/106) of HCC-patients were delisted for drop out. We did not collect any HCC recurrence post-LT.

O-146

Psychosocial characteristics of patients with severe alcoholic hepatitis presenting for early liver transplantation evaluation

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Background: Studies have shown favorable outcomes following early liver transplantation (LT) for severe alcoholic hepatitis (SAH), however optimal selection criteria are unclear. We aim to identify psychosocial characteristics between patients who were accepted or denied for listing.
Methods: Patients transferred to Johns Hopkins for consideration of early LT for SAH with < 6 months sobriety, from 1/1/2017 to 4/15/2018 were studied. Chi-square tests were used to compare patients who were accepted vs. denied.
Results: Fifty-four patients were transferred. Majority were in-state referrals (65%) and from non-academic centers (78%). Among LT candidates, 27 received no medical therapy for SAH prior to transfer, 26 received steroids and 1 received steroids+pentoxifylline. Once transferred, 7 (13%) were not presented to the selection committee due to clinical improvement, 24 (44%) were denied, and 23 (43%) were listed. Reasons for denial included; active substance abuse other than alcohol (63%), medical instability (38%), inadequate social support (29%), medical improvement (25%), uncontrolled psychiatric disease (17%). Among listed, 16 (70%) were transplanted; 2 died while awaiting LT, 2 were sent to hospice, 2 still awaiting LT and 1 was removed due to recidivism. Listed vs. denied were similar in MELD-Na at time of referral (34 vs 32, p=0.932), duration of abstinence prior to transfer (24% vs 46% had < 4 weeks abstinence, p=0.114), history of other substance abuse (52% vs 54%, p=0.839), family history of alcoholism (23% vs 39%, p=0.492), psychiatric comorbidity (48% vs 52%, p=0.652), stable relationship status including marriage (55% vs 42%, p=0.382), and legal history (46% vs 59%, p=0.608). Employment immediately before presentation (41% vs 17%, p=0.082) trended towards significance.
Conclusions: There was no difference in psychosocial parameters or MELD-Na cutoff between listed vs. non-listed patients, though employment trended towards significance. Further studies are required to identify which psychosocial factors may predict candidacy for listing.

O-147

Mitochondrial depolarization, mitophagy and mitochondrial damage-associated molecular pattern molecule (mtDAMP) release, a novel pathway linking mitochondrial adaptations for aldehyde metabolism to alcoholic liver disease pathogenesis

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Liver cirrhosis from alcoholic liver disease (ALD) is a leading indication for transplantation. We explored the role of mitochondrial alterations in ALD pathogenesis with mice gavaged with ethanol acutely or fed ethanol-containing diet chronically. We showed that acetaldehyde generation during ethanol metabolism leads to widespread hepatic mitochondrial depolarization (mtDepo), which accounts for a near doubling of hepatic respiration. In parallel, voltage dependent anion channels (VDAC) in the mitochondrial outer membrane close. Together, stimulated respiration by producing NAD^+ more rapidly and VDAC closure by blocking uptake of normal respiratory substrates promote selective and more rapid oxidation of ethanol to acetaldehyde in the cytosol and then to nontoxic acetate in mitochondria, since membrane-permeant acetaldehyde does not require VDAC to enter mitochondria. VDAC closure also inhibits fatty acid oxidation, leading to steatosis. mtDepo stimulates Type-2 mitophagy, and mitophagy occurred primarily in hepatocytes with depolarized mitochondria in ethanol-treated GFP-LC3 transgenic mice. Acute ethanol also increased mitophagosome processing into lysosomes. After chronic ethanol, mtDepo in association with steatosis also occurred. PINK1, a mitophagy mediator that is ordinarily imported and proteolytically degraded in mitochondria in a membrane potential-dependent fashion, accumulated due to mtDepo. Moreover, LC3-II increased more than LC3-I, indicating disrupted mitophagy/lysosomal processing. Serum mitochondrial DNA, a mtDAMP molecule, and hepatic NLRP3 inflammasome activation also increased, alterations promoting inflammation/fibrosis, as evidence by increased leukocyte infiltration and increased α-smooth muscular actin and collagen-I expression. Taken together, these data suggest that mtDepo associated with adaptive alcohol metabolism increases mitophagic burden. However, after chronic ethanol, mitophagic processing of depolarized mitochondria becomes impaired, leading to extracellular release of mtDAMPs like mitochondrial DNA to promote profibrotic inflammatory responses and enhanced liver injury. We propose that persistence of mtDepo and VDAC closure becomes a tipping point that links adaptive mitochondrial aldehyde metabolism to maladaptive changes initiating onset and progression of ALD (NIAAA).

Plenary Abstract Session II

0-148

Hepatic stellate cells and liver derived endothelial cells improve scaffold-free 3D-bioprinted liver model

Chen A.M.[1], Zhang W.[1], Koehler C.J.[1], Saglam K.[1], Isidan A.[1], Walsh J.R.[1], Naqvi R.A.[1], Gramelspacher E.[1], Smith L.J.[2], Li P.[1], Ekser B.[1]

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Background: Hepatic stellate cells (HSC) comprise about 2-8% of liver cells and are vital to hepatocellular function. Scaffold-free 3D-bioprinting (SF3DBP) allows creation of realistic tissue models without the use of synthetic biomaterials. We hypothesize that co-culturing primary hepatocytes with HSCs and liver derived endothelial cells (LEC) will improve hepatocyte function and accuracy of the SF3DBP liver model.
Methods: We used primary pig hepatocytes and immortalized pig HSCs and LECs to generate spheroids with hepatocytes alone, HSCs alone, or a combination of hepatocytes, HSCs, and LECs. Optimized combination spheroids were printed using a Regenova 3D-bioprinter. Un-printed spheroids were incubated over two weeks for functionality assays (albumin secretion, mRNA transcription, urea clearance) and immunostaining performed for cell composition confirmation.
Results: Hepatocyte:HSC co-cultures (H/H, 2.5:1 ratio), Hepatocyte:HSC:LEC co-cultures (H/H/L 2.5:0.5:0.5 ratio) and HSC-only cells formed round spheroids within 48 hours, whereas the hepatocyte-only condition did not. Functional assays showed superiority in maintenance of albumin secretion and increased urea clearance over 14 days in H/H and H/H/L spheroids compared to hepatocyte culture alone. Real-Time PCR and immunostaining further confirmed that HSCs sustained the expression of hepatocyte marker gene expression (Alb and CK-18). After 4 days of spheroid incubation, optimized H/H combination spheroids were bioprinted. This SF3DBP construct fused 3 days post-bioprinting and could be removed from temporary microneedle support by 6 days post-bioprinting.
Conclusions: SF3DBP of hepatocyte:HSC spheroids in a 2.5:1 ratio demonstrates the potential utility bioprinting has for pharmacological, immunological, and hepatotoxicity testing. Further spheroid optimization using different cell ratios including HSCs, hepatocytes, liver sinusoidal endothelial cells, and cholangiocytes will allow printing of more physiologically accurate liver models.

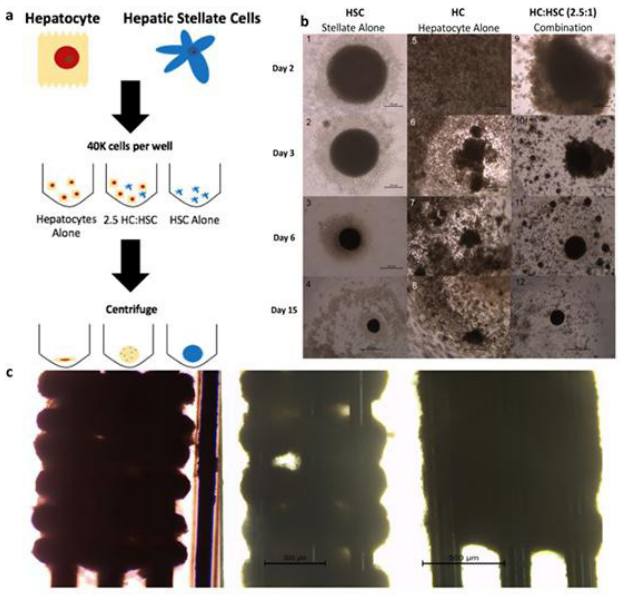

Figure 1. Scaffold-free 3D-bioprinting of pig liver construct. **1a:** Process of forming spheroids using (i) hepatocytes (HC) alone, (ii) hepatic stellate cells (HSC) alone, or (iii) HC:HSC (2.5:1) in low affinity U-bottom plates. **1b:** Formation of spheroids over time using HC, HSC, or their combination with 40,000 cells. Spheroids by HSC alone were uniformly round and smooth. HC alone spheroids failed to coalesce into characterizable spheroids. **1c:** 3D-bioprinted liver construct using combination spheroids on a temporary microneedle support from day 0 to day 3. By day 3, spheroids fused together forming their own extracellular matrix.

[Figure 1]

0-149

Pregnancy outcomes after living liver donation - a multi-institutional survey

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Background: Women who have previously donated a kidney are at increased risk of pre-eclampsia. Nearly half of living liver donors are women of child-bearing age, yet fetal and maternal outcomes after living liver donation are largely unknown.
Methods: We conducted a retrospective cohort study of female

living liver donors whose donations occurred between age 18-49 from five academic transplant centers. Participants were identified and contacted via email with a survey inquiring about pre- and post-donation pregnancies. Comparisons were made between pre-donation pregnancies and post-donation pregnancies.
Results: 378 donors were contacted and 145 donors responded(38% response rate). Of the 42 women who attempted pregnancy after donation, 9 (21.4%) reported infertility and their median age at donation was 26.2[25.7, 28.1]. There were a total of 289 pregnancies; 131/190 (68.9%) of pre-donation pregnancies and 31/99 (70.7%) of the post-donation pregnancies resulted in live births(p=0.76). Compared to pre-donation pregnancies, post-donation pregnancies were significantly more likely to have a higher median maternal age-at-pregnancy (31.0[28.3, 35.5] vs. 26.9[22.9, 31.1], p< 0.01), transaminitis during pregnancy (3.0% vs 0.0%, p=0.04), or deliver via Cesarean section (35.7% vs. 21.2%, p=0.03). Comparing pre-donation and post-donation pregnancies, there was no significant difference in pregnancy-induced hypertension(6.8% vs. 11.2%), pre-eclampsia(9.1% vs. 5.7%), gestational diabetes(3.7% vs. 6.1%), or hemolysis, elevated LFTs, and low platelets (HELLP) syndrome(0.8% vs. 1.4%).
Conclusions: About 20% of women after liver donation report infertility. This needs to be further explored to understand contributing factors, including age at attempting pregnancy. Aside from increased occurrences of transaminitis and Cesarean sections, there was no significant difference in pregnancy outcomes between pregnancies before and after living liver donation but the power is limited by the small number of cases. Future research should continue monitoring this important patient-centered outcome across a larger cohort of donors.

Table 1. Outcomes and complications of pregnancies conceived before and after living liver donation.

	Pre-Donation Pregnancies (N=190)	Post-Donation Pregnancies (N=99)	P-value
Age at Pregnancy, median (IQR)	26.9 (22.9, 31.1)	31.0 (28.3, 35.5)	<0.001
Live-Births, n (%)	131 (68.9%)	70 (70.7%)	0.76
Outcome of Non-Live Births‡, n (%)			
Miscarriage	31 (53%)	25 (86%)	0.01
Abortion	27 (46%)	4 (14%)	
Other	1 (2%)	0 (0%)	
Complications of Pregnancy			
Intrauterine Growth Retardation, n (%)	4 (2.1%)	0 (0.0%)	0.30
Premature Birth*, n (%)	8 (6.1%)	4 (5.7%)	>0.90
Birth Defect, n (%)	3 (1.6%)	0 (0.0%)	0.55
Gestational Hypertension, n (%)	13 (6.8%)	11 (11.2%)	0.20
Pre-eclampsia*, n (%)	12 (9.2%)	4 (5.7%)	0.59
Gestational Diabetes, n (%)	7 (3.7%)	6 (6.1%)	0.35
Abnormal LFTs, n (%)	0 (0.0%)	3 (3.0%)	0.04
HELLP Syndrome*, n (%)	1 (0.8%)	1 (1.4%)	>0.90
Cesarean Section*, n (%)	28 (21.4%)	25 (35.7%)	0.03

‡Analyzed out of non-live birth only (n=88)
*Analyzed out of live births only (n= 201), missing the 88 non-live births

[Table 1. Outcomes and complications of pregnancies conceived before and after living liver donation.]

0-150

Novel approaches in optimising steatotic livers for transplantation

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Introduction: Steatotic livers derive poor outcomes when transplanted and many are discarded. With the global obesity epidemic, an increasing proportion of steatotic livers in the donor pool is inevitable and salvaging them for transplantation is of great importance. The aim of this study is to explore the effects of normothermic machine perfusion (NMP) and de-fatting adjuncts on steatotic livers, providing an insight into how these grafts could be enhanced to enable their successful transplantation.
Methods: Eighteen discarded steatotic human livers were perfused on a NMP circuit for 48h. Livers were divided into 3 groups: NMP alone (group 1, n=6), NMP + lipid apheresis filtration (group 2, n=6) and NMP + lipid apheresis filtration + de-fatting agents (group 3, n=6). To explore any intervention-based effects on liver structure and function, regular perfusate sampling was performed for biochemical analysis of lipid metabolites and biopsies were obtained for lipid quantification. Fatty acids synthesised via *de novo* lipogenesis (DNL) were quantified in tissue via gas chromatography and mass spectrometry.
Results: Donor demographics and pre-perfusion steatosis levels were similar between groups (p=0.84). Lipid apheresis filtration was effective in significantly reducing circulating perfusate triglycerides in groups 2 (2899µmol/L) and 3 (2691µmol/L) compared to group 1 (6071µmol/L) (p=0.03). The addition of de-fatting agents in group 3, significantly increased fatty acid β-oxidation compared to groups 1 (p=0.04) and 2 (p=0.009). A 45% decrease in tissue triglyceride was observed in group 3, compared to a 16% increase in group 1 (p=0.04). The reduction of liver fat observed in group 3 was associated with a decrease in DNL fatty acid synthesis in these livers (7.14µg/mg) compared to groups 1 (18.80µg/mg) (p=0.18) and 2 (26.76µg/mg) (p=0.03).
Conclusion: We demonstrate the ability to manipulate hepatic lipid-metabolism and structure with *ex-situ* interventions. This may result in the successful transplantation of these high-risk grafts.

O-151

Liver viability parameters during normothermic ex-situ liver perfusion in a porcine model of liver transplantation with marginal grafts

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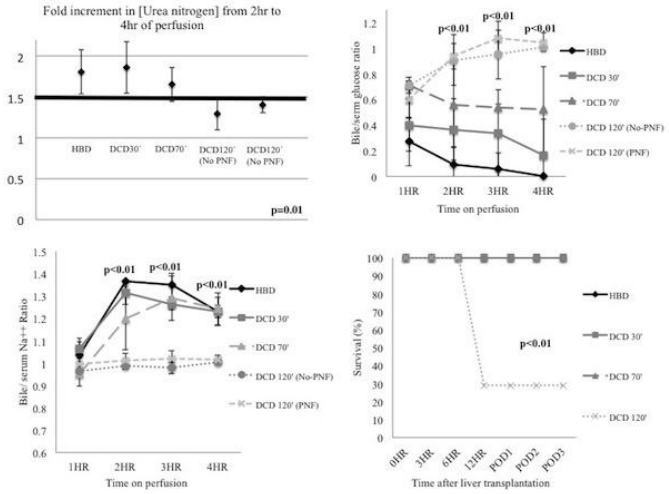

[Predictor parameters of liver viability during NEsLP and animal survival after transplantation]

Background: Normothermic ex-situ liver perfusion (NEsLP) has opened the opportunity of real-time graft assessment prior to transplantation. As of today, there are no established parameters to determine liver viability during NEsLP.
Methods: In this study, we investigated prior assessed parameters and new variables to evaluate liver viability during NEsLP in a transplantation model. We investigated groups with mild [heart beating donors (HBD)], moderate [donation after circulatory death donors with 30 (DCD30´) and 70mins (DCD70´) of warm ischemia time (WIT)] and severe ischemic injury [donation after circulatory death donors with 120mins (DCD120´) of WIT]. Parameters of hepatocellular and cholangiocyte function and injury were assessed during NEsLP and after transplantation.
Results: The HBD, DCD30´ and DCD70´-groups had 100% survival. In contrast, 70% developed primary non-function (PNF) and died in the DCD120´-group. Hepatocellular function during NEsLP showed low lactate (≤1.1mmol/L) in all the groups except the DCD120´-group (>2mmol/L) at 4hr of perfusion (p=0.04). The fold-urea increase was significantly lower in the DCD120´-group (≤1.4) compared to the other groups (≥1.65) (p=0.01). As for cholangiocyte function, bile/perfusate glucose-ratio was significantly lower (< 0.6) in all the groups but the DCD120´-group (≥0.9) after 3hr of perfusion (< 0.01). Bile/perfusate Na+ ratio was significantly higher (≥1.2) after 3hr of perfusion in all the groups except for the DCD120´-group (≤1) (p< 0.01). Three hours after transplantation, the DCD120´-group had a significantly higher INR (>5) compared to the rest of the groups (≤1.9) (p=0.02).
Conclusion: This study demonstrates that parameters of hepatocellular and cholangiocyte function during NEsLP correlate with the degree of ischemic injury and post-transplant function.

O-152

Role of gender and age of liver donor in de novo neoplasms occurrence after liver transplantation

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Background: De novo neoplasms(DNN) are one of the major causes of late-mortality after liver transplantation(LT). Current post-transplant surveillance strategies are largely based on general population guidelines but should be customized in the light of LT-recipients specific risk factors. The influence of donor-recipient sex and age matching on long-term survival after LT is controversial, and data on the possible effect on DNN-risk are lacking.
Material and methods: All patients transplanted among 9 Italian centres between 1985-2014 were enrolled (excluded if: ≤18years-old, follow-up shorter than 90days or cancer diagnosis within 90days after LT). Competing risk approach was applied to estimate 5-year cumulative cancer incidence by time since LT. Hazard-ratios for DNN and 95%CIs were obtained using Cox-models adjusted for recipient gender, age and calendar-year at transplant, and liver disease etiology.
Results: A total of 1927 patients were enrolled. Cumulative DNN-incidence at 5years after LT was 5.4%, with no differences when stratified by donor gender (p=0,45). Considering both donor gender and age, among male-patients receiving a graft from a male-donor, the 5-year cumulative incidence was higher when donor was ≥60years-old (p=0.03). At multivariate-analysis, donor age or gender were not associated with DNN-risk. However, considering their joint effect, at elevated donor age (≥60 years), the DNN-risk increased for recipients from male-donors (HR=2.00, 95%CI:1.02-2.50). When the associations were examined in strata of recipient-gender, a similar pattern emerged among male only (HR=2.26; 95%CI:1.05-4.87 for those receiving an organ from male-donors ≥60years vs< 35years).
Conclusions: In our cohort the risk of DNN occurrence was increased in male-patients receiving a liver graft from older male-donors, irrespectively from recipient age at transplant. Gender and age differences in liver-donors could influence DNN risk due to both donors and recipients biologic and lifestyle factors. These results, if confirmed in other studies, could be useful to further guide post-LT DNN screening-personalization and risk stratification.

O-153

Allograft histology and biopsychosocial health 10 years after liver transplantation in children

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Background: Paediatric liver transplant (pLT) recipients have excellent long-term survival. However, there are concerns regarding the state of allograft health and psychosocial wellbeing of these children. A single-centre experience, evaluating liver allograft histology and biopsychosocial outcomes of pLT recipients.
Methods: A prospective study from 2000-2013 of pLT recipients with stable biochemical and radiological graft status. All participants consented for liver biopsy. Data analysed included incidence of peri-operative complications and allograft histology. Psychosocial data included prevalence of mental health disorders, education/ work status and substance misuse.
Results: Eighty-four patients with stable graft function, at a minimum of 10 years post-transplant were included. The median age at transplantation was 1.3 years (0.2-12.0), with median follow-up of 22.7 years (16.0-31.0). The most common indications for pLT: extrahepatic biliary atresia (n=43), progressive familial intrahepatic cholestasis (7) and hepatoblastoma (4). The rates of acute and chronic rejection were 33% (28) and 21% (18) respectively.
Thrombosis was observed in the hepatic artery in 6 patients and portal vein in 10 patients. Bile leakage occurred in 1 patient and bile duct stricture occurred in 7 patients. Normal liver biochemistry was reported in 73%. The majority of graft biopsies (66.7%) demonstrated Stage 1- mild fibrosis.
Mental health disorders were common, occurring in 26%, most of whom suffered from depression or anxiety. Learning difficulties were common, occurring in 13%; 12% were unable to work or continue studies due to health concerns. 10% of patients smoked tobacco, similar to the UK national average. Excessive alcohol consumption was low compared to UK adults of the same age (4% vs. 16%).
Conclusions: Despite near normal liver biochemistry, pLT recipients develop low-grade graft inflammation and fibrosis. This study also gives new insight into the psychosocial impact of pLT- patients are vulnerable to mental health disorders, learning difficulties, and delays in education and employment.

O-154

Non-contrast-enhanced hepatic magnetic resonance angiography with inflow sensitive inversion recovery technique: Clinical application of vascular evaluation in pre-liver transplantation recipients with impaired renal function

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Background: Image evaluation of the vascular architecture is essential before living donor liver transplant (LDLT). Recent literature has reported inflow sensitive inversion recovery (IFIR) magnetic resonance angiography (MRA) to be a reproducible and noninvasive tool to assess the hepatic vasculature with adequate to good image quality. The purpose of this study is to clinically apply IFIR MRA in liver-transplant recipients and compare the vascular anatomy to intraoperative findings.
Method: From March 2013 to August 2018, thirty-one patients (with renal function impairment) received IFIR MRA as pre-transplant vascular architecture evaluation and underwent subsequent living donor liver transplantation. The image findings were assessed for subjective image quality and were compared to intra-operative findings.
Results: The pre-transplantation vascular anatomy of hepatic arteries, portal vein and IVC identified by IFIR MRA was well correlated with intraoperative findings in whole recipients. A case of portal vein occlusion and 10 cases of portosystemic collaterals were well identified. For subjective assessment of image quality, the overall agreement of scores of IFIR was substantial (kappa values ranged from 0.624 to 0.748). Successful ratings for proper hepatic arteries, portal veins and IVC were 100%, 96.8% and 93.5%. Readable image ratings with imaging quality score ≥ 1 for left hepatic arteries, right hepatic arteries, and gastroepiploic arteries (GEA) were 83.9%, 96.7% and 22.6%. Recipients with higher pre-transplant Model For End-Stage Liver Disease (MELD) score (MELD > 23) have significant lower image quality score in proper hepatic artery and IVC than recipients with lower MELD score.
Conclusion: Vascular architecture evaluated by IFIR MRA is well correlated with intraoperative findings. Despite limited role in GEA and patients with high MELD score, the image is still satisfactory for pre-liver transplant vascular evaluation. In pre-liver transplant recipients with impaired renal function, IFIR MRA is a feasible and reproducible image modality for vascular evaluation

O-155

Rapl protects from non-alcohol steatohepatitis in mice through regulating PPAR-α/PGC-1α network

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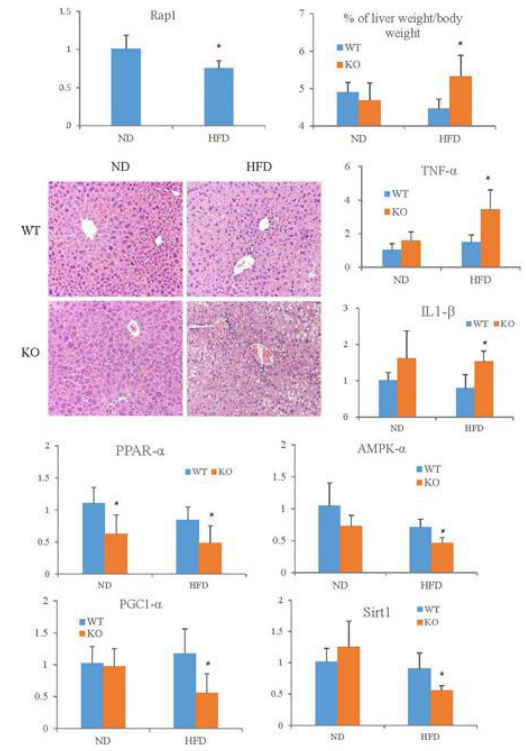
Objectives: Liver inflammation and lipid metabolism are crucial in the pathogenesis of non-alcoholic steatohepatitis (NASH). The mammalian telomere-binding protein Rap1 found to have additional nontelomeric function regulating gene expression. We recently showed that the knockout of Raplattenuated liver graft injury through regulating inflammatory response in normal/fatty liver. In this project, we aim to investigate the role and mechanism of Rap1 in NASH.
Methods: Animal model of NASH was induced by high fat diet for 12 weeks in Rap1 knockout mice and wild type controls. Mouse steatohepatitis, histological damage, liver function, infiltrations of neutrophils and macrophages, and gene expressions were compared between Rap1 knockout and wild type group.
Results: The expression of Rap1 was markedly decreased in both murine model and human subjects with NASH. The knockout of Rap1 promoted diet-induced steatohepatitis, associated with increased expressions of pro-inflammatory cytokines (TNF-a, IL-1b, CXCL10 and MCP-1) and high levels of ALT and AST. The knockout of Rap1 also increased the levels of glucose, cholesterol and triglycerides. We further revealed that decreased expressions of PPAR-α and PGC-1α were also found in Ra1 knockout group. Rap1 can bind to the intragenic F3 region in PPAR-α and PGC-1α genes in the liver. Furthermore, the expression of PPAR-α target genes (such as cpt1 and cpt2) and AMPK/SIRT-1 were also decreased in Rap1-knockout livers
Conclusions: These findings reveal that Rap1 may play a pivotal role in the pathogenesis of experimental steatohepatitis through regulating PPAR-α/PGC-1α network. Rap1 maybe a potential treatment choice for NASH patients.

Figure



[Figure]

O-156

Strategic release of exosomal microRNAs in hepatocellular carcinoma for generation of an immunosuppressive tumor microenvironment

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Background: A recurrence of hepatocellular carcinoma (HCC) after living donor liver transplantation (LDLT) is one of major concerns reflecting the higher mortality of HCC. One of potential mechanisms for posttransplant HCC recurrence is the existence of cellular and non-cellular factors responsible for HCC development and recurrence in the peripheral blood. Recently, tumor-derived microvesicles are highlighted for diagnostic and therapeutic targets. As one of the tumor-derived microvesicles, exosomes are cell-derived small vesicles (40-100 nm diameter), which carry proteins, lipids, mRNAs and non-coding RNAs such as microRNAs. In our previous study, we have successfully identified HCC-relative microRNAs including miR-92b and miR-4669 in experimental and clinical HCC model/patients. This study aimed to explore the impact of circulating exosomal miR-92b and miR-4669 on HCC development and recurrence.
Methods: HCC-relative microRNAs were transfected to Hep3B cells and primary natural killer (NK) cells, and its impact on tumor cell activity and cytotoxicity was evaluated, respectively. Non-HCC patients and HCC patients with/without posttransplant HCC recurrence were enrolled for clinical verification.
Results: Overexpression of miR-4669 enhanced migration ability and epithelial to mesenchymal transition of Hep3B cells. In addition, Hep3B cells overexpressing miR-4669 acquired drug resistance with active secretion of glyceraldehyde-3-phosphate dehydrogenase (GAPDH) for induction of M2 macrophage polarization. On the other hand, Hep3B cells overexpressing miR-92b released exosomal miR-92b, which affected NK cell activity in the tumor microenvironment. Clinically, circulating exosomal miR-92b and miR-4669 may be potential biomarkers for early prediction of posttransplant HCC recurrence.
Conclusions: In summary, we demonstrated the impact of HCC-derived exosomal miR-92b and miR-4669 on the generation of an immunosuppressive tumor microenvironment, resulting in the development and recurrence of HCC after LDLT. The value of exosomal miR-92b and miR-4669 before/after LDLT may predict the risk of posttransplant HCC recurrence.

O-157

A randomized controlled clinical trial of Thymoglobulin® and extended delay of calcineurin inhibitor therapy for renal protection after liver transplantation: A multicenter study

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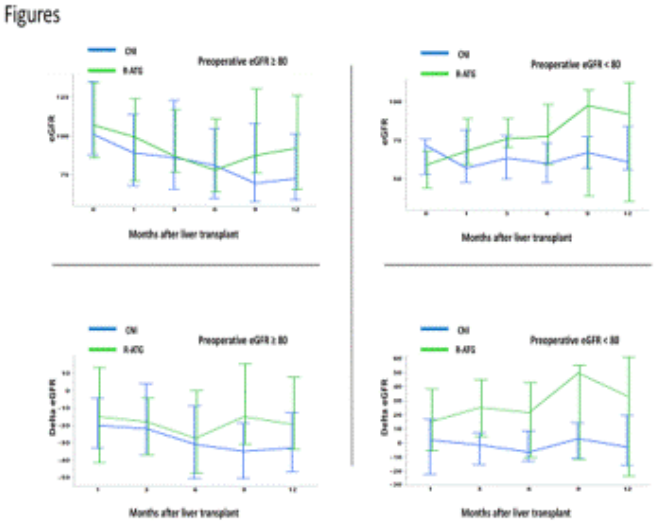
Background: Thymoglobulin® (r-ATG) has been used as induction therapy in liver transplantation (LT). No prospective, randomized, controlled, trial (RCT) has been performed to evaluate effect of r-ATG induction and delayed initiation of CNI on long-term renal function after LT.

Patients and method: 110 patients were randomized to r-ATG induction with delayed initiation of CNI for 10 days after LT, and standard CNI group, at 4 transplant programs. The eGFR and delta GFR were measured at 1, 3, 6, 9, and 12-month milestones for analysis.

Results: The median age, MELD score, baseline creatinine, baseline eGFR, and gender were similar between the two groups (all P>0.05). The median baseline, post-1, -3, -6, -9 and -12 month eGFR in CNI vs r-ATG groups were 88.0 vs. 91.6 (0.18), 82.0 vs. 93.5 (P=0.045), 75.0 vs. 86.0 (P=0.046), 74.0 vs. 79.0 (P=0.15), 69.5 vs. 97.0 (P=0.01), and 73.0 vs.90.0 (P=0.08). The median delta eGFR at 12 months after transplant was better in r-ATG group although it did not reach statistically significant (-21 vs -12, P=0.23). The time-weighted average of CNI levels were similar between two groups (CNI group; 7.2ng/mL r-ATG group 7.5ng/mL P=0.60). The chronological changes of median and interquartile ranges of eGFR and delta eGFR according to pre-transplant GFR (≥ or < 80) were shown in Figure 1. The protective influence of r-ATG was more pronounced in patients with lower initial GFR at LT.

Conclusions: Early initiation of CNI has shown to affect long-term renal function after LT. Induction with r-ATG and delayed initiation of CNI seems to be protective of long-term renal function in LT. This effect is seen at every milestone of follow up but more pronounced in patients with initial degree of renal dysfunction, especially in high-MELD recipients

Figures



[Figure 1]

Vanguard Moderated Poster Discussion

P-001

Complex anatomy precluding right lobe live donor hepatectomy: is there any?

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Introduction: Stringent donor selection ensures donor safety and good recipient outcomes in right lobe living donor liver transplantation (RLLDLT). A high rejection rate is inevitable, this further reduces donor pool.
Methods: We use a detailed 4-Phase donor evaluation protocol including blood investigations/CT liver attenuation index [Phase1], CT volumetry/MRCP [Phase2], systemic evaluation [Phase3], and multidisciplinary team clearance [Phase4].MR fat estimation, and liver biopsy are performed as indicated.Chief donor rejection criteria include expected GRWR < 0.65, future donor liver remnant (FLR) < 30%, macrovesicular steatosis >20%.
Results: For 1709 LDLT's (Jan 2011-Dec 2017),2640 prospective RL donors were evaluated,of these 931 (35%) were rejected;most common reasons being steatosis (57%), low GRWR (11%), and low FLR (20%).Complex bilio-vascular anatomy was present in 236/2640 (9%). Most of these (222/236, 94%) were accepted, and underwent right donor hepatectomy, 14 were rejected (6%,1.4% of all rejected donors,0.5% of all screened donors). Accepted donors had ≥3 right hepatic arteries (RHA) (overlapping supply)[6], Type C (Nakamura Classification) portal vein (PV) alone[27] or with 2 RHA's[14], ≥ 2 right inferior hepatic veins (RIHV) requiring reconstruction[54],or ≥3 right hepatic ducts (RHD's)[120].None of the 222 accepted developed ≥Grade III Clavien complications. Two recipients (0.9%) developed hepatic artery thrombosis,there was no PVT or RIHV thrombosis. Recipient biliary complication rate was 10% (vs.13.5% in our overall series, p=0.14).Complex bilio-vascular anatomy which precluded safe donation[n=14] included:
(A) vascular anomalies:
(i) arterial-intraparenchymal origin of principal segment 8 artery (A8) from A4(1), intraparenchymal A4 from A8(1), and 4 RHA's [all end arteries](1);
(ii) PV-Type E PV(2), segment 8 PV crossover from LPV(1);
(iii) hepatic vein-atretic RHV with 6 RIHV´s draining RL(1), MHV ostial narrowing(1),
(B)-biliary anomalies:
(i) left sided gall bladder(4),
(ii) >3 anticipated RL bile ducts {single LHD,adequate GRWR left lobe preferred}(2).
Conclusion: Most RL donors with complex bilio-vascular anatomy can undergo safe RL donor hepatectomy with good recipient outcomes at experienced LDLT centers.

P-002

Improvement in risk category for liver transplant candidacy in patients with portopulmonary hypertension treated with macitentan: a post-hoc analysis from the PORTICO study

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Background: Portopulmonary hypertension (PoPH) is pulmonary arterial hypertension (PAH) associated with portal hypertension. More than 80% of PoPH patients have cirrhosis and may require liver transplantation (LTx); however, PAH can increase risk of perioperative mortality and severe PAH is a LTx contraindication. PORTICO (NCT02382016) explored efficacy and safety of macitentan, an endothelin receptor antagonist approved for PAH, in patients with PoPH. This *post-hoc* analysis investigated whether changes in hemodynamics with macitentan improve risk category for LTx candidacy.
Method: PORTICO was a multicenter, double-blind, placebo-controlled, prospective, Phase IV study. Eighty-five patients aged ≥18 years with pulmonary vascular resistance ≥320 dyn.sec.cm^{-5} were randomized 1:1 to macitentan 10 mg (N=43) or placebo (N=42) for 12 weeks. Hemodynamic characteristics were measured by right heart catheterization at screening and Week 12. In these *post-hoc* analyses, patients were categorized at baseline and Week 12 by mean pulmonary artery pressure (mPAP) and published risk category thresholds for LTx perioperative mortality (low [< 35 mmHg]; intermediate [≥35 and < 45 mmHg]; high [≥45 mmHg]). Odds ratio for improvement in risk category from baseline to Week 12 with macitentan vs placebo was calculated using exact logistic regression with factors for treatment and baseline risk category.
Results: Baseline mean (SD) mPAP was 46.4 (7.9) mmHg and 43.8 (8.5) mmHg in patients randomized to macitentan and placebo. After 12 weeks, 18 (41.9%) macitentan-treated and 6 (14.3%) placebo-treated patients had improvement in risk category (odds ratio for improvement 3.73 [95%CI: 1.18, 13.40]; p=0.0224). Risk category worsened in 1 (2.3%) macitentan-treated and 7 (16.6%) placebo-treated patients (**Table**). There were no deaths during the double-blind period.
Conclusion: Treatment with macitentan in patients with PoPH can lead to improved hemodynamic parameters. These improvements may increase patient eligibility for LTx and support waitlist priority upgrades.

	Baseline risk category	Week 12 risk category n (%)			
		Low risk	Intermediate risk	High risk	Missing
Macitentan (N=43)	Low risk (n=2)	1 (2.3)	1 (2.3)	0	0
	Intermediate risk (n=16)	5 (11.6)	8 (18.6)	0	3 (7.0)
	High risk (n=25)	1 (2.3)	12 (27.9)	11 (25.6)	1 (2.3)
Placebo (N=42)	Low risk (n=4)	2 (4.8)	2 (4.8)	0	0
	Intermediate risk (n=21)	3 (7.1)	13 (31.0)	5 (11.9)	0
	High risk (n=17)	0	3 (7.1)	13 (31.0)	1 (2.4)

Blue: improved from baseline; red: worsened from baseline

[Table]

P-003

Scaffold-free 3D-bioprinting of human extrahepatic bile duct

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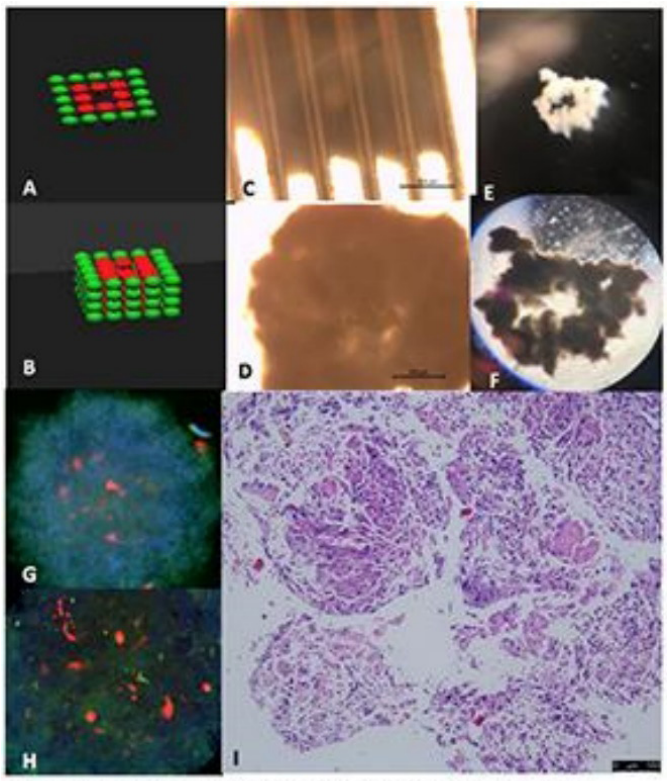
Background: Biliary complications are common in living and deceased donor liver transplantation (LT). Presence of multiple orifices in biliary anastomosis and ischemia, especially in DCD livers, are the leading causes of biliary complications and graft loss. A 3D-bioprinted bile duct may help overcome biliary complications in LT. Human extrahepatic bile ducts are formed by smooth muscle cells, connective tissues, vascular capillaries and luminal cholangiocytes. We 3D-bioprinted scaffold-free tubular bile duct using a combination of human cholangiocytes (CHO), bile duct fibroblasts (FIBRO), and liver endothelial cells (LEC).
Method: Human CHO were obtained commercially. Human FIBRO and LEC were isolated using donor extrahepatic bile ducts and livers. Different cell numbers/ratios were tested and optimized for spheroid formation using a low-binding 96-well plate at 40,000 cells/well. Culture conditions of CHO were also optimized. H&E and immunofluoresence staining were done.
Results: Ratio of CHO-LEC (1:1) and FIBRO-LEC (3:1) were found to be optimal. Two-layer (inner and outer) tubular tissue was designed using 3D-bioprinter's software. While the inner layer was comprised of CHO-LEC spheroids, the outer layer was comprised of FIBRO-LEC spheroids. A total of 96 spheroids were used and each consisted 4x10^{4}cells. The outer layer was composed of 4 levels at 16 spheroids per level and the inner layer was composed of 4 levels at 8 spheroids per level. Immunofluoresence staining using anti-CK7 and anti-CK19 antibodies confirmed cholangiocytes. Anti-CD31 antibody was used for endothelial cells and anti-desmin antibody was used for fibroblasts.
Conclusions: To best of our knowledge, this is the first study building a scaffold-free extrahepatic human bile duct model. Although further improvement is needed to provide manageable tensile-strength, scaffold-free human bile duct model has the potential to be used for repairing injured bile ducts in LT.



Legend: Computer design of two-layer tubular construct, view from above (A), 3D-view from side (B). Bioprinted bile duct on microneedles on day 7, showing well-fused and formed construct (C). Free-standing 3D-bioprinted bile duct on day 7, after removal from the temporary microneedle (D). Naked-eye picture of 3D-bioprinted bile duct (E). Same 3D-construct under the microscope (F). Spheroid with CHO:LEC (1:1) ratio, red=antiCK7, green= anti-CD31 (G). Spheroid with FIBRO:CHO:LEC (2:1:1) ratio, red=anti-CK7, green= anti-desmin, blue= dapi (H). H&E staining show mostly viable cells (I).

[Figure 1]

P-004

Piggyback versus caval replacement, do the kidneys pay the price? Analysis of a large single center cohort

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Background: Surgical technique has shifted from caval replacement (CR) to piggyback (PB) implantation for Liver Transplantation (LT). A 2018 European survey found 50% centers preferentially using PB, 40.5% CR. Acute Kidney Injury (AKI) is associated with increased lengths of stay, subsequent chronic kidney disease, mortality and increased health care cost. It remains controversial if either technique is associated with more postoperative AKI; a recent, and largest existing cohort of 378 LTs showed equivalence. This study evaluates the effect of surgical technique on postoperative AKI in a large single center cohort of 488.
Methods: All deceased donor LTs from our prospective transplant anesthesia outcomes database (TOAD) were reviewed, 06/2012 to 12/2017, excluding those requiring pre-operative RRT. AKI was defined as 'Kidney Disease Improving Global Outcomes' AKI stage ≥2 (2-fold increase in serum creatinine or requiring RRT). Multivariable logistic regression was used to assess if surgical technique is an independent predictor of postoperative AKI.
Results: We included 488 patients, PB was used in 377 (77.2%) cases. There was no difference in baseline MELD components. After adjusting for known risk factors for AKI (baseline creatinine, bilirubin and INR, recipient age and gender, cold ischemia time, DCD or DBD donor, diagnosis and year of transplantation). The PB technique was independently associated with decreased incidence of AKI (odds ratio 0.58, 95% confidence interval 0.36 - 0.94, p = 0.028) when compared to CR.

	Caval Replacement N=111 (23%)	Piggyback N=377 (77%)	P Value
Age (years)	59 [53, 65]	61 [56, 65]	0.116
MELD	15 [10, 20]	13 [9, 29]	0.741
Baseline Creatinine mg/dL	0.89 [0.77, 1.17]	0.93 [0.75, 1.29]	0.599
AKI (≥ Stage 2)	61 (55.0%)	158 (41.9%)	0.020

[Comparison of Caval Replacement and Piggyback Liver Transplants. Data are n (%) or median [interquartile range]. AKI, acute kidney injury.]

Conclusions: In our cohort, PB technique was associated with reduced post-operative AKI stage 2 and above.

P-005

New assessment method: Indocyanine green fluorescence imaging during normothermic ex vivo liver perfusion for DCD graft

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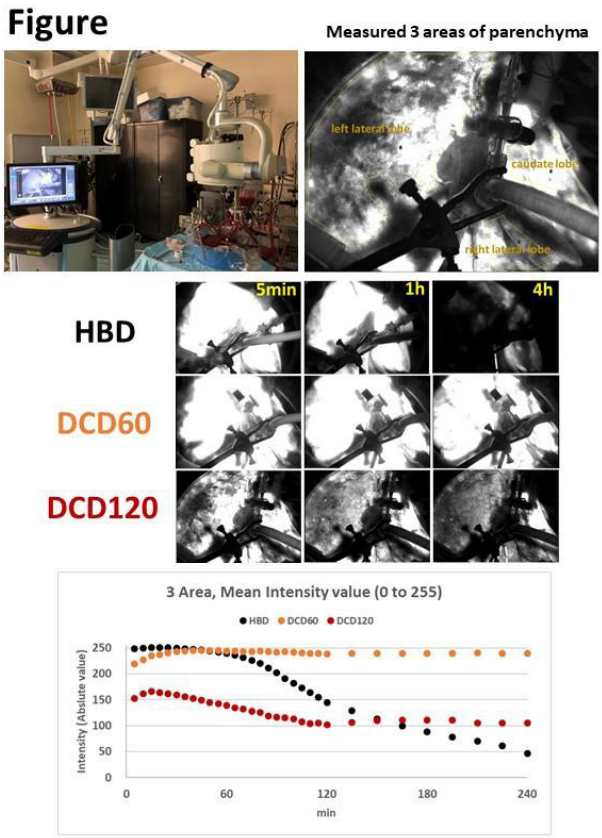
Background: Normothermic Ex Vivo Liver Perfusion (NEVLP) is a novel preservation method for marginal grafts, such as Donation after Cardio-Circulatory Death (DCD). However, there is no accurate parameter reflecting graft injury and function during NEVLP. Indocyanine Green (ICG) is a substance that is cleared by hepatocytes and excreted into the bile. Near-infrared fluorescence imaging with ICG is an emerging modality for image-guided surgery. We evaluated arterial ischemia and metabolic activity of DCD grafts during NEVLP by ICG fluorescence imaging.
Methods: Male Yorkshire pigs were allocated into 3 groups; Heart beating donor (HBD), DCD 60 minutes and DCD 120 minutes, each n = 1. Following induction of warm ischemia with heparinization, procurement and 2-hour cold storage, the livers were assessed with NEVLP. Liver fluorescence was recorded for 4 hours after ICG injection via artery with clamping portal vein for 1 minute. Regional fluorescence data was drawn from SPY Elite® System (Stryker) and analyzed by Image J (National Institutes of Health). The rates of low intensity areas (< 40% of maximum intensity) were defined as the arterial ischemic area.
Results: In the arterial phase, a low intensity rate was higher with longer warm ischemia times; HBD 1.1%, DCD 60minutes 18.9%, and DCD 120minutes 37.5%. HBD liver showed homogeneous fluorescence and quick excretion of ICG from parenchyma. In the DCD 60minutes group, the liver demonstrated low intensity areas in peripheral parenchyma and the high intensity had remained for 4 hours. The DCD 120minutes liver had worse perfusion without central area perfusion and the intensity remained high without clearance.
Conclusions: Our preliminary results suggest that ICG imaging during NEVLP reflects the severity of ischemic injury and graft function.



[Fluorescence imaging and Mean intensity values]

P-006

Experience with Meso-Rex bypass after segmental liver transplant for the treatment of symptomatic portal vein thrombosis

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Background: Portal vein thrombosis (PVT) after pediatric liver transplantation (LT) can produce symptomatic portal hypertension and the need for re-transplantation. The incidence of PVT is higher in patients with pre-existing portal vein hypoplasia. The Meso-Rex bypass (MRB) was originally described for the treatment of PVT after whole LT. Here we present our experience with MRB for the treatment of PVT after segmental LT.
Methods: All patients who were evaluated for MRB after LT in a single pediatric transplantation and hepatobiliary referral center (1998-2018) were identified (n=12). 2 patients had undergone a whole LT and were excluded. 3 patients were not MRB candidates based on their preoperative evaluation.
Results: All 7 patients included were transplanted as infants for biliary atresia with a segment 2-3 graft either from a living donor (n=5) or deceased donor (split liver, n=2). Median age at PVT diagnosis was 1.2 years (range 0.9-4.9). Median age at MRB was 2.2 years (range 1.3-10.7). No patent intrahepatic portal vein could be identified intraoperatively in 2 patients. These underwent a distal splenorenal shunt. The remaining 5 patients benefited from a MRB (internal jugular vein as conduit in 3 patients; deceased donor iliac vein graft for the other 2 patients). At the completion of surgery, MRB was patent in 4/5 patients. Early patency rate (< 30 days) was 60% (3/5). Of those, the 2 with a deceased donor graft suffered from late thrombosis from chronic rejection. Shunt revision was attempted in both, but successful in only 1 (converted to autologous conduit). Overall, 2/5 patients (both with autologous conduit) have a patent MRB at last follow up (1.5-20 years).
Conclusion: MRB after segmental LT is technically challenging, but can successfully treat PVT. Autologous conduits should be favoured, as deceased donor conduits have a high rate of chronic rejection despite immunosuppression.

P-007

What matters is quality not quantity - bile production in liver grafts on normothermic machine perfusion

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Background: Extended criteria liver grafts are increasingly being used to meet the demand-supply mismatch. They are at increased risk of non-function and biliary issues. One way to assess the functional status is normothermic ex-situ liver perfusion (NESLiP). There are already set parameters to assess hepatocellular compartment but to confidently assess Cholangiocyte function is still a challenge. In this study we looked at the biochemical composition of bile in livers on NESLiP and if bile production per se has any predictive value.
Methods: Livers with high donor risk index (DRI) were placed on NESLiP after a variable period of static cold storage and perfused with normothermic blood-based perfusate. The volume of bile

produced was measured and analysed using point of care blood gas analyser (Roche Cobas b 221).
Results: 56 livers (DBD 17; DCD 39) underwent NESLiP for either clinical or research use. 30 (53.6%) livers were transplanted with favourable parameters on machine and 4 (13.3%) patients developed clinical evidence of cholangiopathy on follow-up.
Bile production was more than 10 ml in 26 (46.4%) livers with mean bile volume of 35 ml over a mean perfusion time of 367 minutes. Out of these, 17 were transplanted and all 4 cholangiopathies were reported in this group. In 30 (53.6%) livers where bile production was less than 10 ml, 13 (43.3%) were transplanted with no episodes of primary non-function or cholangiopathy. Three livers didn´t produce any bile out of which one was transplanted without any complication.
Median bile pH, glucose and perfusate-bile glucose gradient in transplanted livers were 7.72, 1.7 mmol/L and 8.65 mmol/L respectively.
Conclusions: Bile production may be a misleading parameter for assessment of cholangiocyte compartment on ex-situ machine perfusion. Bile biochemistry may be more useful to assess bile duct viability. A large cohort follow-up may enable identification of predictive parameters.

P-008

The intention-to-treat effect of bridging therapies in the setting of Milan-in patients waiting for liver transplantation

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Background: In patients with hepatocellular cancer (HCC) meeting the Milan Criteria (MC), the value of loco-regional therapies (LRT) in the context of liver transplantation (LT) is still debated. The conflicting data reported are due to initial selection biases among treated and untreated patients. With the intent to overcome these shortcomings, an inverse probability of treatment weighting (IPTW) analysis was done in a large patient cohort. After using a competing-risk analysis, the primary end-point of the study aimed at identifying the risk factors of HCC-specific LT failure, defined as pre-LT tumor-related drop-out or post-LT recurrence.
Methods: An initial population of 1,083 MC-IN cases (NO-LRT=182; LRT=901) was balanced using eight variables available at first referral: age, male gender, MELD, HCV and HBV status, the diameter of the largest lesion, number of nodules, and alpha-fetoprotein (AFP) level. After the IPTW, a pseudo-population of 2,019 patients listed for LT was analysed, and two homogeneous groups of no-treated (n=1,077) and LRT-treated (n=942) patients were compared. The study was registered at http://www.ClinicalTrials.gov (ID: NCT03723304).
Results: Post-LRT progressive tumour disease at last radiological evaluation was the most important independent risk factor for HCC-related failure (sub-hazard ratio=5.6; p< 0.001). Other independent risk factors were the largest tumour diameter, AFP, MELD, patient age, male gender and waiting-list time. One LRT was protective compared with no treatment (SHR=0.5; p< 0.001); this effect remained present when 2-3 treatments were performed (SHR=0.7; p=0.02), however being lost if four or more treatments were applied (SHR=0.8; p=0.3).
Conclusions: In Milan-IN patients, up to three locoregional therapies are beneficial for an intention-to-treat LT success, with a 35-50% reduction of failure risk compared to non-treated patients. This benefit is lost if ≥4 LRT are applied. Initial tumour aggressiveness and poor response to LRT are correlated with a higher risk of HCC-specific LT failure.

P-009

Predictive factors for 28-day mortality in acute-on-chronic liver failure patients admitted to the intensive care unit - a case for liver transplant?

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Background: Acute-on-chronic liver failure (ACLF) is an entity comprising an acute deterioration of liver function in cirrhotic patients, associated with organ failure(s) and high short-term mortality. We aimed to identify predictive factors for short-term mortality in patients admitted with ACLF that may benefit most from liver transplantation.
Methods: Retrospective analysis of patients admitted in ACLF to a tertiary intensive care unit between 2013 and 2017 was performed. The EASL-CLIF Acute-on-Chronic Liver Failure in Cirrhosis (CANONIC) criteria were used to define ACLF grade (grades 1-3) and the CLIF-SOFA score for organ failure(s). Multivariable analysis using 28-day mortality as an end-point was performed, including severity-of-disease scores and clinical parameters.

Results: Seventy-seven patients were admitted in ACLF over the study period. The commonest aetiology of liver disease was alcohol related 52/77(68%) and the commonest precipitant of ACLF was variceal haemorrhage 83/77(49%). Twenty-six out of seventy-seven patients (34%) were considered as potential candidates for liver transplantation, of which 10/26(38%) died before being listed. Overall 28-day mortality was 42/77(55%) [ACLF grade-1:3/42(7%); ACLF grade-2:10/42(24%); and, ACLF grade-3:29/42(69%);p=0.002]. Diverse factors were associated with early-mortality at the univariate analysis during admission and after 48-72 hours, however on multivariable analysis only MELD≥26 [odds ratio(OR)=11.559; 95% confidence interval(CI):2.820-47.382;p=0.001], ACLF grade-3 (OR=3.287; 95%CI:1.047-10.325;p=0.042) at admission and requirement for renal replacement therapy (OR=5.348; 95%CI:1.385-20.645;p=0.015) were independently associated with 28-day mortality.
Conclusion: Patients admitted with ACLF to intensive care have a high mortality rate. Defined early thresholds at admission can identify patients at the highest risk that may benefit most from liver transplantation.

P-010

Renoportal anastomosis in liver transplantation: results from a propensity score-based outcome analysis

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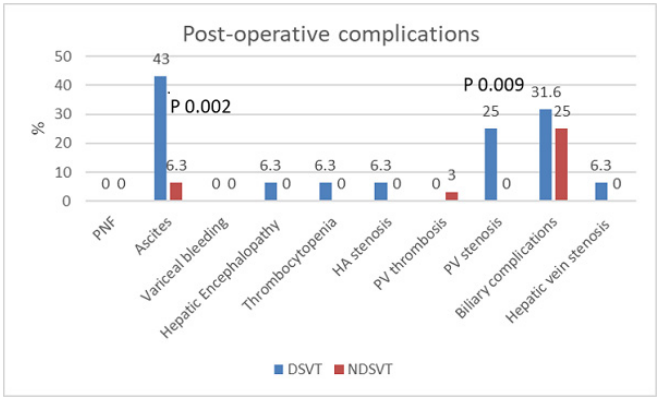
Background: Diffuse splanchnic venous thrombosis (DSVT) remains a serious challenge for the liver transplant (LT) surgeon, despite ongoing advances in surgical techniques. Reno-portal anastomosis (RPA) has previously been reported as a valid option for the management of patients with DSVT during LT.
Methods: A propensity score (PS) model was used to compare patients with DSVT to a cohort of patients without DSVT. The following variables were considered as covariates: age, sex, year of LT, Model for End-Stage Liver Disease score, donor risk index, renal function pre-LT, and liver weight. A 1:2 matching model with replacement was utilized. The analysis was performed over 5 years of follow-up.
Results: 1250 patients underwent LT between January 2005 and December 2017. 16 patients had DSVT that required RPA (using a venous jump graft) at the time of LT; all were noted to have concurrent spleno-renal shunt (SRS). The 16 patients with DSVT were compared to 32 matched patients without thrombosis (NDSVT group). Post-operative complications are summarized in Figure 1. All cases of post-operative ascites resolved within 3 months of LT. The eGFR decreased by 23% in the DSVT group and by 21.5% in the NDSVT group at 5 years (p 0.3). 5- years patient and graft survival were similar for patients with DSVT and NDVST (93.7% vs 96.8%, p=0.9).
Conclusions: Our report is the first to demonstrate similar long-term renal function in patients undergoing RPA for DSVT when compared to patients undergoing conventional LT. We suggest that RPA be considered in patients with DSVT with and without SRS as a method by which to negate alternative approaches to DSVT, such as cavoportal hemitransposition or multivisceral transplant.



[Figure 1. Post-operative complications]

P-011

Flow measurements in adult deceased donor liver transplantation - luxury or necessity

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Introduction: Portal vein (PV) and hepatic artery (HA) flow measurements with inflow modifications are useful in living donor liver transplants to decrease the incidence of post-transplant vascular thromboses and graft failures. We hypothesized that flow measurements in deceased donor liver transplants would lead to a similar finding.
Methods: We retrospectively compared our rates of post-transplant vascular thromboses and outcomes between recipients with (FL+) and without (FL-) post-reperfusion flow measurements. We performed vascular inflow modification as indicated by post-reperfusion flow meter measurements, similar to our current practice in living donor liver transplantation.
Results: Between 2011 and 2018, we performed 433 adult deceased donor liver transplants. Patient and transplant characteristics are attached.

	FL+	FL-	p value
Average Age (years)	58.9	56.4	0.019
Proportion Male (%)	69.0	69.1	0.984
Pre-transplant MELD	26.3	27.2	0.351
Body Mass Index	29.6	29.7	0.910
Proportion Malignant Indications (%)	23.0	37.6	0.011
Pre-transplant Functional Status (%)	52.3	51.6	0.636
Pre-transplant Employment (%)	24.1	26.0	0.721
Waitlist Time (days)	171.6	227.5	0.0495
Deceased Donor Average Age (years)	46.1	46.4	0.904
Cold Ischemia Time (hours)	5.98	6.38	0.080

[Patient and Transplant Characteristics]

Overall average PV flow pre-modification was 1483 mls/min (278-3550). Overall average HA flow pre-modification was 207 mls/min (40-800). In the two patients requiring HA flow modification, average pre-modification flow was 47.5 mls/min which increased to 115 mls/min post-modification. There was a notable corresponding decrease in PV flows (pre-modification 2925 mls/min to post-modification 1950 mls/min). In the five patients requiring PV flow modification, average pre-modification flow was 648 mls/min which increased to 1174 mls/min post-modification. There was an expected marginal decrease in HA flows (pre-modification 182 mls/min to post-modification 165 mls/min).

The incidence of pre-transplant portal vein thrombosis was significantly different (FL+ 21.8% versus FL- 10.7%, p=0.0057); majority of these were treated with eversion thrombectomy. Post-operative PV thrombosis was 0% versus 0.58% (FL+ versus FL-, p=0.478). HA thrombosis was 0% in FL+ versus 4.3% in FL- (p=0.0418). Our rate of early graft failure was not significantly altered (FL+ 5.8% versus FL- 10.8%, p=0.2353).

Conclusion: Intraoperative flow measurements performed post liver reperfusion should be considered in all cases of liver transplantation to increase intraoperative detection of potentially correctable vascular or flow-related complications.

P-012

Risk factors for antibody-mediated rejection after adult ABO-incompatible living-donor liver transplantation in the era of rituximab desensitization: a single center experience

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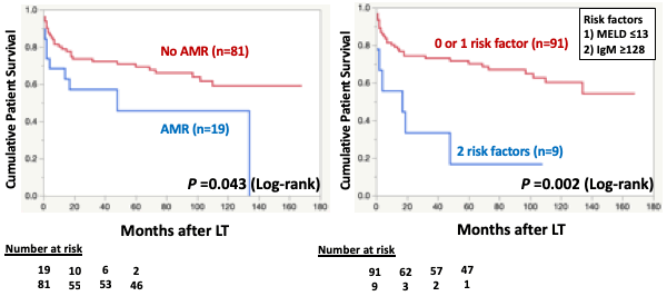
Background: Blood-type incompatible living-donor liver transplantation (ABOi-LDLT) is a necessary alternative in countries where brain-dead donors are insufficiently obtained. Pre-transplant desensitization with rituximab has dramatically changed the outcome of ABOi-LDLT, however, risk factors for antibody-mediated rejection (AMR) after rituximab desensitization remain unclear.

Methods: Of our 577 cases of adult LDLT (≥18 years, 2004-2018), 129 (22.4%) were ABOi-LDLTs with rituximab pretreatment. Various clinical factors, including recipient/donor age and gender, liver etiologies, MELD scores, anti-ABO IgG/IgM-titers, CD19-/20-positive B-lymphocytes, doses/timings of rituximab, blood loss, warm/cold-ischemic time, and with/without splenectomy, were investigated. AMR was comprehensively diagnosed based on clinical, serological, and histological findings. Unusual cases, such as re-LTx (8 cases), acute liver failure (7), inadequate doses/timings of rituximab (12), and deviated immunosuppression protocols (2) were excluded.

Results: A total of 100 ABOi-LDLT recipients (male/female: 45/55; median age: 54 years [IQR: 42-59]) were enrolled. Primary diseases included HCV/HBV (27/17), PBC (17), and alcoholic cirrhosis (9). Median MELD score was 18 (14-21). Pre-treatment anti-ABO IgG/M-titers were 32 (8-256)/64 (32-128), respectively. Rituximab, 500mg/body (33) or 300mg/body (67), was administered 14 days or earlier before transplants (81) or shorter (19), resulting in significant reduction of CD19+/20+ counts to 0.1% (0.0-0.3%)/0.0% (0.0-0.0%), respectively. Splenectomy was performed in 47. Of these, AMR occurred in 19, showing significantly-worse recipient survival than in those without (*P*=0.043, Fig.1-A).In univariate analysis, risk factors for AMR were MELD score ≤13 (*P*=0.004) and anti-ABO IgM-titer ≥128 (*P*=0.049). Multivariate analysis also identified MELD ≤13 (OR 5.74 [1.83-18.0], *P*=0.003) and IgM-titer ≥128 (OR 3.14 [1.04-9.53], *P* =0.043) as independent risk factors for AMR, combination of those was associated with significantly worse recipient survival (*P*=0.002, Fig.1-B).

Conclusion: Lower MELD score(≤13) and higher anti-ABO IgM-titer before desensitization (≥128) were independent risk factors for AMR in adult ABOi-LDLT.

Figure 1-A ***Figure 1-B***



[Recipient survival after ABOi-LDLT]

Poster Round I, Session 1, 2, 3: Anesthesia/Critical Care Medicine

P-013

TOAD: Transplant Outcomes in Anesthesia Database. A proof of concept granular perioperative data warehouse

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Background: Outcomes research in health care continues to be plagued by fragmented data collection, which is even more pronounced in organ transplantation with additional stakeholders such as organ procurement organizations (OPOs). While registries have been developed to address this data fragmentation, they are not granular enough for detailed perioperative studies. Our goal was to create the first published, comprehensive, sustainable data warehouse for liver transplant (LT) recipients.
Methods: Preoperative, intraoperative, and postoperative data for LT patients at UCSF from June 2012 onwards is sourced from the Epic electronic medical record via Clarity, TITUS (transplant surgery electronic medical record), and the UCSF Liver QI database (manually-entered database maintained by anesthesiologists). Data is stored on a secure PostgreSQL server within the UCSF IT network.
Results: The database contains ~15 million perioperative data points for over 1000 LTs at UCSF. Important predictive and outcome metrics, such as graft function, acute kidney injury, intraoperative hypotension, etc, are dynamically calculated with new case additions. The database is modular (for addition of new types of data or metrics) and updates seamlessly with new cases. Data can be accessed securely and loaded directly into mainstream third-party platforms, such as R or Python, for analysis.
Conclusions: We were able to curate and deploy the Transplant Outcomes in Anesthesia Database (TOAD), a multidisciplinary data warehouse with organ donor and perioperative recipient data for LTs. We anticipate TOAD will reduce redundant data mining from multiple sources over different projects, data collection turnaround time for serial projects, and overall barriers to data access. TOAD simplifies much of the cumbersome process of data acquisition for perioperative research in order to maximize data quality, and promotes and facilitates academic inquiry. TOAD, as a proof of concept, encourages the creation of similar databases, and, if standardized, could lead to collaboration between programs.

P-014

Early postoperative myocardial injury is associated with perioperative cardiovascular complications after liver transplantation

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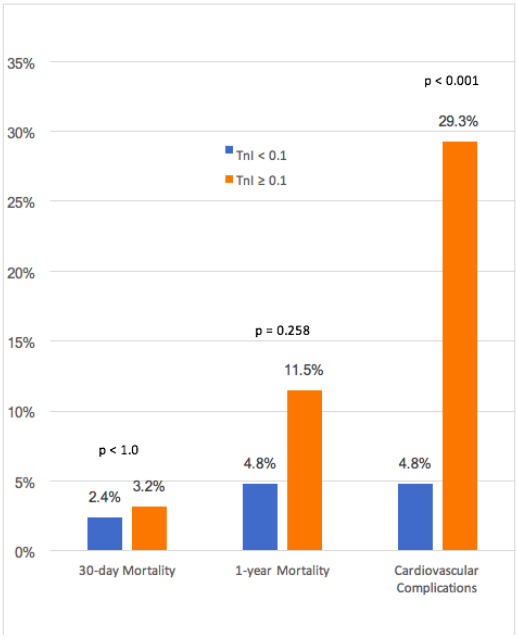
Perioperative myocardial injury, as evidenced by increased cardiac troponin levels, is an area of active research in liver transplantation (LT), where cardiovascular complications remain a leading cause of early postoperative mortality. Previously we reported the highest known prevalence (76%) of myocardial injury in a single-center consecutively sampled LT cohort. The impact of myocardial injury on post-transplant outcomes is of significant clinical interest.
We performed a retrospective chart review of all adult primary LT patients at the University of California, Los Angeles from January 1, 2015 to July 31, 2017, to evaluate the impact of myocardial injury on mortality and cardiovascular complications.
322 patients underwent LT during the study period. 220 patients had serial serum troponin I (TnI) measured within 72 hours of LT. 102 patients had TnI testing either omitted or performed after the 72-hour period. 21 patients were excluded because of preexisting CAD, arrhythmia, ventricular dysfunction, or combined cardiac-LT surgery. The prevalence of myocardial injury (TnI $\geq$ 0.1 ng/mL) was 79% (n=157/199). 30-day mortality in those with and without myocardial injury was 3.2% (n=5/157) and 2.4% (n=1/42), respectively ($p < 1.0$). 1-year mortality in those with and without myocardial injury was 11.5% (n=18/157) and 4.8% (n=2/42), respectively (p=0.258). The prevalence of perioperative cardiovascular complications including cardiac arrest, severe arrhythmia, and ventricular dysfunction on echocardiogram was higher ($p < 0.001$) in those with myocardial injury (29.3%, n=46/157) compared to those without (4.8%, n=2/42). There were no differences between the groups in their average age, MELD score, or need for preoperative dialysis or life support.
Early postoperative myocardial injury after LT is extremely prevalent and strongly associated with perioperative cardiovascular complications. There was no significant association between myocardial injury and either 30-day or 1-year mortality. Further investigation is warranted.



[Post-LT Outcomes in Patients With and Without Myocardial Injury]

P-015

Application of goal-directed fluid therapy in fluid management after liver transplantation

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Objective: To investigate the safety and effectiveness of application of goal-directed
fluid therapy (GDT) in the fluid management after liver transplantation (LT).
Methods: One hundred and nine patients who underwent orthotopic LT in the First Affiliated Hospital of Xi´an Jiaotong University between January 2015 and July 2016 were enrolled in this prospective study. According to the postoperative manage measures, the patients were divided into the GDT group (n=51) and control group (n=58). In the GDT group, 38 cases were males and 13 were females, aged (45±18) years old on average, and GDT was used in the patients. In the control group, 43 cases were males and 15 were females, aged (47±17) years old on average, and conventional postoperative manage measures were used in the patients. The informed consents of all patients were obtained and the local ethical committee approval was received. The first exhaust time, defecation time and postoperative length of ICU stay in two groups were compared using t test. The incidence of complications was compared using Chi-square test.
Results: The first exhaust time, defecation time and length of ICU stay after orthotopic LT in the GDT group was respectively (2.1±0.4), (3.1±1.3), (3.5±0.9) d, significantly shorter than (3.2±2.1), (4.9±1.8) and (5.4±1.3) d in the control group (t=-3.681, -5.912, -8.753; P< 0.05). The incidence of postoperative volume-related complications in the GDT group was 10%(5/51), significantly lower than 26%(15/58) in the control group ($\chi 2$=4.671, P< 0.05).
Conclusions: GDT is a safe and efficacious approach for fluid management after LT, and it can accelerate the postoperative recovery of the patients.

P-016

Intraoperative oliguria with decreased SvO_2 predicts acute kidney injury after living donor liver transplantation

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Background: Acute kidney injury (AKI) is a frequent complication after living donor liver transplantation (LDLT) associated with increased mortality. However, the association between intraoperative oliguria and the risk of AKI remains uncertain for LDLT. We sought to determine the association between intraoperative oliguria alone and oliguria coupled with homodynamic derangement and the risk of AKI after LDLT.
Methods: We evaluated the hemodynamic variables including mean arterial pressure, cardiac index and mixed venous oxygen saturation (SvO_2). We reviewed 583 adult patients without baseline renal dysfunction and who did not received hydroxyethyl starch during surgery. AKI was defined using the Kidney Disease Improving Global Outcomes criteria according to the serum creatinine criteria. Multivariable logistic regression analysis was performed with and without oliguria and oliguria coupled with a decrease in SvO_2. The performance was compared regarding area under the receiver operating characteristic curve (AUC).
Results: Intraoperative oliguria < 0.5 and < 0.3 ml/kg/h were significantly associated with the risk of AKI, however, their performance to predict AKI was poor. The AUC of single predictor increased significantly when oliguria is combined with decreased SvO_2 (AUC 0.72, 95% confidence interval [CI] 0.68-0.75 vs. AUC of oliguria alone 0.61, 95% CI 0.56-0.61, P < 0.0001; vs. AUC of SvO_2 alone 0.66, 95% CI 0.61-0.70, P < 0.0001). Addition of oliguria coupled with

SvO_2 reduction also increased the AUC of multivariable prediction (AUC 0.87, 95% CI 0.84-0.90 vs. AUC with oliguria 0.73, 95% CI 0.69-0.77, $P < 0.0001$; vs. AUC with neither oliguria nor SvO_2 reduction 0.68, 95% CI 0.64-0.72, $P < 0.0001$).
Conclusions: Intraoperative oliguria coupled with a decrease in SvO_2 may suggest the risk of AKI after LDLT more reliably than oliguria alone or decrease in SvO_2 alone. Intraoperative oliguria should be interpreted in conjunction with SvO_2 to predict AKI more accurately.

P-017

Albumin dialysis with MARS® in the treatment of cirrhotic patients with acute on chronic liver failure (ACLF) with a transplant perspective

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Background and aims: MARS® is the main liver support currently available and often used in patients with a perspective of liver transplantation (LT). The aim of this study is to evaluate in a recent era, efficacy and safety of the device in patients with ACLF.
Methods: Data of all consecutive patients that received at least 1 session of MARS were collected from two university-hospital centers using an e-CRF on line. More than 250 variables were collected per patient.
Results: 62/162 treated patients (70.1% male) with a mean age of 52.4±11.1 years had ACLF and were treated with 170 MARS® sessions. Etiology of cirrhosis was alcoholic (62%), viral (13%) autoimmune (9%) and others (16%). Median delay between admission and MARS therapy was 12.5 days (range 0-74 days). Survival was observed in 56% and 47% of the patients respectively at 1 and 3 months. Seventeen patients (27.4%) underwent LT with 100% post-transplant survival rate at 3 months vs. 28% in non-transplanted. Short-term survival at day 14 and 28 was significantly higher in those who received ≥ 2 MARS'sessions. Patients with CLIF-SOFA > 13 or CLIF-SOFA OF ≥ 4 had the lowest survival respectively 22% and 9% at 90 days. All liver and ICU scores at admission were significantly associated with mortality, but in the multivariate regression analysis, CLIF-SOFA score (OR: 1.39 (95%CI: 1.69-1.14; p=0.001) was predictive of death at 28 days of ICU admission. Main AEs related to MARS therapy were clotting of the membrane (11.7%), catheter site bleeding (9.4%).
Conclusion: In patients with ACLF who received MARS®, CLIF-SOFA score at admission was the main predictive factor of mortality. MARS® is futile in patients with CLIF-SOFA OF ≥ 4. Early medical management in combination to MARS® treatment improved short-term survival allowing an optimal window opportunity for LT with an excellent post-transplant survival.

P-018

A prospective cohort study assessing the use of peripheral saphenous venous pressure monitoring as a marker of transhepatic venous pressure gradient in liver transplantation surgery

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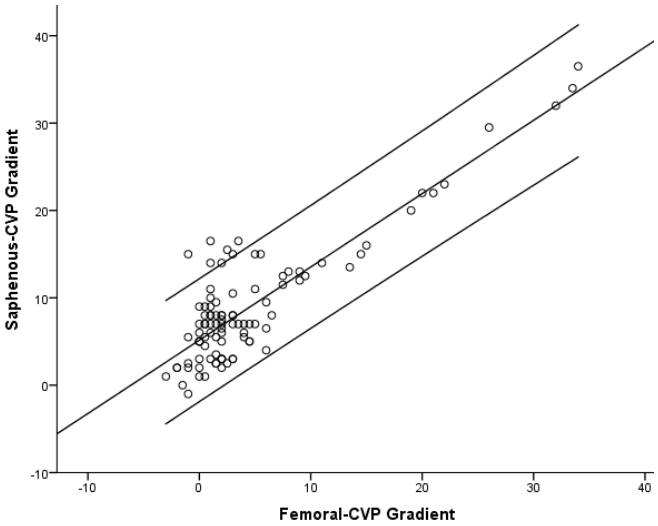
Background: During orthotopic liver transplantation the femoral to central venous pressure gradient provides information on transhepatic venous congestion and the venous gradient during 'piggy-back' or caval cross-clamp. Large gradients provide a prompt to reposition the clamp to reduce venous obstruction with potential haemodynamic benefits and reduced renal engorgement. However, this requires the insertion of a femoral venous line with the attendant risks in coagulopathic patients. Peripheral saphenous venous pressure (PSVP) measurement may provide an alternative to femoral venous pressure (FVP) measurement; we therefore investigated the ability of PSVP to reflect changes in FVP throughout liver transplantation surgery.
Method: Central venous pressure (CVP) was measured via a quad lumen cannula in the right internal jugular vein and FVP was measured via a single lumen CVC in either femoral vein. A standard 18G cannula was inserted in the long saphenous vein or alternative large vein below the ankle. Mean venous pressures from the internal jugular, femoral and saphenous cannulae were recorded.
Results: Twenty-two patients were included in this study. Combined data from all surgical phases demonstrated a significant correlation between the PSVP and FVP ($r = 0.701$, $p < 0.001$). Multivariable linear regression analysis, adjusting for ventilatory and physiological variables, retained this association for the whole of surgery ($r = 0.875$, $p < 0.001$) and importantly the anhepatic phase. There were good correlations between the femoral-CVP and saphenous-CVP gradients throughout surgery (Spearman $r = 0.621$, $p < 0.001$, see Figure) as well as during the anhepatic phase.



[Gradients for all surgical timepoints across all cases. Line of best with individual 95% CIs.]

Conclusion: The saphenous venous pressure presents a reliable surrogate for femoral venous pressure in determining the infrahepatic venous pressure. The ability to accurately infer the transhepatic gradient through saphenous cannulation obviates the need for femoral vein cannulation with the associated risks and morbidity.

P-019

Intraoperative blood loss during living donor liver transplantation: an analysis of 950 recipients at a single centre

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Background: Living-donorliver transplantation (LDLT) has been an important option in the treatment of patients with end-stage liver disease. Massive intraoperative bloodloss can occur during LDLT, mandating blood transfusion. The purpose of this study was to present blood loss data from the recipients of LDLT, to assess the effect of massive intraoperativeblood loss on prognosis, and to establish the reliability of preoperative factors in predicting intraoperative blood transfusion requirements in LDLT.
Study design and methods: A total of 950 patients who underwent LDLTs between 2011 and 2018 at our hospital were retrospectively investigated. The volume of blood loss, prognosis, and preoperative variables were analysed statistically.
Results: Intraoperativeblood loss ranged from 5.27ml to 516.6 mL per kg (mean, 76 mL/kg). Massive blood loss negatively affected survival not only immediately after operation (high blood loss [HBL]:low blood loss [LBL] ratio, 82.5%:95.9% at 1 month) but also over the long term (HBL:LBL, 68.4%:86.8% at 5 years). Preoperative risk factors for massive blood loss were determined to be recent spontaneous bacterial peritonitis, fibrinogen (< 100mg/dL), haematocrit (< 27%), total bilirubin (>20.0 mg/dL), direct bilirubin (>16.0 mg/dL), and serum creatinine levels (>2.0 mg/dL).
Conclusions: The risk factors associated with massive intraoperativeblood loss during LDLT were identified. This is the first analysis of blood loss during LDLT at a single centre from Indian subcontinent.Massive blood loss is a predictor of poor prognosis in LDLT patients.

P-020

Assessment of physician performance in a liver transplant program

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Performance of individual anesthesiology physicians in a liver transplant program is important to both benchmark and encourage best practice. We collected data on 281 consecutive adult cadaveric liver transplant cases at our academic center from January 1, 2015-March 1, 2018. Eight different anesthesiology physicians participated in transplants, with varying numbers of cases performed during this time period. The beginning of the case is strongly controlled by the anesthesia team, including positioning the patient, attaching monitoring devices, induction of anesthesia, securing the airway and placement of invasive lines. We measured the time from patient entry into the operating room to incision (as a marker of anesthesiologists efficiency) and the percentage of patients who were extubated immediately in the operating room at the conclusion of the procedure.The Table presents each individual physician´s metrics compared in the categories of number of cases performed, average MELD, in-room to incision time, and percentage of patients extubated in the OR. The overall average time for in room to incision was 48 minutes (standard deviation 3.0). The average immediate extubation was 67% (standard deviation 10). We believe it is important to track measures of individual physician performance and share with our group to encourage best practice and uniformity in approach to care of the transplant patient.

Physician	Number of Cases	MELD	In Room to Incision Time, minutes	Extubated in OR
1	40	25	50	70%
2	30	26	41	53%
3	65	27	46	55%
4	35	25	46	74%
5	32	28	50	69%
6	39	26	48	65%
7	27	26	46	44%
8	17	26	55	59%

[Anesthesiology Physician Performance]

P-021

Liver-kidney transplantation in a patient with hypertrophic obstructive cardiomyopathy (HOCM)

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A 58-year-old female, MELD 15, with severe HOCM was referred for second opinion in evaluation for liver-kidney transplantation (ETOH/CKD with GFR 27 >4 months, not on dialysis). Patient complained of dyspnea on exertion, limited exercise tolerance, and +3 peripheral edema. Echocardiography demonstrated severe left ventricular outflow tract (LVOT) obstruction, LVEF 81%, mildly thickened mitral valve, systolic anterior motion of the mitral leaflet with severe mitral insufficiency, and grade 2 diastolic dysfunction. Left and right heart catheterization demonstrated unremarkable coronary arteries and right heart pressures with LVOT gradient of 110 and 150mmHg at baseline and during Valsalva, respectively. Alcohol septal ablation for a 1.6cm asymmetric septal thickening was deemed not indicated. The patient was optimized with metoprolol and adjustment of diuretic, and LVOT gradient decreased to 50 and 90 at baseline and during Valsalva, respectively. She was listed as a high-risk candidate. A 7-year-old donor after cardiac death became available and we proceeded with transplant. In the OR, an awake radial a-line was placed. General anesthesia was induced, two central lines and TEE were placed, and femoro-jugular veno-venous hemodialysis was initiated. Flotrac hemodynamic parameters (via femoral a-line) monitored with TEE guided fluid replacement, as well as the titration of esmolol, phenylephrine, and vasopressin infusions to avoid tachycardia and increased contractility, and maintain preload and afterload. Partial clamping of the IVC was tolerated while dialysis blood flow was increased to 500ml/min. A slow and gradual unclamping of the portal vein minimized the hemodynamic instability during reperfusion. Thirty minutes after reperfusion, hemodynamic instability and diffuse coagulopathy/fibrinolysis on TEG occurred, which required Amicar and transfusion of multiple blood products. Several episodes of tachycardia (HR 90-115) and hypotension (MAP 45-50) requiring metoprolol with esmolol/vasopressin and phenylephrine infusions. Hemodynamic recovery occurred with correction of coagulopathy and she was transferred intubated to the ICU in stable condition.

P-022

Does Renal Resistive Index predict acute kidney injury in patients undergoing living related liver transplantation - a prospective pilot study

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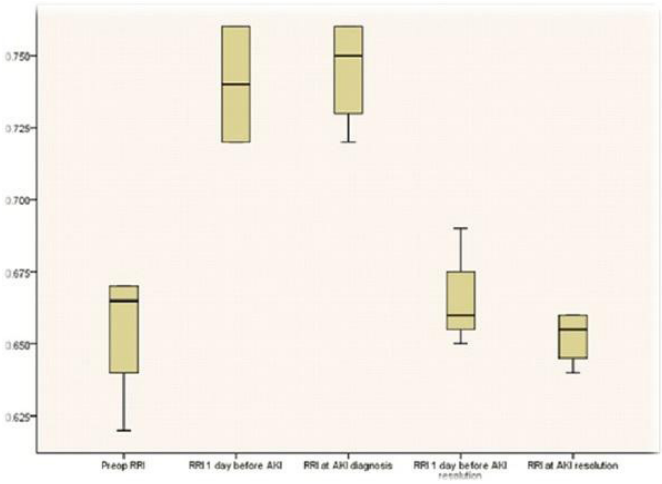
Background: Acute Kidney injury (AKI) is commonly seen in the post-operative period of Liver Transplantation and is associated with significant morbidity & mortality. The cause of post-operative AKI can be multifactorial. Early detection of Acute kidney Injury is likely to hasten the diagnosis & also help in implementing remedial measures to preserve renal function. We attempted to determine whether doppler derived Renal Resistive Index (RRI) helped in predicting AKI in patients undergoing Living related Liver Transplantation.
Methods: This pilot study was conducted in 21 adult patients who underwent Liver transplantation at our centre. In addition to the demographics, pre- operative and post - operative laboratory values, we also measured the RRI pre-operatively and subsequently during the first 7 post - operative days. AKI was graded into 3 grades as per KDIGO criteria.
Results: The results are summarized in figure 1. 17 patients developed AKI within 7 post-operative days following LDLT. AKI group had higher age, BMI and MELD score & lower GFR at presentation. Mean RRI a day before [RRI(-1), 0.72±0.03] and on the day of diagnosis of AKI [RRI(0), 0.73±0.03] were significantly higher than preoperative RRI [RRI(preop), 0.65±0.02, P< 0.001] and RRI(-1) and RRI(0) showed strong positive correlation (r=0.97, p< 0.001) and no difference in means (P=0.165). Mean RRI on resolution of AKI retuned to the baseline values (Figure 1). On logistic regression, age, BMI, MELD score, preoperative GFR and GRWR were significantly associated with the likelihood of occurrence of AKI.

Conclusion: Our study demonstrated that RRI Predicts onset of AKI in patients undergoing liver transplantation. RRI could be a useful monitor in the post - operative period in aiding early diagnosis of AKI & also might help in early initiation renal protective strategies.



[figure1]

P-023

Temporary portocaval shunt during liver transplantation has no effect on postreperfusion syndrome: a matched retrospective study

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Background: Postreperfusion syndrome (PRS) has been associated with severe adverse effects such as acute kidney injury, graft loss or post-operative death. The objective of this study was to estimate the effect of a temporary portocaval shunt (PCS) during liver transplantation on PRS occurrence.
Methods: From a monocentric cohort of 340 liver recipients between 2009 and 2016, 70 recipients with PCS were matched with 132 controls without PCS, using *coarsened exact matching*. The matching covariates were: indication for transplantation, MELD and Child-Pugh scores, presence of esophageal varices, donor age and BMI. PRS was defined as cardiac arrest or a decrease of mean arterial pressure (MAP) with values below 70% of the baseline value for at least 1 minute within 5 minutes after portal reperfusion.
Results: In the matched sample, median patient age was 56 years old, median MELD was 11, Child-Pugh score was A in 107 (53%) patients, and main indication for transplantation was hepatocellular carcinoma. PRS occurred in 58 (29%) patients and was associated with an increased risk of early allograft dysfunction and biliary complications. Risk factors of PRS were presence of esophageal varices, use of University of Wisconsin preservation solution, and high MAP prior to reperfusion. In multiple regression, PCS was not associated with PRS (OR [95% CI]: 1.17 [0.53, 2.58], p = 0.70).
Conclusion: PCS use during liver transplantation did not prevent PRS occurrence in this matched sample, in which most patients had compensated liver cirrhosis. Whether an effect exists in patients with severe liver disease needs to be further investigated.

P-024

Resolution of coagulopathy and decrease in bleeding events by day 7 after liver transplantation

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Background: Patients undergoing liver transplantation (LT) are at high risk of postoperative haemorrhagic and thrombotic complications but changes in coagulation in the immediate post-LT period have not been described comprehensively. We investigated postoperative changes in each component of the haemostatic system (primary haemostasis, coagulation, fibrinolysis, endothelial function) and their relationship with postoperative bleeding/ thrombotic events. We are reporting a sub-component: changes in conventional coagulation tests (CCTs) and thromboelastography (TEG) parameters post-LT.
Method: We measured TEGs and CCTs in a prospective cohort of patients undergoing elective deceased donor LT immediately pre- and postoperatively, and on postoperative days 1, 2, 5, 7 & 10 (D1-10). We recorded all postoperative bleeding and thrombotic complications, alongside blood product use. We describe trends in the INR, platelet count, reaction time (R-time), and maximum amplitude (MA) and also the timing of bleeding events requiring ≥ 2 units of packed red cells (PRCs).
Results: Serial changes in coagulation indices of 23 patients are displayed in Figures 1 and 2. R-time increases from baseline until D1, followed by a gradual decrease. MA was reduced at end of surgery, remaining low until D3. By D7 the R-time was within the normal range (< 9min) in 95% of patients and 89% of patients had a normal (>40mm) MA. Fourteen significant bleeding events and the transfusion of 62 units of PRCs occurred before D7. After D7 there were only 3 bleeding events and 28 units of PRCs transfused,

consisting mostly of single-unit transfusions.
Conclusion: We describe the disruption and subsequent resolution of CCT and TEG parameters in patients undergoing LT. By postoperative day 7, TEG demonstrates normal clot initiation and strength for the majority of patients. This corresponds with a reduced incidence of haemorrhage and transfusion requirement after this time point. Further analysis is underway to clarify mechanisms underlying these changes.

P-025

Impact of hyponatremia on early postoperative outcome after living donor liver transplantation

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Background: Hyponatremia is associated with reduced survival in cirrhotic patients awaiting liver transplantation. We investigated the effect of hyponatremia at the time of Living donor Liver Transplantation (LDLT) on postoperative complications and short term mortality.
Method: We retrospectively analysed, prospectively collected data of 298 patients who underwent LDLT from February 2017 to September 2018. Patients were divided in two groups according to their preoperative serum sodium (Hyponatremia (HN) ≤130 mEq/L, n=72 and Normonatremia (NN) ≥ 131 mEq/L, n=226). Impact of hyponatremia on early postoperative complications and short term mortality was assessed.
Results: Mean serum sodium in HN was 125±3.83 vs 136±3.39 in NN group. Autoimmune hepatitis and hepatocellular carcinoma was significantly more seen in NN group. MELD (24.69 ± 8 vs 17.72 ± 8, P =0.0001), CTP (10.82 ± 1.8 vs 9.56 ± 2.2, P = 0.0001) and ascites was significantly higher in HN group. 24 hour change in serum sodium was significantly higher in HN group (6.5 ± 3.71 vs 3.15 ± 2.76, P < 0.0001) along with significantly higher requirement of intraoperative blood products transfusion (Packed RBC units 6.29 ± 4.75 vs 3.78 ± 4.1, p = 0.001). Incidence of class 2 and 3 Acute kidney injury (AKI) defined by Kidney disease: improving global outcome (KDIGO), Early allograft dysfunction (20% vs 11.5%, P=0.045) and sepsis (15% vs 7%, P= 0.045) was significantly higher in HN group .There was no difference between the groups regarding rejection episodes, postoperative dialysis and neurological complications. There was no statistically significant difference regarding hospital stay (23.91±16 vs 21±10.91 days, p=0.16) and 30 days mortality (12.5% vs 7.52% p=0.20) between 2 groups.
Conclusion: Patients with preoperative hyponatremia are high risk for perioperative complications such as severe AKI, allograft dysfunction and sepsis. However Hyponatremia had no impact on early post LDLT mortality and hospital stay.

P-026

Immediate extubation in liver transplant recipients: 3 years single centre experience

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Background: Reducing postoperative mechanical ventilation in patients undergoing liver transplantation has clinical benefit and a more efficacious use of resources. Few small series have reported immediate postoperative extubation in liver transplant recipients [both deceased donor liver transplant (DDLT) & living donor liver transplant (LDLT)]. We report a series of 168 liver transplant recipients who were extubated immediately after operation.
Methods: In this prospective study, 168 out of 200 patients consecutively undergoing liver transplantation between January 2016 and November 2018 were extubated in the operating theatre at the end of surgery. There were no prefixed criteria for extubation. Based on a relative uneventful intraoperative course, haemodynamic stability at the end of reperfusion of graft, and improvement of metabolic parameters after implantation and vascular anastomosis, a decision for immediate postoperative extubation was made by the anaesthesiologist in consultation with the operating surgeon at the time of biliary anastomosis, which allowed adequate time to start weaning the patient.
Results: One hundred and sixty eight (110 DDLT & 58 LDLT) of the 200 patients (84%) were extubated immediately after the completion of the surgical procedure. 148 were males,mean age was 46.78+/- 13.66 years, mean BMI was 25.32+/- 4.58 kg/m2 and mean MELD score was 22.28+/- 5.42. Associated comorbidities included diabetes mellitus in 80, hypertension in 25 , coronary artery disease in 9 and hypothyroidism in 18 patients. Mean duration of surgery was 394+/- 60 minutes. Two patients required reintubation for surgical reasons and none had pulmonary complications.
Conclusion: Immediate extubation after liver transplantation is possible in a substantial percentage of liver transplant recipients; confidence and habit are decisive factors in encouraging anaesthesiologists to extend this practice to the largest possible number of recipients. A successful immediate extubation may be an important indicator of perioperative quality of care in liver transplantation.

P-027

The impact on long-term outcome after acute kidney injury following living donor liver transplantation

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Background: Acute kidney injury (AKI) is a common postoperative complication after liver transplantation (LT). The occurrence of postoperative AKI after LT (Post-LT AKI) is associated with inferior patient and graft outcomes. The aim of the present study was to determine incidence, etiology, progression of long-term chronic kidney disease (CKD), cardiovascular event (including MI, stroke and heart failure) and mortality in a single-center series of adult LDLT.
Patients and methods: We review medical records of 512 consecutive LDLT recipients during January 2009 to December 2013, with a mean follow-up of 7.3±1.5 years after LDLT. We defined AKI using consensus KDIGO criteria and classified into four stages according to severity of acute rise in creatinine. The chronic kidney disease (CKD) is defined as eGFR ≤60 ml/min/1.73 m^2 for at least 3 months.
Results: The prevalence of post-LT AKI is 35.2% (n=179). The most common etiology of AKI was surgery-related (50.0%, n=89), followed by tacrolimus-induced AKI (15.6%, n=28) and massive ascites (11.7%, n=21) in the AKI group. Post-LT AKI group showed higher incidence of postoperative cardiovascular disease, CKD, ESRD and all-cause mortality (7.8% versus 3.6%, $p< 0.05$; 44.1% versus 18.6%, $p< 0.001$; 6.2% versus 1.2%, $p=0.002$; 20.1 versus 5.2%, $p< 0.001$; respectively) compared with post-LT no AKI group. The mortality risk is proportional to AKI functional severity (stage 1: 18.5%, stage: 22.2%, stage 3: 33.3%, dialysis requirement: 50%, $p< 0.001$).
Conclusions: Our results reveal that post-LDLT AKI associated with higher long-term risks of cardiovascular disease, CKD, ESRD and death in this cohort. Enhanced post-discharge follow-up of LT recipients who have complicated with postoperative AKI may be warranted.

P-028

Perioperative viscoelastic assay use for coagulation monitoring among U.S. liver transplantation centers

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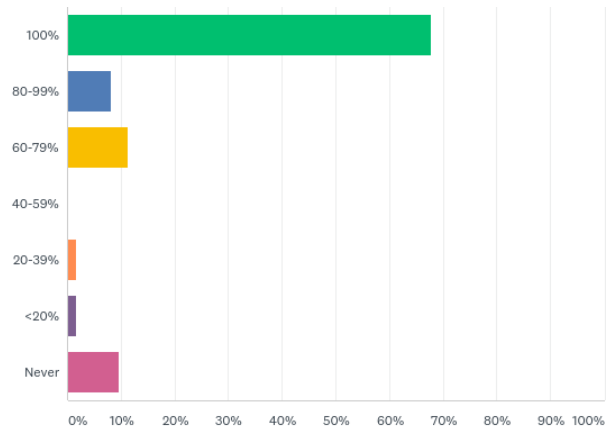
Introduction: The use of viscoelastic essay in liver transplantation has been constantly increased in recent years. It has been shown to be valuable during liver transplantation to evaluate hemostasis. The objective of this study was to evaluate the pre-, intra-, and postoperative use of viscoelastic assay among U.S. liver transplantation programs.
Methods: A 21-item-survey was sent to anesthesia directors at 137-liver transplantation centers in the U.S. Primary outcome measures were the ratio of viscoelastic assay use in the perioperative management of liver transplantation. Secondary outcome measures were institutional demographics, physician training level, and device demographics.
Results: 61 of 137 centers responded to the survey. 77%(n=48) of liver transplantations were performed in university settings and 21%(n=13) in private practice with a modal of 11-50 liver transplantations a year. 74% of all centers performed transplantation in adult patients only. 92%(n=57) of the institutions, had access to either ROTEM or TEG during liver transplantation. Out of those, 67.7% used it every single time intraoperatively during liver transplantation. 20% of the institutions used it in 60-99% of the time. 59%(n=35) institutions used viscoelastic assay preoperatively, and 84%(n=51) postoperatively. 68% of the users learned usage and interpretation through self-education, 21.1% through an official training, and 10.5% during fellowship or from colleagues. Device was located in 16.4% in the liver transplantation operating room, 7.3% in another operating room and 61.8% in the laboratory. Real time delivery of results occurred in 74.1%.



[Percentage of ROTEM/TEG use during intraoperative management of liver transplantation]

Conclusion: Currently viscoelastic monitoring is widely available and routinely used intraoperatively and postoperatively in most U.S. liver transplantation centers regardless of university or private practice setting. However, the preoperative use is limited to two third of the institutions. Official training for device usage and interpretation was lacking and formal training courses or education guide is needed.

P-029

Complications of peripherally inserted large-bore rapid infusion catheters for patients undergoing orthotopic liver transplantations: a review of 852 cases

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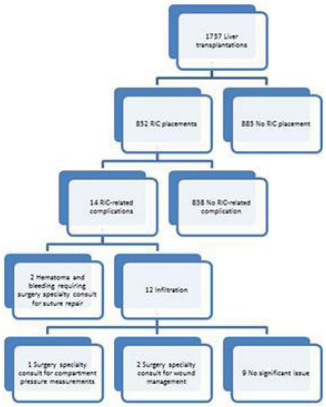
Background: The rapid infusion catheter (RIC) (Arrow Rapid Infusion Catheter Exchange Set, Teleflex, Morrisville, NC, USA) is an 8.5 French peripherally inserted catheter for high-flow administration of intravenous fluids and blood products during liver transplantations. Although commonly used, data on RIC-related complications was unavailable. This study aimed to estimate the incidence of RIC related complications in liver transplantation patients.
Method: After obtaining institutional review board approval, 852 out of 1737 liver transplant surgeries from 2008-2018 were identified with intraoperative RIC placements. A retrospective chart review was performed to find complications such as hematoma formation or infiltration. We deemed complications to be severe if the RIC site required surgical intervention (e.g. suturing or repair for a hematoma) or consultation with a surgical specialty due to infiltration (e.g. evaluation for compartment syndrome or wound management). The following variables were also obtained: age, sex, duration of surgery, body mass index (BMI), history of difficult intravenous access, pre-operative coagulation lab values, total intravenous fluid administered, and total blood products administered.
Results: Of the 852 liver transplantation surgeries with RIC placements, 1.6% (n=14) were found to have RIC-related complications with 0.6% (n=5) needing surgery specialty consult for the management of the complications (Figure). Of the 14 complications, 9 were placed by CRNAs and 5 were placed by resident physician anesthesiologists. No long-term complications were noted in the 852 patients.
Conclusion: The incidence of all complications related to RIC placement was relatively low (1.6%) with 0.6% of patients requiring surgical consultation. Given the significant morbidity and mortality associated with this operation in this patient population, we conclude that these risks are acceptable when compared to the alternative of placing an additional central venous catheter.

Figure. Rapid Infusion Catheter (RIC)-Related Complications



[Rapid Infusion Catheter (RIC)-Related Complications]

P-030

Preoperative left ventricular systolic dysfunction in association with increased consumption of intraoperative pressor in liver transplantation

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Background: Preoperative left ventricular systolic dysfunction (LVSD) has been shown to associate with increased postoperative morbidity and mortality in various settings, but the intraoperative impact of preoperative LVSD in liver transplantation (LT) is unknown. This study was conducted to investigate if preoperative LVSD was associated with increased consumption of intraoperative vasopressor in patients undergoing LT.
Methods: After the institutional review board approval, preoperative transthoracic echocardiography and perioperative data of all adult patients undergoing LT between January 2006 and October 2013 were reviewed. Patients with or without LVSD (defined as left ventricular ejection fraction (LVEF) < 50%) were compared using a student T-test, Pearson's chi-square test or Fisher's test. Risk factor

analysis was conducted using multivariate logistic regression.
Results: During the study period, 1055 patients who underwent LT and had complete LVEF data were included. There were 11 patients (1.0%) whose LVEF were < 50% by preoperative echocardiographic examination (median 45%). Comparison analysis showed that preoperative variables were similar between patients with and without LVSD except for age and the preoperative pressor use (patients with LVSD were younger and required more pressor). Intraoperatively, a greater portion of patients with LVSD required vasopressors following anesthesia induction (71.4% vs. 20.5%, P=0.001), immediately after reperfusion (100% vs. 62.1%, P=0.049) and at the end of transplant (100% vs. 38.5%, P=0.001) compared to patients without LVSD. Multivariate logistic analysis showed that LVSD was an independent risk factor (OR, 4.7, 95% CI 1.0-21.3, P=0.043) of increased consumption of intraoperative vasopressor along with other risk factors including encephalopathy, preoperative pressors, male gender, higher MELD score and longer cold ischemia time. Patients with preoperative LVSD had comparable 1-year mortality compared with patients without LVSD (18.2% vs. 16.1%, P=0.792).
Conclusions: Preoperative LVSD is associated with the increased consumption of intraoperative pressors in LT.

P-031

Perioperative coronary artery disease care in liver transplantation survey

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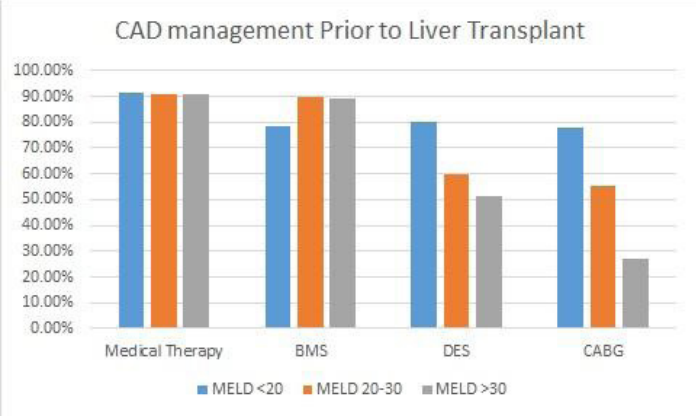
Introduction: The presence of cardiovascular disease in liver transplant (LT) candidates is a predictor of poor prognosis, therefore, the identification of those at risk remains vital in improving outcomes. This survey focuses on how LT centers around the world assess and manage perioperative coronary artery disease(CAD).
Methods: A 10-item survey was sent to LT anesthesia directors around the world to investigate how they assess the perioperative CAD evaluation and management prior to LT.
Results: 72 out of 190 recipients responded to our survey. Fifty-six percent would recommend cardiac stress tests despite good functional status. Patients with three or more cardiac risk factors and poor functional capacity are the main indications for cardiac stress test.
The three main indications for coronary angiography are positive cardiac stress test (96%), known CAD (64%), and baseline EKG abnormalities such as Q wave, LBBB, RBBB, or other concerning abnormalities(41%).
Absolute contraindications to LT are obstructive CAD that is not amenable to revascularization (75%) or requires surgical revascularization in Child-Pugh Class B/C cirrhosis (41%).
Most centers would manage significant CAD with medical therapy (90%) and bare metal stents (90%) irrelevant to MELD-score. Nevertheless, the responses were different when treating patients with drug eluting stents (80%, 60%, 51%, for patients with MELD< 20, 20-30, and >30 respectively) and performing Coronary artery bypass graft (CABG) (78%, 55%, 20%, for patients with MELD< 20, 20-30, and >30 respectively).



[Coronary Artery Disease Management]

Most centers (74%) would not perform simultaneous CABG with LT.
Conclusion: Fifty-six percent of responses would recommend cardiac stress tests despite good functional status. Most centers recommend medical therapy and bare metal stents irrelevant to MELD score; however, the percentage of centers recommending drug eluting stents and CABG decreases with increase in MELD-score. Three-quarter would not perform simultaneous CABG with liver transplantation.

P-032

Severe congestive heart failure after liver transplantation

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Severe congestive heart failure (CHF) is a rare, but devastating complication after liver transplantation (LT) and its incidence and impact on 30-day mortality have not completely elucidated. In this retrospective study, we investigated the incidence of severe CHF

and 30-day mortality after LT.
After institutional review board approval, patients who underwent LT between January 2006 and August 2013 were identified. Medical data including admission status, anesthesia record, operative note, consultation note, preoperative echocardiography and postoperative echocardiography were reviewed. Severe postoperative CHF was defined by the clinical presentation of CHF and echocardiograph showing left ventricular ejection fraction < 30% within 30 days after LT. Patients with and without severe postoperative CHF were compared by univariate and multivariate analyses.
Among 1210 adult patients who underwent primary LT during the study period, 12 patients (0.99%) developed severe CHF. Majority (91.7%) of severe CHF occurred during the first postoperative week. All patients with severe postoperative CHF had normal value of left ventricular systolic function before LT. Among 12 CHF patients, 3 experienced atrial fibrillation with rapid ventricular response, 3 had acute myocardial infarction, 2 experienced ventricular tachycardia, and 1 had sinus bradycardia. Out 12 patients, 3 (25%) died within 30 days after LT.
In conclusion, severe CHF occurred at a rate of 0.99% within 30 days after LT and was associated with increased 30-day mortality.

P-033

Perioperative extracorporeal membrane oxygenation support for a patient with respiratory failure in liver transplantation: a case report

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Background: Despite the wide use of liver transplantation, severe cardiac or pulmonary dysfunction remains a life-threatening contraindication to operation. Extracorporeal Membrane Oxygenation (ECMO), as an extracorporeal life support system for critical cardiopulmonary dysfunction generally used in intensive care unit, can also help patients with severe pulmonary artery hypertension to maintain the perioperative respiratory function in surgery. However, performance of ECMO in the patient of severe pulmonary artery hypertension during liver transplantation has not been reported yet.
Methods: The case describes a 56 year old male with advanced hepatocellular carcinoma and decompensated liver cirrhosis. However, the patient suffered severe respiratory failure because of an unknown pulmonary fibrosis which indicated high mortality rate for liver transplantation. Fatal 44mm of main pulmonary artery diameter and 70/40mmHg of severe pulmonary artery pressure were measured before operation. Mechanical ventilation was administrated and parameters are listed as follows: PEEP 5cmH2O, FiO2 30%, SaO2 70-80%, PO2 84mmHg. Considering all the factors, venoarterial ECMO were performed 1 hour before liver transplantation and maintained working during liver transplantation. We adjusted the ECMO index according to the patient´s condition so that cardiopulmonary functioned well in the perioperative period.
Results: ECMO support was removed 1 day post operation and the tracheal intubation were removed 2 days after operation. There is no complications of ECMO or operation found and the patient discharged 1 mouth after transplantation.
Conclusions: It is practicable to ensure the safety of recipient with severe pulmonary artery hypertension during liver transplantation by the use of ECMO.

P-034

Effect of ventilation on extravascular lung water during liver transplantation

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Background: The extravascular lung water (EVLW), measured using transpulmonary thermodilution (TPTD), has been suggested as a useful marker for early diagnosis of pulmonary complications after surgery. The previous study on liver transplantation (LT) patients showed EVLW and the pulmonary vascular permeability index (PVPI) values obtained at the end of surgery were useful for predicting prolonged mechanical ventilation. About a half of patients develop pulmonary edema after LT, which compromises the postoperative course. In this study, we examined whether the method of mechanical ventilation (MV) could affect on the EVLW and PVPI during LT.
Method: Adult patients scheduled for LT were recruited. MV was set with a tidal volume of 8 to 10 ml/kg with no PEEP in conventional ventilation group and a tidal volume of 6 to 8 ml/kg with PEEP 5 to 7 cmH_2O in protective ventilation group. The respiratory rate was set to maintain an end-tidal carbon dioxide of 35 to 40 mm Hg. All patients had a radial arterial line and pulmonary arterial catheter (PAC). We used a VolumeView catheter (Edwards Lifesciences, Irvine, CA) that was introduced into the right femoral artery and connected to the EV1000 system. TPTD measurements were recorded at 8 time points during surgery.
Results: Preliminary data of thirteen patients were analyzed as a pilot study. Actual tidal volume was applied with a tidal volume of

8.7±0.7 ml/kg with PEEP 2.4±0.4 cmH_2O in conventional ventilation group and a tidal volume of 6.0±0.2 ml/kg with PEEP 6.5±0.8 cmH_2O in protective ventilation group by the spirometry of ventilator. EVLW and PVPI on the end of surgery were 8.9±1.8 and 1.8±0.5 in conventional group, 8.0±3.1 and and 1.6±0.3 in protective group, respectively.
Conclusion: Our preliminary data showed that there was no significant difference of EVLW and PVPI according to the use of tidal volume.

P-035

Effects of polymyxin B hemoperfusion in patients with septic shock after liver surgery: the pilot study

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Introduction: Polymyxin B direct hemoperfusion (PMX-DHP) which removes plasma endotoxins is considered an effective treatment for sepsis, particularly intra-abdominal infection with gram-negative bacteria. There are limited data on the clinical experience of the PMX-DHP for septic shock in liver disease with immunologic deficits.
Methods: From August 2016 to September 2017, 10 patients underwent PMX-DHP treatment for septic shock after liver surgery (3 cases of hepatectomy and 7 cases of liver transplantation) in surgical intensive care unit. The PMX-DHP treatment was performed one or two times in each patient. Two patients who died within 24hr after PMX-DHP were excluded. We analyzed the change of the patient's hemodynamics and infection marker before and after PMX-DHP treatments (before, 24hr, 48hr, 72hr, 7 day).
Results: Most of the patients had gram-negative bacteremia. The 28 days-mortality was 50%. The Mean value of sequential organ failure assessment (SOFA) score and serum lactate before PMX-DHP treatments were 17.6 (13.0-22.0) and 8.3mg/dL (2.0-26.7mg/dL). After the PMX-DHP treatment, serum lactate, vasoactive-inotropic scores (VIS), vasopressor dependency index (VDI), and PaO_2/FiO_2 ratio significantly decreased. Also, the C-reactive protein (CRP) as infection marker decreased after the PMX-DHP treatment.
Conclusion: Our pilot study suggest that the PMX-DHP treatment significantly improves hemodynamics in patients underwent liver surgery with septic shock.

	before (n=8)	24hr(n=8)	48hr(n=7)	72hr(n=7)	7day(n=6)	P-value
CRP	10.7 ± 5.6	9.6 ± 6.9	7.9 ± 5.3	8.9 ± 4.3	5.0 ± 3.5	0.009
SOFA score	17.6 ± 2.7	17.4 ± 2.9	17.4 ± 3.5	17.7 ± 4.7	15.2 ± 3.7	0.254
Lactic acid (mg/dL)	8.3 ± 8.0	6.7 ± 6.2	6.5 ± 5.8	5.5 ± 4.9	1.8 ± 0.6	0.003
VIS	46.5 ± 49.6	25.3 ± 30.6	20.7 ± 24.5	1.6 ± 2.1	1.7 ± 2.0	<0.001
VDI	0.9 ± 1.0	0.4 ± 0.5	0.4 ± 0.5	0.3 ± 0.3	0.03 ± 0.04	0.003
PaO2/FiO2	113.6 ± 39.0	141.4 ± 60.0	167.1 ± 80.3	186.6 ± 87.5	185.3 ± 127.4	0.026

[Hemodynamics of the patients after the PMX-DHP treatment]

P-036

Impact of flushed fluid potassium concentration on postreperfusion acute hyperkalemia and significant arrhythmias in deceased donor liver transplantation

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Background: Acute hyperkalemia is a relatively common, but also often neglected phenomenon during the early reperfusion period in deceased donor liver transplantation (DDLT). However, the impact of flushed fluid potassium concentration (FFK) on the prevalence of acute hyperkalemia and significant arrhythmias has not been noted previously.
Methods: A retrospective cohort study of 75 adult patients submitted to DDLT between November 2016 and September 2018 was conducted. Patients were divided into two groups depending on the FFK level (< or ≥ 6.75 mmol/L), as measured by a point-of-care blood gas analyzer at the end of the portal vein flush: HFFK group (n = 42) versus LFFK group (n = 33). Independent risk factors of acute hyperkalemia and significant arrhythmias during the early reperfusion period were identified by mutivariate logistic regression. Propensity score (PS) analysis was designed to control selection bias.

Results: Even after PS matching, patients who received a higher FFK liver graft had higher incidences of acute hyperkalemia and significant arrhythmias (93.3% vs. 53.3%, p = 0.035; 80.0% vs. 33.3%, p = 0.025, respectively). Mutivariate analysis showed that higher FFK (odds ratio [OR]: 1.4) and serum potassium before reperfusion (K_0) (OR: 2.5) were independent predictors of acute postreperfusion hyperkalemia, and higher FFK (OR: 1.6) and serum potassium at 1 minute after reperfusion (K_1) (OR: 3.0) were independent risk factors for suffering postreperfusion significant arrhythmias. Additionally, the HFFK group showed a higher K_1 level (5.5±1.0 vs. 6.5±0.9, p < 0.001), and more frequent development of vasoplegic syndrome during the late reperfusion period (53.3% vs. 6.7%, p = 0.014) and early allograft dysfunction after DDLT (83.3% vs. 16.7%, p < 0.001).
Conclusions: High FFK is an independent unfavorable factor for suffering postreperfusion acute hyperkalemia and significant arrhythmia in DDLT.

P-037

Postoperative diabetes insipidus in liver transplantation: a case report

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Postoperative Diabetes insipidus is an uncommon presentation after liver transplantation . We present a case of idiopathic central diabetes insipidus in a 77 year male with Hepatitis B related CLD and HCC who underwent living donor related liver transplantation(LDLT). **Intraoperative urine output was 50ml/hour but increased to about 150-200ml/hour after reperfusion**. The patient was extubated on postoperative day (POD)1 . **On POD 1, the urine output increased to around 500ml/hour**. Fluid restriction was done and samples were sent for serum electrolytes, urine specific gravity, urine and serum osmolality and plasma ADH levels. The investigation reports pointed towards diabetes insipidus although serum electrolytes were in the normal range. Desmopressin nasal spray was started.But there was a decrease in the portal flows on Doppler ultrasound and increasing lactate levels after about 6hours of fluid restriction. This was a major dilemma and it was decided to replace at least 50% of the urine output in addition to the maintenance fluids with portal flow and lactate levels being regularly monitored. On POD 1 the patient had a urine output of 8ml/kg/hour on an average. A magnetic resonance imaging of the brain was also done to rule out any damage to the hypothalamus or pituitary and no abnormality was detected. The frequency of desmopressin spray was increased and the urine output slightly decreased to 5ml/kg/hour on POD 2. On POD2, the urine osmolality and specific gravity increased from the previous day's levels. On POD3, the urine output decreased further to about 1-2ml/kg/hour and desmopressin was discontinued. All throughout the electrolyte levels, lactate levels and portal flows were monitored. Central diabetes insipidus is a rare presentation after LDLT but can affect the mortality and morbidity significantly and thus it becomes imperative for anesthesiologists and intensivists in the LDLT settings to consider this uncommon presentation.

P-038

Severe preoperative QT prolongation is associated with overall mortality after liver transplant: a pilot study

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Background: Prolongation of corrected QT (QTc) is a minor criterion of cirrhotic cardiomyopathy, but it is also a major factor that may cause malignant arrhythmia during surgery. It remains controversial whether prolongation of QTc affects the overall mortality of patients following liver transplantation. The aim of this study was to investigate the effect of prolonged preoperative QTc on the overall mortality of patients after liver transplantation.
Methods: Between November 2008 and July 2018, 50 LT recipients [median age 53 (46-57), Male 31 (62%)] were retrospectively evaluated. As defined by European regulatory guidelines, a QTc >450 ms for males and a QTc >470 ms for females was considered prolonged. Patients with QTc prolongation were subdivided into three categories for analytic purposes: mild (451-470 ms in males; 471-490 ms in females), moderate (471-490 ms in males; 491-510 ms in females), and severe (> 490 ms in males; > 510 ms in females). Kaplan-Meier survival curves was performed to examine the association between the prolonged preoperative QTc and overall mortality rate.
Results: There was 14 (28%) deaths during a median follow-up of 2.8 years. When divided according to the QTc criteria mentioned above, normal was 27 (54%) and abnormal was 23 [mild 8 (16%), moderate 11 (22%), and severe 4 (8%)]. The survival rate of patients was statistically significant among 2 groups (group 1 : normal, mild, and, moderate, vs. group 2: severe) according to QTc considering sex (log-rank test, P=0.018). However, the survival rate of patients was not statistically significant among 4 groups (normal, mild, moderate, and severe) (log-rank test, P=0.09) and among 2 groups (normal and abnormal) (log-rank trst, P=0.341) according to QTc considering sex.
Conclusions: Our results showed that severe preoperative prolonged QTc has an impact on overall mortality in LT recipients, although not mild or moderate QTc prolongation.

P-039

Preoperative opioid use correlates with higher opioid requirements after liver transplantation

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Background: All liver transplant (LT) patients require large doses of opioids for adequate pain control, but pain management for recipients already taking opioids for comorbid conditions is made more complicated due to tolerance and an increased risk of toxicity with higher doses. We sought to investigate the severity of pain after LT as well as the analgesic requirements of patients with preoperative opioid use.
Method: All cases of cadaveric LT performed at the University of Washington between 2008 and 2016 were reviewed. Cases that qualified for the study were divided into two groups of recipients, those with no prior opioid use and those on opioid therapy. Opioid requirements were stratified by calculating morphine-equivalent dosages. Demographic and perioperative outcome variables were also compared between the groups.
Results: Of 322 LT recipients (out of a total of 624), 61 patients were taking opioids before transplantation while 261 patients had no usage prior to surgery (control group). In the control group, opioid requirements were highest in the first 24 hours post-transplant (60.4±33.6 mg) and steeply declined by 72 hours (21.8±18.1 mg). Patients already taking opioids required three times more opioid in the first 24 hours (205.9+318.5 mg, $p < 0.0001$) and continued to have significantly higher requirements at 7 days after transplant (57.0±70.6 mg, $p < 0.0001$) (Figure 1). The first 24 hour opioid requirements were correlated with daily opioid doses before transplant ($r2=0.97$).
Conclusion: Liver transplant recipients with no prior opioid use require 60 morphine milligram equivalents during the first 24 hours post-transplant. Patients who take opioids have significantly higher, dose-related opioid requirements after surgery compared to those not previously taking opioids. Opioid-associated comorbidity in these patients warrants further investigation.

P-040

Catastrophic events during liver transplantation - strategies for team work and organs utilization

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Background: Intracardiac thrombosis (ICT) and pulmonary embolism (PE) during liver transplantation are rare, but potentially lethal complications. Several publications discuss incidence, risk factors, early diagnostic methods, and possible treatment algorithms. There is no information in the literature that addresses an importance of the team based decision process in this critical situation. Our observational study introduces team approach aiming to improve patient care and organs utilization
Methods: We obtained consents from the families for presentation of these two cases.
Results: The first case is a 67 year old patient with recurrent Hepatitis C, ascites, and encephalopathy presenting for re-transplantation with a MELD score of 32. Veno-venous bypass with a heparin-coated circuit was used because the patient was unable to tolerate cross-clamping. The patient was stable after reperfusion, but ninety minutes after discontinuation of bypass, complete circulatory collapse occurred. CPR protocol was initiated. TEE study showed massive thrombus under the aortic valve. A team decision was made to proceed with administration of t-PA. Shortly after administration of t-PA, complete resolution of the thrombus was observed and the patient regained stability.
The second case was a 63 year old male with Hepatitis B, cirrhosis, and kidney failure on hemodialysis. The MELD score was 40. During dissection which required 10 units of blood and 5 units FFP, sudden hemodynamic collapse refractory to high doses of vasopressors and direct cardiac massage occurred. TEE demonstrated a cavo-atrial junction thrombus extending to the pulmonic valve. After consultation with the surgical team and cardiac surgeon, a decision was made to stop resuscitative efforts and use the liver graft for a different recipient.
Conclusion: A multidisciplinary approach addressing analysis of the complication patient status, and a differential of solutions is extremely important in providing the optimal care for patients suffering from this devastating complication.

P-041

Factors associated with immediate extubation after liver transplantation in adults

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Immediate extubation after liver transplant may lead to improved patient satisfaction, reduced costs and shorter length of stay. We retrospectively collected data on 148 consecutive adult OLTs from June 2, 2017 to November 12, 2018 to analyze factors associated with immediate extubation in the operating room after completion of the procedure. The piggy-back surgical technique was used and general anesthesia consisting of inhalation agent and low dose narcotics. The table demonstrates factors associated with immediate extubation. No patients required re-intubation. Comparison of listing MELD and % extubation showed MELD ≤20 was 85%, MELD 21-25 was 82%, MELD 26-30 was 68%, MELD 30-39 was 50% and MELD ≥40 was 33%. Factors most associated with immediate extubation were procedures < 4 hours operating room time, minimal blood transfusions (0-4 units) and completion of cases during daytime hours. Obesity did not reduce extubation as patients > 100 kg were extubated 69% of the time.
Immediate extubation may decrease morbidity, reduce costs, improve patient satisfaction and shorten length of stay after liver transplantation. Our approach did not lead to any re-intubations post-operatively. Understanding what factors are associated with immediate extubation may assist physicians in identifying opportunities for improving care of OLT patients.

Overall Extubation	68%
OR Time < 4.0 hours	80%
Resident Case	64%
CRNA Case	76%
Weight >100 kg	69%
Finish 10pm-6am	50%
SLK	32%
0 Units RBC	97%
1-4 Units RBC	61%
>4 Units RBC	0%

[Factors Associated with Immediate Extubation in OLT]

P-042

ROTEM values vary among liver transplant recipients according to etiology of liver failure and MELD score

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Background: Rotational thromboelastometry (ROTEM) is a global test of coagulation that measures whole-blood clot formation, strength and lysis. ROTEM has been used to assess bleeding risk and guide administration of pro-coagulants in liver transplantation (LT). Patients with advanced liver disease frequently exhibit abnormal coagulation based on ROTEM and conventional coagulation tests. Our primary aim was to determine whether ROTEM values varied among patients with different etiologies of liver failure presenting for LT.
Methods: We included 408 adults presenting for LT at UCLA between 7/2015 and 8/2018 and excluded re-do transplants, combined cardiac procedures, patients on medications that may affect coagulation, and patients for whom no ROTEM data was available. After anesthesia induction and prior to incision, arterial blood samples were collected. Etiology of liver failure was determined from the attending surgeon's operative report. MELD scores were determined from UNOS data, except for patients who received MELD-exception points, in which case MELD was recalculated using laboratory values from blood samples within 24-hours prior to transplant (Lab-MELD). Five ROTEM parameters (CT-EXTEM, CT-INTEM, Alpha angle-EXTEM, MCF-EXTEM and MCF-FIBTEM) were analyzed.
Results: 328 patients had a single etiology of liver failure and were subdivided into six groups (NASH, alcoholic, viral, cholestatic, fulminant hepatic failure and other). Patients with cancer were included in the aforementioned groups. Linear regression demonstrated all five ROTEM parameters were significantly different between groups ($p < 0.05$). Additionally, multivariate regression models including both etiology of liver failure and MELD demonstrated all ROTEM parameters except CT-EXTEM were significantly different among groups.
Conclusion: In this pilot study of a LT cohort, ROTEM profiles differed among patients with various etiologies of liver failure. Etiology of liver failure and chemical-MELD score are important considerations when assessing anticipated abnormalities in coagulation and bleeding risk during surgery.

Clinical characteristics given as either number, percentage, or mean (SD)	Total, n=396	NASH, n=76	Alcoholic, n=87	Viral, n=81	Cholestatic, n=22	Fulminant, n=20	Other, n=42	P
Etiology of liver disease (%)		23.2%	26.5%	24.6%	6.7%	6.7%	12.8%	
Gender M/F (%)	57.8/42.2	31.6/68.4	75.6/24.4	83.9/16.1	31.8/68.2	26.3/73.7	34.9/65.1	<0.001
Age (yr)	55.3 (11.3)	59.2 (9.2)	51.4 (10.9)	61.3 (6.9)	49.1 (12.2)	47.3 (16.8)	50.8 (13.7)	<0.001
BMI (kg m-2)	28.5 (7.3)	31.4 (9.9)	27.7 (6.1)	27.7 (5.6)	26.0 (6.9)	30.3 (7.7)	27.1 (5.4)	0.002
Lab-MELD	33.1 (11.3)	35.7 (9.6)	37.2 (7.2)	22.9 (13.6)	34.8 (9.4)	37.8 (4.4)	35.3 (9.7)	<0.001
Hepatobiliary Cancer	25.6%	18.4%	5.8%	66.7%	9.1%	0%	11.9%	<0.001
ROTEM parameters given as median (IQR)	Reference range for healthy subjects	NASH, n=76	Alcoholic, n=87	Viral, n=81	Cholestatic, n=22	Fulminant, n=20	Other, n=42	P
CT-EXTEM	43-82 s	101.5 (74-135)	111 (85-148)	75 (62-100)	99 (72-151)	95 (75-188)	78 (70-110)	0.002
CT-INTEM	122-208 s	246.5 (206-303)	252 (223-297)	202 (166-256)	219 (187-264)	230 (202-300)	197 (175-241)	0.001
Alpha angle-EXTEM	65-80 degrees	49 (40-57)	47 (37-56)	57 (44-71)	59 (41-73.5)	52 (36-68)	56 (45-56)	0.002
MCF-EXTEM	52-70 mm	36 (29-42)	33 (27-40)	41 (32-53)	44 (30-55)	39 (33-47)	40 (33-52)	<0.001
MCF-FIBTEM	7-24 mm	6 (4-9)	5 (3-8)	8 (5-14)	7 (5-17)	6 (4-9)	8 (5-13)	0.002

SD = standard deviation; NASH = non-alcoholic steatohepatitis; BMI = body mass index; MELD = model for end stage liver disease; ROTEM = rotational thromboelastometry; IQR = interquartile range

[Clinical characteristics of study LT recipients according to etiology of liver failure.]

P-043

Change to the universal use of male FFP product and decreased mortality after FFP transfusion in liver transplant recipients

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Background: Transfusion of fresh frozen plasma (FFP) donated by female donors with a history of pregnancy is associated with increased risk of mortality, being possibly due to pregnancy-related antibody production and lung injury. In Korea, FFP production has been allowed only for blood donated by males since July 2009. We hypothesized that conversion to universal male FFP use decreases mortality after FFP transfusion. In this study, we compared the association between perioperative FFP transfusion and post-transplant mortality before versus after the conversion to universal male FFP use in patients who underwent living donor liver transplantation.
Method: We analyzed the data of 686 recipients who underwent a first living donor liver transplantation in our hospital between July 2004 and July 2013 (representing 4 years before and after the conversion to universal male FFP use). The primary outcome was post-transplant overall survival. Survival analysis was performed by using the Cox model. We evaluated the association between FFP transfusion and survival probability in mixed donation group and in male donation group, respectively.
Results: The median follow-up time was 55 months. In mixed donation group, FFP transfusion was significantly associated with survival in univariable analysis ([HR=1.039 (1.025-1.052), P=0.000) and in multivariable analysis (HR=1.06 [1.032-1.094], P=0.000). In male donation group, FFP transfusion was not significantly associated with survival in univariable analysis (HR=1.002 [0.992-1.013], P=0.646) and in multivariable analysis (HR=1.003 [0.993-1.014], P=0.519, Table 2).
Conclusion: FFP transfusion negative affected survival of liver transplant patients when FFP units were produced irrespective of donor sex. In contrast, we found no evidence that FFP worsens post-transplant survival when FFP units were produced only from male donors. Also, we found that the conversion to universal male donation improved survival after perioperative FFP transfusion.

P-044

Does intra-operative use of albumin affect post-operative outcomes in patients undergoing living related liver transplantation - a single center experience

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Background: The use of albumin in critically ill patients has been extensively debated since most studies have shown mixed results. However many anesthetists use albumin intra-operatively during liver transplantation as most of the patients are hypoalbuminemic & also for the fact that albumin is presumed to protect the integrity of endothelial glycocalyx.As there are few studies which have analyzed whether intra-operative use of albumin affects post operative outcomes, we attempted to do the same.
Materials and methods: We queried a prospectively maintained database of 179 Liver transplantation recipients between 2015-2016 out of which 109 patients received albumin during the operation whereas 70 did not. The post operative outcomes analyzed were duration of mechanical ventilation,inotropic support,Incidence of AKI,post operative ileus, respiratory complications,early sepsis, duration of stay in ICU&1-month mortality.
Results: The results are summarized in table 1. The incidence of post operative ileus,respiratory complications,mean ICU stay & SOFA score were significantly higher in the non-albumin group, however there was no statistically significant difference in post-operative sepsis, AKI & 1-month mortality.
Conclusion: Our retrospective analysis concludes that use of albumin intra-operatively reduces post - operative morbidity viz ileus & respiratory complications, along with reducing ICU stay. However no significant reduction in AKI, sepsis & 1 month mortality was noticed.

Post Operative Outcomes	Albumin Group	No albumin Group	P- Value
SOFA Score at Day 10	6.5±2.96	11.2±1.7	<.001
Ileus	11.9%	55.7%	<.001
AKI	28.4%	40%	.075
Respiratory Complications	38.5%	52.9%	.042
Early Post Op Sepsis	25.7 %	27.1 %	.481
Mean ICU Stay	10.4±2.2	12.4±1.5	<.001
1 Month Mortality	8.3%	10%	.442

[Post Operative Outcomes]

P-045

Protective effect of ischemia-free liver transplantation procedure on remote organs

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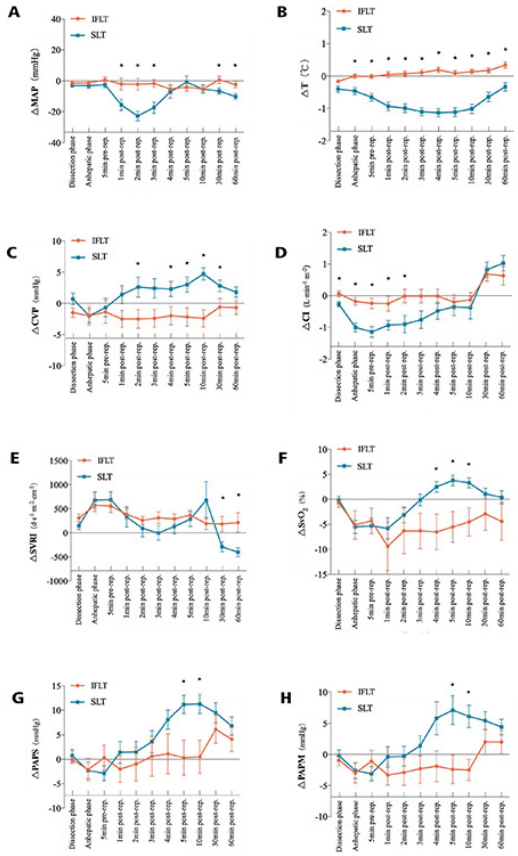
Background: Hypothermia, hypoxia and ischemia-reperfusion injury (IRI) in standard liver transplantation (SLT) are the main factors that affect graft function and cause damage to remote organs. We aimed to compare the hemodynamics and multi-organ function between ischemia-free liver transplantation (IFLT) and SLT using cold storage as a preservation method.
Methods: We prospectively collected perioperative data from IFLT and SLT, and compared the stability of hemodynamics, the incidence of post-reperfusion syndrome, and the function of heart, lung, kidney between the two groups.
Results: Between July 2017 and April 2018, a total of 14 cases of IFLTs and 28 cases of traditional standard liver transplantations were included in our study. Compared with IFLT group, the SLT group had a significantly decreased blood temperature (T) (△T -0.46±0.58 vs. 0.00±0.24, p=0.007) and cardiac index (CI) (△CI-1.00±0.69 vs. -0.18±0.40, p=0.000) in anhepatic phase. After reperfusion, the mean arterial pressure (MAP) of the SLT group (△MAP2min -22.8±17.0 vs. -2.3±14.2, p=0.000) declined dramatically, meanwhile pulmonary artery systolic pressure (△PAPS5min 11.2±7.7 vs. 0.3±11.4, p=0.006) and central venous pressure (CVP) (△CVP5min 3.0±5.8 vs. -2.2±4.9, p=0.017) and mixed venous saturation (SvO2) (△SvO25min 3.8±4.3 vs. -5.5±10.2, p=0.014) increased significantly compared to that of the IFLT group. In postoperative period IFLT group had a lower incidence of renal replacement therapy (7.1% vs. 17.9%, p=0.640), and shorter intensive care unit (ICU) stay (41.6h vs. 65.2h, p=0.040).
Conclusions: Compared with the SLT procedure, patients with IFLT have more stable intraoperative blood temperature and hemodynamics. The IFLT is associated with minimal effects on multiple organs such as heart, lung and kidney. Therefore, IFLT can reduce the perioperative risks for the recipients.



[Fig. 1]

P-046

Hyponatremia prior to liver transplantation is not associated with post-operative encephalopathy

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Background: Hyponatremia occurs in about 15% of patients with end-stage liver disease with associated waiting list mortality; however, its impact on post-operative encephalopathy and survival after transplantation remains unclear.
Methods: Patients with pre-operative hyponatremia, defined as a serum sodium (SNa) < 130 mmol/L and a SNa shift within the first 24 hours following liver transplantation, have been evaluated between January 2004 and December 2016 retrospectively. Liver disease, hepatic encephalopathy, intra-operative / peri-operative SNa levels and shift of SNa were compared between patients with and without neurological symptoms.
Results: While 8.1% (16/198) of patients presented with pre-operative hyponatremia a rapid increase of SNa (ΔNa > 10 mmol/L) was observed in 16.7% of patients. There were 12 patients (6.1%) with neurological symptoms and 1 patient (0.5%) developed central pontine myelinolysis (CPM) with a ΔNa > 12 mmol/L; however, both hyponatremia and rapid increase of SNa did not have any impact on neurological symptoms (p>0.1). Further there was no significant correlation between neurological symptoms and both hyponatremia and rapid increase of SNa.
Conclusion: Hyponatremia is not a contraindication for liver transplantation; however, a rapid increase of SNa shall be omitted to prevent CPM. Thus a careful monitoring of SNa is a prerequisite for the patients' safety during liver transplantation.

P-047

Four wavelengths cerebral oximetry was not affected by hyperbilirubinemia

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Aim: Regional cerebral oxygen saturation (rSO_2) measurements can detect disturbances in cerebral oxygenation. However, the accuracy of rSO_2 using two wavelength sensors has been shown to be compromised in patients with hyperbilirubinemia. The effect may be due to the bilirubin that is deposited throughout all tissue layers absorbing 730 nm wavelength which is similar to the absorption spectrum of deoxyhemoglobin, causing falsely low rSO_2 levels (1). It was speculated that rSO_2 using multiple wavelengths may overcome this problemby Nielsen and Larsen (2). In this paper, we present rSO_2 performance in five liver transplantation recipients with hyperbilirubinemia (higher than 15 mg/dL).
Methods: Before induction of general anesthesia, rSO_2 using two-wavelength sensors showed lower than 40% (mean 28 from both forehead sensors) in all five patients with hepatic failure (Child's score: 11.8 (mean); MELD: 25.6 (mean)). The two-wavelength rSO_2 probes were removed and exchanged for sensors using four wavelengths.Repeated rSO_2 measurement on the same sites showed a mean 60% in left side and 58.2% in right side. During the liver transplantation operation, rSO_2 was measured to be within 20% of basal level. Preoperative mean value of total bilirubin was 21 mg/dL (range 18 to 26 mg/dL) and mean Hb was 9.6 mg/dL (range 8.2 to 10.6 g/dL).
Conclusions: End-stage liver disease patients undergoing liver transplantation,we found that rSO_2 using two wavelengths was impacted by very high total bilirubin values. However, rSO_2 measured with a four-wavelength sensor (O3™, Masimo, Irvine, CA) was not affected by very high total bilirubin.
References:
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P-048

Intraoperative management to prevent cardiac collapse in a patient with large amount of pericardial effusion and paroxysmal atrial fibrillation during liver transplantation: a case report

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Background: The pericardial effusion was frequently described in patients with end-stage liver disease. This case report outlines intraoperative management without re-pericardiocentesis to prevent circulatory collapse on critical surgical timing, including manipulation of major vessel and graft reperfusion.
Case report: A 47-year-old female patient (height 161 cm; weight 81 kg) with hepatitis B was scheduled to undergo deceased donor liver transplantation (LT). Large pericardial effusion was preoperatively identified using transthoracic echocardiography (TTE), and paroxysmal atrial fibrillation was occurred. 2 days before surgery, preemptive pericardiocentesis was performed and 1,150 mL effusion was drained. Intraoperatively, recurrence of large pericardial effusion was identified using transesophageal echocardiography (TEE). During inferior vena cava manipulation, the transplant surgeon consulted the transplant anesthesiologist to evaluate the hemodynamic changes. After three times trials, the transplant team was able to find the most appropriate anastomosis site to less impact cardiac function. As a preventive regimen

over severe postreperfusion syndrome (PRS), on 20 min before portal vein declamping, 10% $MgSO_4$ of 2 g was gradually infused; and immediately before graft reperfusion, epinephrine of 100 µg bolus was administered. During graft reperfusion, there were no evidences to develop heart chamber collapse or flow disturbance in TEE findings. Postoperatively, the patient was completely recovered to discharge the hospital. 6 months after the surgery, there was no pericardial effusion in follow-up TTE finding.
Conclusions: Our intraoperative strategy could be one of applicable methods to prevent cardiac collapse without re-pericardiocentesis during LT. Additionally, intraoperative TEE may play an important role to guide hemodynamic management in patients who impaired cardiac dysfunction.

P-049

Liver transplantation in cirrhotic patients in the intensive care unit with acute on chronic liver failure (ACLF)

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Introduction: Liver transplantation (LT) in cirrhotic patients with ACLF admitted to the ICU is a major debate. The aim of this prospective study was to evaluate the feasibility of LT, outcome and factors associated with mortality of these patients.
Methods: All consecutive patients admitted to the ICU with ACLF, were included in our study.
Results: From July 2017 to September 2018, 120 patients were admitted to the ICU with 131 admissions. Reasons for patients' admission were septic shock (23.6%), upper digestive bleeding (23.6%), acute kidney injury (17.6%) and acute respiratory distress syndrome (12.2%). The 28-days mortality was 41.3% (n= 77) and the 90-days mortality was 55.7% (n= 58). At admission, 19.2% had ACLF grade 0, 17.5% grade 1, 20% grade 2 and 43.3% grade ≥3. The 28 days mortality rate was 4.3% in patients without ACLF and respectively 33.3%, 33.3% and 67.3% in ACLF grade 1, grade 2 and grade ≥3 patients. Fifty-five patients were evaluated for the LT (45.8%) and 31 were listed (25.8%). Overall, 18.3% of the patients were transplanted with 100% 90 days post-LT survival; 8 patients died while on list and 1 patient is still on the waiting list. In univariate analysis, coma at admission, mechanical ventilation at admission (for neurologic failure or respiratory failure), SAPS 2 score, SOFA score, number of organ failure at day 2 and the use of catecholamine during ICU stay were associated with less transplantation. MELD score and age were not associated with liver transplantation.
Conclusion: The global mortality of cirrhotic in ICU was 56.7% and day-28 mortality rate was 41.7%. LT in selected patients was associated with excellent survival. Coma at admission, SAPS 2 and SOFA score, CLIF-OF at day 2 and the use of catecholamine were associated with less access to LT.

P-051

Effect of type of intra operative fluid on post operative liver function tests in donor hepatectomy: large retrospective study in 890 patients

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Background and aims: Ensuring best outcomes for the donor is necessary in the background of living donation. There is limited literature evaluating the impact of intraoperative fluids on liver function profiles in living donor hepatectomy. This study was done to compare the impact of type of fluid therapy (balanced solution vs. isotonic saline) on the postoperative liver function tests in these patients.
Methodology: The data for 890 patients, who underwent living donor hepatectomy at Apollo Hospitals, New Delhi, was retrospectively analysed. These patients were divided into two groups, group A comprising 583 patients who received isotonic saline intraoperatively, and group B of 307 patients who received balanced solutions. Basic profile of all patients with respect to age, gender, weight, height, intraoperative duration was noted. Assessment of clinical data for both the groups was carried out for following post-operative parameters - total serum bilirubin, serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and serum albumin.. Statistical tool used for evaluation and analysis of the clinical data is student's t-test at (95% confidence level).
Results: All the above post-operative parameters were measured for both the groups on 1st, 3rd and 7th day of the surgery. The mean bilirubin levels, AST,ALT and serum albumin levels were analysed. Difference between two groups on the basis of these measurements were found to be statistically insignificant.
Conclusion: Our study shows that there is no statistically significant difference in the postoperative liver function tests on the basis of type of intraoperative fluid used. However, randomized multicentric trials with larger numbers of patients may be needed to further evaluate the effect intraoperative fluid on donor outcome.

P-052

Successful living related liver transplantation in a scenario with both donor and recipient having sickle cell trait: a case report

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Orthotopic liver transplantation in a patient with sickle cell disease presents many new challenges to the transplant team. We describe the case of a 48-year-old patient with sickle cell disease and hepatitis C virus-induced cirrhosis who required liver transplantation. Various prospective donors were put through a battery of tests and only suitable donor was found out to be sickle cell trait. Recipient had vaso-occlusive crisis prior to transplant in the form of joint pains, which were managed conservatively using Hydroxyurea and Non steriodal anti-inflammatory drugs. Hypoxaemia, acidosis and a decrease in body temperature are common occurrences that can cause sickling in the peri-operative period, putting the patient at risk of sickle-cell crises or graft dysfunction in case of recipient. Hb electrophoresis was performed in both donor and recipient which revealed HBS fraction of 33.5% in donor and 36.3% in recipient. Perioperatively the haemoglobin S fraction was maintained below 30% and the total haemoglobin level was maintained between 8 and 10 g/dL (in recipient) through intermittent blood-letting and replacement blood transfusion . Post operatively both donor recipient was put on antiepileptic prophylaxis. None of them developed any vaso-occlusive crisis post operatively. Rest of the postoperative course was also uneventful. Donor was discharged after 7 days and recipient after 21 days as per institute protocol. Requisite counselling was done with regards liver transplant and sickle cell trait related future care.

P-053

Use of high-flow nasal cannula vs standard oxygen therapy via venturi mask in liver transplantation after extubation to prevent the hypoxemia: a matched-controlled study

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Post-operative hypoxemia is common after liver transplantation (LTx). High flow nasal cannula (HFNC) oxygen therapy is a innovative therapy used in patients with acute respiratory failure. We conducted a matched-controlled study aiming to compare the effectiveness of preventive oxygen therapy delivered by HFNC versus Standard Oxygen Therapy (SOT) via Venturi mask after extubation in adult LTx patients. Primary end-points were the reduction of hypoxemia (defined as partial pressure of arterial oxygen to fraction of the inspired oxygen ratio [Pa_{02}/FI_{02}] < 300) at 1 and 24 hours post-extubation. Secondary end-points were re-intubation or non-invasive ventilation (NIV) requirement rate, ICU length of stay (LoS) and 28-days mortality. Twenty-nine ICU LTx patients, admitted to our ICU intubated and mechanically ventilated, received HFNC after extubation (HFNC group) and were matched 1:1 with 29 controls (SOT group) chosen from a historical group of 90 patients admitted in the previous 36 months. Matching criteria were: age, MELD, Simplified Acute Physiology Score II, and BMI. HFNC and SOT were applied for 24 hours after extubation. Incidence of hypoxemia was similar between HFNC and SOT group at 1 hour (41% vs 48%, p=0.81) and 24 hours (45% vs 34%, p=0.63) after extubation. However, the Pa_{CO2} value 1 hour after extubation was lower in the HFNC group compared to the SOT group (p< 0.05). In HFNC group incidence of re-intubation and NIV requirement was lower compared to SOT group (3% vs 7% and 3% vs 17%, respectively) but not significant. ICU LoS and 28-days mortality were similar between groups.Early application of HFNC in LTx patients did not reduce the incidence of hypoxemia after extubation compared to SOT and did not modify re-intubation or NIV requirement rate, ICU LoS and 28-days mortality. Further studies are needed to identify the best candidates to HFNC.

P-054

Intravenous methylene blue versus hydroxocobalamin as treatment for intraoperative vasoplegic syndrome in liver transplant patients

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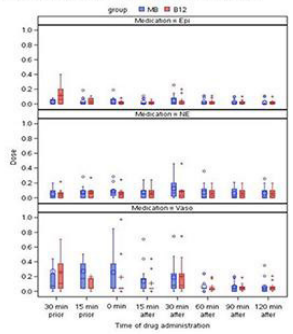
Background: Intraoperative vasoplegic syndrome(VS) with hypotension, increased cardiac output, and low systemic vascular resistance(SVR) is a common complication in liver transplantation (LT). VS has been treated via methylene blue(MB) and hydroxocobalamin(Cyanokit, Meridian Medical Technologies, Inc., Columbia, MD, USA), a form of vitamin B12. The development of VS contributes to the morbidity and mortality following LT. Identifying the most effective treatments for VS may greatly improve outcomes and survival rate in patients undergoing LT.

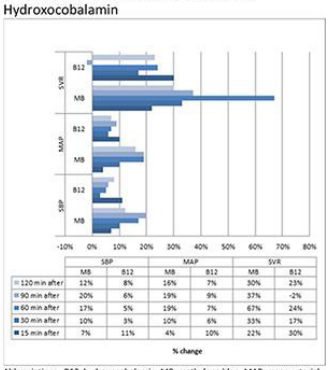
Method: A retrospective chart review was conducted for LT surgeries performed between January 2016 and June 2018. If MB or hydroxocobalamin was used to treat VS during the procedure, the SVR, mean arterial blood pressure(MAP), systolic blood pressure(SBP), and vasopressor requirements at 0, 15, 30, 60, and 90 minutes after the medication administrations were recorded. If both medications were used during the procedure, the hemodynamics and vasopressor requirements after the second medication administration were still recorded and the first medication was marked as ineffective on treating VS.
Results: 401 LT were performed during the study period, 14 patients presented with intraoperative VS and received MB as the first-line VS treatment. 9 of the 14 patients received hydroxocobalamin after MB was ineffective on reducing pressor requirements and/or on improving hemodynamics. Figures show the pressor dosages and changes of hemodynamics after VS treatments.
Conclusion: Due to the institutional protocol, hydroxocobalamin was only administered after MB was deemed ineffective. Without significant differences of pressor requirements between the medications, the MB group appeared to have higher percentage of SVR increase as the patients with responses to MB would not further receive hydroxocobalamin. No clear comparison between the medications was possible. The findings support future prospective, randomized study on the effectiveness of MB versus hydroxocobalamin as VS treatment in LT surgeries.

Figure 1. Pressor Dosages in Liver Transplant Patients with Vasoplegic Syndrome Treated with Methylene Blue versus Hydroxocobalamin



Dose units: mcg/kg/min for Epi and NE. units/min for Vaso.
Abbreviations: B12, hydroxocobalamin; Epi, epinephrine; MB, methylene blue; NE, norepinephrine; Vaso, vasopressin.

Figure 2. Hemodynamic Changes after Administration of Methylene Blue versus Hydroxocobalamin



	SBP		MAP		SVR	
	MB	B12	MB	B12	MB	B12
120 min after	12%	8%	16%	7%	30%	23%
90 min after	20%	6%	19%	9%	37%	-2%
60 min after	17%	5%	19%	7%	67%	24%
30 min after	10%	3%	10%	6%	33%	17%
15 min after	7%	11%	4%	10%	22%	30%

Abbreviations: B12, hydroxocobalamin; MB, methylene blue; MAP, mean arterial pressure; min, minutes; SBP, systolic blood pressure; SVR, systemic vascular resistance.

[Figures 1 and 2]

P-055

To evaluate the incidence, causes and management of early postoperative neurological complications in recipients who undergo adult living-donor liver transplantation at a high volume centre

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Background: Neurological complications (NC) are especially common following liver transplantation due to poor pre-operative clinical conditions of patients (prolonged surgery, electrolyte imbalance, malnutrition, coagulopathy, etc). They cause significant morbidity and mortality.
Methods: Analysis of prospectively collected data was done, patient demographics, indication for transplantation, comorbidities, pre-transplant investigations, immunosuppressant used, occurrence and nature of neurologic complications, length of stay post-transplant and outcomes were studied.
Results: Neurological complications were observed in 149 patients out of 1778 patients included in the study (8.3%). In our study, NCs were most widely seen in males (124 as compared to 25 females- 83.2%), those aged 45 and above (91 patients- 61%). The primary cause of liver disease was alcohol in 37.5% patients, followed by cryptogenic in 23.4% and hepatitis C in 18.1%. The most common presenting symptoms observed were seizures (44/149- 29.5%) and psychosis (43/149- 28.8%). More fatal symptoms were cerebrovascular disorder (CVA- 13.4%) and Central Pontine Myelinolysis (CPM- 3.3%). Approximately one-third of these managed by reducing/altering immunosuppressant (27.5%) or conservative management (7.3%). Antipsychotic medication was started in (34.2%) & antiepileptic medication in (33.6%). Only 2% (3/149) required surgical intervention of which 2 recovered.
Index admission mortality was seen in 12/149 patients (8.1%) which was not different from mortality seen in non- neurological complication group.
Other complications observed were immunosuppression neurotoxicity (4.7%), neuromuscular disorders (11.0%) and altered behaviour/stroke/delirium (20.0%). The mean length of stay in ICU was 7.32 days in these patients as opposed to 6.12 days for those who did not have any NC ($p< 0.05$). The total hospital stay was also longer in these patients-20.57 days.
Conclusion: NC among transplant recipients is common and lead to longer ICU stay. Awareness and anticipation of such neurological complications is vital. The majority are managed conservatively with or without change in immunosuppression. Neuro-surgical intervention is seldom indicated.

P-056

Successful orthotopic liver transplantation in severe persistent bradycardia recipient: a case report

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Background: Cardiac electrophysiological disturbances is common in end-stage liver disease (ESLD) patient[1].It is a challenge for anaesthesiologist to detect cardiac abnormality and provide a good care for the patient.
Case report: A 58 years-old, male patient was diagnosed as hepatitis B cirrhosis with HCC (MELD score 24) and sent to do orthotopic liver transplantation (OLT). His co-morbidities included obesity (BMI 32kg/m^2) and chronic kidney disease stage V (no hemodialysis requirement). Investigation revealed mild anemia, thrombocytopenia, rising of creatinine, normal electrolytes and INR 1.47. His CXR showed cardiomegaly. ECG showed sinus bradycardia, rate 45/min with prolonged QT interval. Echocardiography revealed dilatation of all cardiac chambers with normal ejection fraction (65%), good RV function, mild pulmonary hypertension (mPAP 29 mmHg) without significant valvular abnormality. After uneventful induction and intubation, he also received non-invasive CO monitoring and CVP as additional. He started with sinus bradycardia, 35 - 40 bpm, in-charged staff started to infuse dobutamine 3 and titrate up to 10 mcg/kg/min, with no response, but stable blood pressure and CO(5-6L/min). Epinephrine was started just before anhepatic phase, but his heart rate stayed slow. He passed trial clamp with severe bradycardia but acceptable blood pressure, CO result disappeared. External pacing pads with defibrillator were then prepared. His ABG showed mild acidosis without electrolyte abnormality. Reperfusion phase went successfully. He was remained intubation and transferred to ICU. Twelve-lead ECG was performed and cardiologist was consulted. Two to one AV block was diagnosed and transvenous pacing was inserted at rate 80/min for 48 hours, then his heart rate was at 50-60 bpm without treatment. He was extubated at 36 hours after surgery and discharged at postoperative day 10.
Conclusion: Cardiac conduction abnormality in ESLD patient presented with various form[2]. Proper preoperative assessment, adequate monitoring and good team communication result in good patient outcome[3].

P-057

Transfusion strategy for ABO incompatible living donor liver transplantation: our first experience a case report

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Introduction: ABO incompatible living donor liver transplantation (ABOi LDLT) is a treatment option for saving lives from end-stage liver disease. Although graft and patient survival have been improved by various treatment options in the recent years, no standardized treatment protocols for ABOi LDLT exist.
Case presentation: 55 year old Chinese male with history of hepatocellular carcinoma presented with worsening signs and symptoms of portal hypertension. Liver transplant was offered to him as a curative treatment option as patient was not a suitable candidate for liver resection or radiofrequency ablation of the tumor. Due to the acute worsening of his condition, patient was planned for ABOi LDLT.
Careful planning and preparation was done prior to the surgery as patient's blood group is B+ and the donor's group is A+. Therapeutic plasma exchange and apheresis were performed. Immunosuppressant therapy was administered for further eradiation of antibody producing cells. Anti-A antibody titer in the recipient's plasma was trended. Leukocyte depleted B+ red blood cell consistent with recipient's blood group was cross-matched preoperatively for the need of intraoperative transfusion. AB+ type of fresh frozen plasma, cryoprecipitate and pooled platelet were also prepared which are universal donors as they lack of any antibodies. Patient was sent to intensive care unit for closer monitoring post-operatively. Anti-A antibody titer was closely monitored. No hyperacute antibody mediated rejection was noted.
Discussion: ABOi LDLT is an option used in emergency situations which require careful planning. The use of immunosuppressant regime as well as therapeutic plasma exchange and apheresis has improved ABOi graft survival rates.[1] Preoperative arrangement of patient compatible blood products is also critical for the success of operation.
References: 1. Rummler S et al. Current techniques for ABO-incompatible living donor liver transplantation. *World Journal of Transplantation* 2016; **6**: 548-55.

P-058

Changes in glutathione homeostasis during living donor hepatectomy

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Background: Glutathione, a tripeptide molecule, plays a key role in the regulation of many enzymatic reactions. It is an important scavenger molecule, participating in metabolism of various drugs. The bulk of plasma GSH originates from the liver, which plays a central role in the interorgan homeostasis of GSH. Thus, dysregulation of hepatic GSH synthesis after hepatectomy can have impact on GSH homeostasis systemically. Animal models have shown that hepatic GSH levels increase 12 hours after partial hepatectomy but no trial have been done in humans.
Importance of the proposed project: This study will help in assessing the changes in plasma glutathione levels after living donor partial hepatectomy and will help future research on the need of drug dosage modification after hepatectomy.
Methodology: In the study, 3ml venous sample was withdrawn for glutathione estimation before induction of anesthesia, 30 minutes after hepatectomy, 12 and 24 hours after hepatectomy. Plasma Glutathione levels were estimated by ELISA method.
Results: The mean plasma glutathione value was 38.03 + 9.57 µg/ml at baseline, which decreased significantly to 19.99 + 5.49 µg/ml, 30 minutes after hepatectomy. As the liver started regenerating, it was evident that plasma glutathione started rising 12 hours after hepatectomy (24.7 + 6.87 µg/ml) and remained almost similar at 24 hours post hepatectomy (24.89 + 7.93 µg/ml). However, this decrease in plasma glutathione at 30 minutes post hepatectomy did not correlate with the residual liver volume.
Conclusion: Plasma glutathione levels decrease significantly after hepatectomy and may require the dose modification in drugs utilising glutathione in their metabolism, e.g. paracetomol, diclofenac. Further research is required in this field.

P-059

Effect of fecal microbiota transplant on the recovery of patients after liver transplantation

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Objective: Gastrointestinal symptoms are the first symptoms of liver disease. The intestinal dysfunction or intestinal flora imbalance always accompany with the progress of liver diseases. After liver transplantation, the use of various drugs (especially antibiotics) further damage the intestinal flora, result in bloat, diarrhea even malnutrition and infection, which seriously affects the prognosis of patients. This paper we investigate the effects of fecal microbiota transplantation on patients after liver transplantation.
Methods: 49 Patients with severe hepatitis were randomly divided into two groups after liver transplantation. In the testing group, 20 patients (18male,2female) was received retention enema with 200ml feces solution every three days after liver transplantation. The fecal donor was the same sex healthy member from the family of the receptor and had no smoke, no drink, no drugs in the last three months. 29 patients (24male, 5female) in the control group were received retention enema with 200ml Physiological saline every three days after liver transplantation. The nutritional status, Infection status, liver function were compared on postoperative day 10 and 20. The prognosis, and the length of hospitalization in ICU of the patients were also compared between the two groups.
Results: There were no different betwent two groups on day 10 postoperative. But on day 20 postoperative, the level of AST, ALT, total bilirubin, urea nitrogen, rate of infection and the length of hospitalization in ICU in testing group were all lower than that in control group ($P < 0.05$). The pro-albumin level were higher than that in control group ($P < 0.05$).
Conclusion: Gut microbiota imbalance is a common problem for patients with severe liver diseases. Fecal microbiota transplant can help restoring the balance of intestinal flora, reducing toxin and infection, all of which is beneficial to recovery of liver function after liver tansplantation.

P-060

Intraoperative Reverse Takotsubo cardiomyopathy in liver transplantation - an anesthesiologist's nightmare

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Reverse Takotsubo cardiomyopathy, rarest type of stress cardiomyopathy typified by a transient systolic dysfunction of the basal segments of left ventricle, in the absence of obstructive coronary artery disease.We present an extremely challenging case of intraoperative Reverse Takotsobo Cardiomyopathy in LDLT. A 19 year male, with extrahepatic biliary atresia was taken up for transplantation. There was no history of any cardiac comorbidity and echocardiography was normal with an ejection fraction of 60%. Induction was done with fentanyl, propofol and atracurium. In the dissection phase, the patient suddenly had an episode of ventricular tachycardia which reverted on its own after 30 seconds. Then he had atrial fibrillation, amiodarone was given as bolus dose followed by infusion. The ECG started becoming variable with rhythms like ventricular tachycardia, junctional rhythm, atrial ectopics, atrial fibrillation, alongwith small periods of sinus rhythm. The patient also developed hypotension and noradrenaline infusion was started. A TEE was done, and it showed posterobasal and anterolateral hypokinesia with apical sparing, with an EF 20% and severe mitral regurgitation. The cardiologist diagnosed it to be reverse Takotsubo cardiomyopathy, and as per advice, noradrenaline was replaced with adrenaline and isoprenaline infusions, and cardiac biomarkers and plasma catecholamine levels were sent. The reperfusion phase was uneventful, the patient had severe bradycardia and hypotension just before end of surgery and was managed with isoprenaline and increasing inotrope levels. On POD1 and POD2, the patient had to be cardioverted multiple times, and isoprenaline was tapered off. On POD4, the patient was extubated and the echo showed EF 30% with moderate MR. The ecg rhythm reverted to sinus from POD7 onwards, and the EF increased to 50% on POD10. The patient did not have any subsequent cardiovascular instability. To our knowledge, this is **the first literature on intraoperative Reverse Takotsubo in liver transplantation**

P-061

The "Tricky Triad" of anemia, coagulopathy and massive fluid overload managed with intraoperative phlebotomy and hemofiltration

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A 34-year-old male was admitted with acute decompensation of alcoholic cirrhosis and acute renal failure with a MELD score of 41. He was transferred to our center for combined liver-kidney transplantation.
He presented with shortness of breath, fever and diarrhea. His hemoglobin was 5.9g/dL, platelets 34, and his INR was 3.3. The patient required continuous renal replacement therapy (RRT) and inotropes. He was subsequently intubated for encephalopathy.
He was bleeding from his nose and catheter insertion sites, which was interpreted as coagulopathy and drove transfusions: In the week prior to transplant, he received 15 packed red blood cells, 21 units of platelets, and 67 units of fresh frozen plasma (FFP). He was anuric, RRT was aiming for a neutral balance. An echocardiogram confirmed good ventricular function. A right heart catheterization demonstrated a post capillary wedge pressure of 35mmHg and a pulmonary artery pressure of 46mmHg. There was no continuous CVP monitoring.
In the operating room, an additional central line was placed prior to transplant. His initial CVP was 50mmHg, hemoglobin was 7.8g/dL. A high CVP during liver transplant can compromise graft perfusion and must be avoided. The team had 3 hours to optimize the patient until reperfusion:
1) We removed 1L of blood from the central line using cell-saver
2) We initiated intraoperative RRT with a hemofiltration rate of -999mL/hr for the 3 hours during the dissection phase.
By the time of portal vein clamping, we had reached the target CVP of 8mmHg, and the transplant was completed successfully.
This case illustrates the misinterpretation of venous ooze from venous congestion as coagulopathy. The "tricky triad" of fluid overload, anemia and coagulopathy was managed using hemofiltration and intraoperative phlebotomy.
This case was one of only 4 cases of intraoperative RRT in our cohort of 1500 transplants in the past 9 years.

P-062

Intensivist-led deceased organ donor management

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Introduction: Despite the recent increase number of deceased donors, the demand for transplantable organs continues to exceed the supply. We hypothesized that intensivist-led management of deceased organ donors would increase the number of organs procured for transplantation.
Methods: We retrospectively analyzed data from all adult deceased organ donors during before (2012.01-2014.12.) and after (2015.01.-2017.12.) implementation of an intensivist-led donor management.
Result: Total 116 adult deceased organ donors were included. After intensivist-led donor management, number of an expanded criteria donor (ECD) (n = 24, 50%. vs. n = 16, 23.5%, p = 0.003) was significantly higher than before. Mean arterial pressure before organ procurement was higher (96.50 ± 19.602, vs. 88.16 ± 17.558, p = 0.018) than before. However, vasopressor index score (20.80 ± 23.796, vs. 42.77 ± 64.511, p = 0.012) and vasopressor dependency index (0.22 ± 0.261, vs. 0.54 ± 0.900, p = 0.008) were lower than before. After adjusted for ECD, more than 4 organs procured from a donor was increased (OR 2.50 (95% CI 0.937-6.639), p = 0.067). And that was significant in lungs (OR 3.87 (95% CI 1.469-9.931), p = 0.006) and pancreas (OR 6.00 (95% CI 1.592-22.616), p = 0.008).
Conclusion: Management of deceased organ donors by intensivists may be a profitable strategy to increase organs available for transplantation.

P-063

Short term outcome of liver transplant for acute on chronic liver failure (ACLF) ad acute decompensation (AD): an intention to treat analysis

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Background: ACLF is a serious complication of liver disease characterized by the onset of an event of acute decompensation, organ failure and high mortality rate. A fast track to LT in eligible patients seems to be the only effective therapeutic option. ITT analysis aiming to evaluate the benefit of liver transplant in patients with ACLF are still limited.
Aim: To evaluate the short term overall survival of pts with ACLF and AD according to an ITT analysis.
Methods: From June 17 to June 18,45 pts(22 ACLF and 23 AD) were consecutively enrolled and prospectively followed until last clinical visit, death, drop-out,re-LT.
Results: The main clinical features shown in table 1. Infections were the most frequent trigger event (46.7%; ACLF-59.1% vs AD 34.8%; p=ns). Mean time of hospitalization was longer in ACLF group (50 +30.5 d vs 43.9 + 65.2 d; p=0.028). None of the AD patients needed admission to ICU before OLT. Among ACLF group 5 pts were admitted to ICU and 8 to HDCU. 19 pts were not eligible for LT (10 ACLF and 9 AD) because of active drugs use(42%), age>70y(21.1%), severe comorbidities (21.1%), unwillingness (5.3%) and stable improvement (10.5%-in AD pts). OLT rate were:52.2 % in AD vs 40.9% in ACLF; p=0.45. AD pts had a longer time of observation (212.7 ± 116.4 d) compared to the others(114.5 ± 107.8 d, p=0.005). The rate of the composite endpoint: LT+mortality was 72.7% in ACLF and 52.2% in AD group (p=0.155). Time to endpoint was shorter in ACLF (43.5 d[20-98]vs 85d [54-236]; p=0.005). OS was stratified for ACLF/AD and OLT. The 6 months OS of ACLF and AD pts undergoing OLT was overlapping (78% and 83%, respectively), while the OS of ACLF pts without OLT was very poor (32%; log rank=0.001).
Conclusions: As described in literature, also in our population infections were the leading cause of ACLF/AD. The very poor outcome of non-transplanted pts with ACLF should induce a possible expansion criteria in selected categories (age > 70 and comorbidities > 65 y).

	N	Tot (N = 45)	ACLF (n = 22)	AD (n = 23)	p*
Age - *mean ± SD*	45	59.2 ± 10.6	57.6 ± 12.9	60.8 ± 7.8	0.306
Male - *n (%)*	45	28 (62.2%)	11 (50.0%)	17 (73.9%)	0.098
CP score					
A	45	3 (6.7%)	0 (0.0%)	3 (13.0%)	0.004
B		5 (11.1%)	0 (0.0%)	5 (21.7%)	
C		37 (82.2%)	22 (100.0%)	15 (65.2%)	
Comorbidities	45	32 (71.1%)	18 (81.8%)	14 (60.9%)	0.189
Cardiovascular		*18 (40.0%)*	*13 (59.1%)*	*5 (21.7%)*	*0.011*
Diabetes		*7 (15.6%)*	*1 (4.5%)*	*6 (26.1%)*	*0.096*
Obesity		*5 (11.1%)*	*2 (9.1%)*	*3 (13.0%)*	*1.000*
Psychiatric disorder		*2 (4.4%)*	*2 (9.1%)*	*0 (0.0%)*	*0.233*
Renal impaiment		*2 (4.4%)*	*2 (9.1%)*	*0 (0.0%)*	*0.233*
Broncopneumpathy		*1 (2.2%)*	*0 (0.0%)*	*1 (4.3%)*	*1.000*
Etiology	45				
HBV		*8 (17.8%)*	*3 (13.6%)*	*5 (21.7%)*	*0.079*
HCV		*13 (28.9%)*	*5 (22.7%)*	*8 (34.8%)*	
Autoimmune		*6 (13.3%)*	*1 (4.5%)*	*5 (21.7%)*	
Alcohol		*15 (33.3%)*	*10 (45.5%)*	*5 (21.7%)*	
Nash		*3 (6.7%)*	*3 (13.6%)*	*0 (0.0%)*	
HCC	45	10 (22.2%)	3 (13.6%)	7 (30.4%)	0.284
Previous ACLF episodes		3 (6.7%)	3 (13.6%)	-	-
Previous AD episodes		36 (80.0%)	17 (77.3%)	19 (82.6%)	0.722
Biochemistry	45				
Bilirubina tot - *median (Q1,Q3)*		7.8 (3.3, 15.1)	11.2 (8.1, 19.5)	3.9 (2.3, 7.6)	0.001
WBC - *median (Q1,Q3)*		8.3 (4.4, 11.3)	10.6 (6.2, 13.0)	5.0 (3.4, 9.9)	0.028
Creatinine - *median (Q1,Q3)*		1.0 (0.7, 1.6)	1.6 (1.0, 2.2)	0.8 (0.6, 1.1)	0.002
Na - *median (Q1,Q3)*		134.0 (131.0, 137.0)	132.0 (130.0, 135.0)	135.0 (134.0, 138.0)	0.039
MELD score					
baseline - mean ± SD	45	22.5 ± 7.4	26.9 ± 6.5	18.3 ± 5.5	0.000
At OLT - mean ± SD		24.8 ± 8.5	30.1 ± 7.5	20.0 ± 6.2	0.005
Causa ACLF/AD	45				
Bleeding		9 (20.0%)	2 (9.1%)	7 (30.4%)	0.173
Infections		21 (46.7%)	13 (59.1%)	8 (34.8%)	
Acute Alcholic hepatitis		2 (4.4%)	2 (9.1%)	0 (0.0%)	
Unknown		8 (17.8%)	3 (13.6%)	5 (21.7%)	
Others		5 (11.1%)	2 (9.1%)	3 (13.1%)	

[Baseline features of the population enrolled]

P-064

Dengue shock syndrome fever complicated with multiple organ failure: case series from a tertiary care centre

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Background: Dengue is a common arboviral infection with a clinically diverse spectrum from mild form catastrophic form. Although hepatic dysfunction is commonly identified along with multiple organ failure in dengue shock syndrome, fulminant liver failure is rare. Dengue shock syndrome (DSS) and Dengue Hemorrhagic fever (DHF) is known for high mortality despite aggressive management.
Material: We wish to share our experience of 10 DSS cases who have multiple organ failure along with liver involvement where we worked with advanced hemodynamic monitoring to titrate fluid and vasoactive drugs and other supportive therapies. We used monitoring depending upon hemodynamic instability and cardiac status ranging from arterial pressure to uncalibrated cardiac output monitoring including SVV and SVRI. In three cases we used calibrated, global ejection fraction and extravascular lung water to titrate fluid therapy and vasoactive drugs. CRRT was also used in patients with acute renal failure and fulminant liver failure.
Results: These patients had high hematocrit, high hemoglobin, high lactate levels and severe metabolic acidosis. Most of patients had high transaminases in range going up to 18000 units per ml and high urea levels. Some patients had poor cardiac contractility. We found that advanced monitoring had impact on the choice of vasoactive drugs and fluid titration.
Discussion: As DSS is associated with capillary leak which is limited for 24-48 hours. Most of the patients die of capillary leak leading volume deficit with high hematocrit resulting in rapidly developing hypovolemic shock and multiple organ failure with high mortality. Aggressive timely managed optimal hemodynamic support with closed monitoring can help to restore hemodynamics stability in a better way during crisis.
Conclusion: Early hemodynamic monitoring using stroke volume variation and systemic vascular resistance in these patients help to titrate fluid and vasoactive drugs to better hemodynamic stability.

P-065

Improving patient handover from OR to ICU following liver transplant

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Background: Safe and effective handovers are recognized as shared mental model of high performing teams to foster quality of care and work team satisfaction. The complexity of liver transplantation requires integration of multiple care services during the immediate post-operative period ensuring that adequate care is provided to these patients. Handover of care from the operating room to the intensive care represents a vulnerable check point, as these patients remain intubated, hemodynamically tenous, and require communication of complex care plans. Quality & Improvement study was conducted to address the need and improve upon a structured handover process in liver transplant recipients.
Methods: A 10 step patient transfer protocol was developed to

standardize the transition from the OR to the ICU (**Figure 1**). The COLD and SBAR tools were used to improve communication between services (**Figure 2**). Two plan-do-study-act (PDSA) cycles were completed after a preliminary data collection period. A comparison between preliminary and the PDSA cyle one and two were performed measuring handover performance.
Results: Preliminary data showed poor communication between care teams. Compliance with team member introduction and roles definition was lacking. **Table 1.**
The results will be discussed.
Conclusion: The conclusion will be presented. Patient transfers represent a checkpoint where poor communication of patient care plans results in inadequate handover of care. Standardizing patient transfer process and communication will improve the quality of care provided to these patients.

P-066

Anaesthetic challenges in a patient for living donor related liver Re-transplant with MELD of 40: a case report

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Liver transplant in a patient with a high MELD score can prove to be very challenging especially if it involves re-transplant. In our institute we performed a re-transplant in a patient aged 34 years, who had undergone his first transplant two years back in view of Hepatitis C related end stage liver disease. The patient required a re-transplant in view of graft dysfunction secondary to poor treatment compliance.
Our challenge was to optimize this patient who had a MELD score of 40 and was admitted with decompensation in form of grade III hepatic encepahalopathy, hepato renal syndrome (HRS),coagulopathy, spontaneous bacterial peritonitis and refractory ascites. The other associated problems were of sepsis, hyponatremia, generalized edema and long term immunosuppressants. Serum osmolality was gradually raised to decrease the intracranial pressure, terlipressin for treatment of HRS and appropriate antibiotics were started. Two sessions of plasma exchange therapy were instituted as a bridge to transplantation. Proper psychological counseling was provided to the donor and patient's family as the survival outcome reported in literature is approximately 50%. Intraoperative course proved to be equally challenging since dense adhesions required massive blood transfusions. Patient had a prolonged period of hypotension requiring high vasopressor and inotropic support. Preparedness for hemodialysis in the perioperative period was ensured in view of decreased urine output, progressive metabolic acidosis and hyperkalemia. But following implant of the new graft, patient had a gradual improvement in all the above mentioned parameters. Rest of the post operative course was uneventful.

P-067

Intraoperative management of a patient with impaired cardiac function undergoing simultaneous ABO-compatible liver and ABO-incompatible kidney transplantation from two living donors: a case report

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Background: Combined liver and kidney transplantation is a very complex surgery. To date, there has been no report on the intraoperative management of patients with impaired cardiac function undergoing simultaneous ABO-compatible liver and ABO-incompatible kidney transplantation from two living donors.
Case report: A 60-year-old man underwent simultaneous ABO-compatible liver and ABO-incompatible kidney transplantation from two living donors because of IgA nephropathy and alcoholic liver cirrhosis. The preoperative cardiac findings revealed continuous aggravation, shown by large left atrial enlargement, severe left ventricular hypertrophy, a very prolonged QT interval, and a calcified left anterior descending coronary artery. Severe hypotension with very weak pulsation and severe bradycardia developed, with an irregular junctional rhythm noted immediately after the liver graft was reperfused. Although epinephrine was administered as a rescue drug, hemodynamics did not improve, but only central venous pressure (CVP) and mean pulmonary arterial pressure (mPAP) increased to potentially fatal levels. Emergency phlebotomy via the central line was performed. Thereafter, hypotension and bradycardia recovered gradually as the CVP and mPAP decreased. The irregular junctional rhythm returned to a sinus rhythm, but the QTc interval was slightly more prolonged. Because of poor cardiac capacity, the volume and rate of fluid infusion were increased aggressively to maintain appropriate kidney graft perfusion after confirming vigorous urine production of the graft.
Conclusions: A heart with impaired function due to both end-stage liver and kidney diseases may be less able to withstand surgical stress. Further study on the cardiac dysfunction will be helpful for the management of patients who undergoing complex transplantation surgery.

Poster Round I, Session 1, 2, 3: Comorbidities and Complications

P-068

Remodulation of early allograft dysfunction estimation: steatosis and liver weight count

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Background: The most common used definition of Early Allograft Dysfuntion (EAD) is based on the classification of Olthoff et al, in which a combination of trasaminases peaks and the last available values of total bilirubin and INR at 7thday are considered. However, EAD has shown an overall sub-optimal ability to predict the post-transplant 90-day patient death, with areas under the curve (AUC) typically < 0.7. Moreover, Olthoff criteria are based on too large parameters, typically including a great part of the investigated population. Starting from these assumption, we investigated the role of liver macrosteatosis and graft weight with the intent to "normalize" the transaminases peak, recalibrating the EAD definition in light of this normalization.
Methods: 193 adult (≥ 18 years) patients underwent a first transplant during the period September 2014-August 2018 in the two Roman University Centers. All donor liver underwent protocollary biopsies.
Results: One-hundred-twenty four(64.2%) patients exceeded the Olthoff-EAD criteria. We normalized the transaminases peak considering as referral point the median liver weight of our grafts, corresponding to 1500 mg. After this, we created a scoring system based on the following criteria: normalized transaminases < 2,000 IU/L=0, 2,000-3,999=1, ≥4,000=2; total bilirubin < 10.0 mg/dL=0, 10.0-19.9=1, ≥20.0=2; INR < 1.60=0, 1.60-1.99=1, ≥2.00=2; macrosteatosis < 5%=0, 5-19=1, ≥20=2. Modified EAD (modEAD) had an AUC=0.71 (p< 0.001) for the risk of 90-day death after transplant, being superior to EAD (0.67, p=0.002). Stratifying the population according to the different modEAD classes, patients with a value ranging 0-3 (n=147; 76.2%) had a 90-day death rate of 11.6 vs 39.1% in patients with a score ranging 4-8 (n=46; 23.8%) (log-rank p< 0.001).
Conclusions: EAD recalibration according to macrosteatosis and graft weight may be taken into account due to its ability to improve the diagnostic ability of the score. External validation of the proposed score is needed.

P-069

Immune tolerance secondary to graft-versus-host disease after liver transplantation: a case report

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Graft-versus-host disease after liver transplantation is a rare but usually fatal complication. We present, to our knowledge, the first successfully treated case induce to immune tolerance because of graft-versus-host disease after liver transplantation. A 46-year-old male with recurrent hepatocellular carcinoma receive liver transplantation from a 35-year-old male donor after brain and cardiac death with anti-interleukin-2 receptor monoclonal antibody induction followed by maintenance with tacrolimus, mycophenolate mofetil and steroids. Twenty days posttransplant, the patient present with fever, skin rush, and decreased blood cell counts. Skin biopsy showed focal liquefaction degeneration of the basal cells and lymphocytic infiltration in the dermis consistent with GVHD. Their HLAs showed a donor-dominant one-way match, not at HLA-DR but at HLA-A, HLA-B, and HLA-C (recipient; A 31/33, B 51/54, C 1/14, DR 9/11, donor; A 31/-, B 51/-, C 14/-, DR 8/11). Short tandem repeats (STR) enriched for CD3+ cells from peripheral blood showed a mixed chimerism. He was successfully treate by withdrawal immunosuppression, and improved high-dose steroids therapy. 281 days posttranplant, he totally withdrawal steroids, four years till now with normal liver function hrombocytopenia and no evidence of peripheral blood donor chimerism who got immune tolerance. In conclusion, early diagnosis of GVHD after liver transplantation may allow successful treatment. STR enriched for CD3+ may be useful to evaluate the response to therapy. High level or withdrawal tacrolimus may not effect the result of therapy of GVDH, and the improved steroids therapy will reward. Decreased blood cell counts may contribute to the reconstruction of immune system induce tolerance.

P-070

Technique of venous outflow reconstruction and incidence of hepatic venous outflow obstruction (HVOO) following liver transplantation

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Introduction: Hepatic venous outflow obstruction (HVOO) after liver transplantation (LT) is a recognised complication with resultant graft dysfunction that could necessitate revisional surgery or re-transplantation. The aim of this study was to see whether the technique of venous reconstruction correlates with the occurrence of HVOO following LT.
Methods: Consecutive adult patients who underwent whole deceased LT over a ten year period (2008-2017) were recruited into the study. Redo liver transplants were excluded. The techniques of venous reconstruction were: Type A - Piggyback (Two vein extension or Three veins); Type B - Caval replacement; Type C - Side to side cavo-cavostomy. Data were retrospectively reviewed and screened for occurrence of HVOO. HVOO was defined as radiological evidence of outflow obstruction by CT scan, confirmed by cavography and pressure studies showing a hepatic venous gradient of 12mmHg or more post LT.
Results: During the study period, 1,677 consecutive patients underwent LT. 157 patients who underwent redo transplantation were excluded. 1,369 patients received whole grafts and were recruited into the study. The techniques used were as follows: Type A, n= 1005; Type B, n=208; Type C, n=156. 54 patients (4%) had large volume ascites. 15 patients (1%) had confirmed HVOO, with 14 patients having Type A reconstruction, none having Type B and 1 having Type C reconstruction, which was statistically significant at p< 0.005 (Chi ^{2}, MonteCarlo analysis). Mean hepatic pressure gradient was 19mmHg (range 10 - 39mmHg). Four patients were treated medically, 4 had radiological dilatation/stenting, 6 had operative correction and 1 patient had re-transplantation. Graft weight recipient weight (GWRW) ratio was assessed as a possible independent risk factor for HVOO using categorical analysis (Kruskal-Wallis test) and there was no correlation (p=0.61).
Conclusion: Our results favour caval replacement and side to side cavostomy as having a statistically significant less chance of HVOO.

P-071

Different perceptions of sustainable case-mix for liver transplantation between surgeons and hepatologists: an Italian multicenter study

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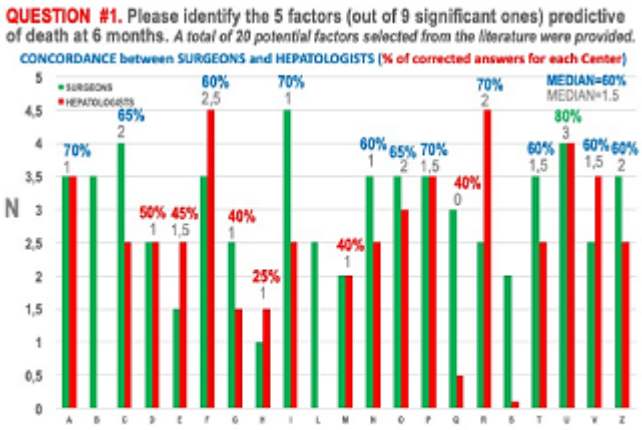
A national study on case mix is ongoing in Italy. A preliminary report has been submitted to this congress. Surgeon's perception of sustainable case-mix may be different from the hepatologist's one, even within the same team. As an add-on study the evaluation of perception of sustainable case mix between different Italian liver transplant (LT) Centers has been performed using a 30-item questionnaire.
Surgical directors and senior hepatologists from 21 Italian LT Centers were asked to quantify perception of the risk of "graft failure" and of "patient death" at 6 months after LT for each supposed risk factor and possible fatal combinations. Answers were assessed by visual-numerical analogue scale (0% = no impact; 100% = max impact, Spearman's Rho test). Surgeon-hepatologist concordance within the same Center and between Centers was evaluated. The case-mix database (1633 LTs, 2016-2017) was used as reference. The number of correctly identified factors was low for surgeons and hepatologists (median 1.5, figure). However, when the answers were globally evaluated in the same Center a 60% of correctly identified factors (figure) was observed.
A better fit was observed when the question was to identify the "multifactorial fatal combination" (ɻ‡ 0,64; p=0.005).
The detrimental effect of donor age ≥85 or DCD status was erroneously overestimated in the majority of cases. Instead, the detrimental effects of Yerdel 3-4 portal thrombosis, pre-transplant dialysis, pre-transplant mechanical ventilation, and surgical complexity were underestimated in the majority of cases.

In conclusion, perception of case mix is different between surgeons and hepatologists. Overall, adherence to the reality (case-mix factors affecting survival) is low. Integration between surgeon's and hepatologist's perspective increases the accuracy of case mix perception. To improve adherence to reality, surgeons and hepatologists should group together when evaluating the risk of a complex case-mix.



[Question #1]

P-072

Impact of early kidney dysfunction in the incidence of major cardiovascular events after liver transplantation

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Background: Major cardiovascular events (MACE) are frequent after liver transplantation (LT), and their risk factors are not well defined. We aimed to investigate the incidence of post-LT MACE and evaluate their risk factors, particularly the relationship between renal dysfunction and MACE in the long-term.
Method: Retrospective, single-centre study that included all LT recipients between January 1st 2007 and December 31st 2017. The incidence of MACE after LT was investigated, and risk factors before LT (cardiovascular risk factors, kidney function, liver disease, age, gender), at discharge from transplant episode and 12 months after LT (cardiovascular risk factors, kidney function, immunosuppression) were evaluated.
Results: We included 627 patients, 117 (19%) of whom suffered at least one MACE during follow-up. Cumulative incidence of MACE was 8% and 20% at 12 and 60 months after LT. Age at LT, male gender and serum creatinine at LT were associated with the incidence of MACE during the first month after LT at univariate analysis, with age (p< 0.001) and serum creatinine (p=0.014) being independent risk factors at multivariate analysis. Male gender, age at LT, personal history of diabetes, arterial hypertension and MACE before LT, immunosuppression with cyclosporine A at transplant episode discharge, arterial hypertension 12 months after LT and serum creatinine at transplant discharge and 12 months after LT were associated with the incidence of MACE >12 months after LT at univariate analysis. At multivariate analysis, age at LT (p=0.019), male gender (p=0.025), pre-LT personal history of MACE (p=0.03) and serum creatinine 12 months after LT (p=0.05) were independent predictors of the risk of MACE >12 months after LT.
Conclusion: Renal dysfunction during the first months after LT is an early marker of cardiovascular risk in LT recipients. Whether renal-sparing immunosuppressive regimens also result in a decreased incidence of MACE should be evaluated in prospective studies.

P-073

MELD-Na alterations on the liver transplant waiting list and its impact on listing outcome

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Background: Currently, MELD Score listing is state of the art for liver transplant recipients. Our department could show by our own data and confirmed by an ET- cohort that dynamic MELD deterioration (Delta MELD) during waiting time has a significant impact on postoperative survival. Aim of this study was to analyze the impact of MELD score (Delta MELD) alterations on waiting list behavior of liver transplant candidates.
Method: More than 42000 patients were listed in the UNOS data for a liver transplantation between 2011 to 2015.
Patients were analyzed according to their delisting reasons, which were defined as transplanted, still listed, died on list, too good, too sick for transplantation or other.
Difference in outcome between MELD and MELD-Na were compared.
Results: Half of the listed patients (50.1) are already transplanted, 18.6% are still actively listed, 11.5% were removed due to poor conditions, 11% died on list, 2.6% were removed due to recovery and

6.3% of patients were removed due to other reasons.
MELD and MELD-Na values are shown in table 1.
Conclusion: Dynamic alterations in the MELD/MELD-Na during waiting time have significant impact on waiting list behavior for liver transplant candidates. Patients finally receiving a graft showed lower listing MELD scores /MELD-Na and an only minimal increase during waiting time. In contrast patients who died on list presented with significantly higher listing MELD/MELD-Na and showed a significant deterioration during their waiting time. Patients who died on list had a significantly higher Delta Max as well a Delta compared to the other groups.

	TX	too good	too sick	died	other	waiting
ON	18.2/20.3	13.4/15.4	18.0/20.3	19.6/22.1	14.0/16.3	13.2/15.2
OFF	21.6/23.4	11.1/12.5	24.6/26.1	27.3/28.9	15.4/17.5	13.5/15.1
DELTA	3.3/3.0	-2.3/-2.9	6.6/5.9	7.7/6.8	1.4/1.2	0.3/-0.1

[MELD/Meld Na values according to waiting list outcomes]

P-074

Analysis of intraoperative cardiac arrest during adult liver transplantation

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Liver transplantation is a high risk procedure that occurs in extremely ill patients. Intraoperative cardiac arrest (ICA) has been reported to occur in from 1-5.5% of patients undergoing transplant. We conducted a review of 798 consecutive adult liver transplants that took place from 2005-2014 at Kansas University Hospital. ICA occurred in 32 patients during this study period, with an incidence of 3.9%. Pre-operative creatinine average was 2.2 mg/dl (7 patients had Cr > 3.0). MELD average was 24(7 patients had MELD >30). Five patients expired in the operating room, with 84% successfully resuscitated. Two additional patients expired within 30 days of transplant (post op day 1 and post op day 5) and one further patient died within one year of transplant. One year survival of patients who experienced ICA was 75%. In patients who survived, there was no graft loss at either 30 days nor 1 year. Post-reperfusion syndrome occurred in 23 of 31 patients with ICA. Three patients resuscitated after ICA required ventilation support for >72 hours, with the rest successfully weaned from mechanical ventilatory support. Persistent neurological deficits were present in 2 of 27 survivors at discharge from the hospital. Acute kidney injury occurred in 2 of 27 patients who survived ICA. The average length of stay in patients who survived to discharge was 15.2 days (range 5-43 days).
Cardiac arrest during liver transplantation is not an uncommon event. Patients most frequently experience ICA upon reperfusion of the new graft and demonstrate post-reperfusion syndrome. Despite the occurrence of ICA, 84% of patients had a successful resuscitation, with one-year survival of 75%. Also of note, graft survival was 100% at one year in survivors who were discharged from the hospital. Only 2 of 27 (7%) patients experienced a new neurological deficit at the time of discharge from the hospital.

P-075

Poor long-term outcome in liver transplant recipients with renal insufficiency prior to liver transplantation

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Background: Due to the MELD based allocation system the number of patients undergoing orthotopic liver transplantation (OLT) with severely impaired renal function has markedly increased. Therefore, we here investigated long-term outcome of OLT recipients with advanced renal dysfunction.
Methods: All adult patients with chronic kidney disease (CKD) stage 4/5 undergoing OLT at our institution between 2011-2015 were included. Patient survival and renal outcome were retrospectively assessed.
Results: Altogether 60 patients (CKD 4: n=22, 37%, CKD 5: n=38, 63%) with a median follow-up of 1099 days were analysed. In the immediate postoperative period 42 (70 %) patients required dialysis for median 21 days. On long-term follow-up 18/60 (30%) required dialysis, only 5 of these patients (28%) subsequently underwent kindney transplantation (KTx) after a median period of 274 days (IQR 201-1461).
After OLT 29 patients (48%) had CKD 4/5 or had undergone KTx at end of follow-up. There was no difference in terms of age, CKD stage, time on dialysis prior to OLT, length of stay on ICU, type of immunosuppression, presence of diabetes, arterial hypertension or hyperlipidemia between patients with compensated renal function and those with poor renal outcome (CDK 4/5 or KTx) at last follow-up (p=n.s.). The only risk factor for poor renal outcome was post-operative need for dialysis. Overall 3- and 5-year patient

survival was 60% and 42%, respectively. 1- and 5- year mortality was significantly higher in patients with poor compared to compensated renal outcome (59% vs. 13%, p< 0.001 and 72% vs. 28%, p< 0.001, respectively).
Conclusion: In this long-term follow up study, about half of the patients with CKD 4 and 5 prior to OLT had poor long term renal outcome, going along with a very low 5 year patient survival rate. Future studies should investigate if combined OLT and KTx improves outcome of these patients.

P-076

Role of cardiac troponin T in pre-transplant renal function evaluation and its possibility as prediction marker of acute kidney injury following liver transplantation

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Background: A precise assessment of preoperative renal function, or even detecting even mild insufficiency, is crucial in identifying liver transplantation (LT) recipients at a higher risk of renal failure following LT. Recently, elevated serum cardiac troponin T (cTnT) is reported to be associated with renal impairment. This study is aimed to evaluate the relation of preoperative cTnT to other conventional renal function markers and to estimate cTnT as a potential predictive factor for developing acute kidney injury (AKI) after LT.
Methods: Adult LT recipients who had survived for at least 4 weeks were enrolled. We excluded patients on dialysis prior to LT and patients with preoperative renal dysfunction caused by specific etiology unrelated to liver disease. The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault formula. Twenty-four hours creatinine clearance (24CrCl) was also calculated using 24-hour urine specimen in living donor liver transplant (LDLT) cases. The optimal cut-off values were determined by receiver operating characteristic curves.AKI was defined to meet the injury (I)-class according to RIFLE criteria within 4 weeks postoperatively.
Results: Nighty LT recipients, including 64 LDLT recipients, were investigated. In the pretransplant evaluation, cTnT value showed weak correlation with serum creatinine (p=0.049, r=0.21), eGFR (p=0.05, r=-0.21), and Cystatin C (Cys-C) (p=0.002, r=0.32) and moderate correlation with 24CrCl (p< 0.001 r=-0.50). Twenty-four recipients (26.6%) developed AKI. In univariate AKI risk analysis, pre-transplant creatinine > 1.5mg/dL, Cys-C > 1.2mg/L, and cTnT > 0.015ng/ml, operative time > 750 minutes, and intraoperative packed RBC transfusion > 23units were significantly associated with AKI development. Among them, only cTnT and intraoperative packed RBC transfusion remained significant in multivariate analysis.
Conclusion: cTnT value might be useful for the assessment of preoperative renal function. In addition, the elevated cTnT can be the predicting factor for development of postoperative AKI in LT recipients.

P-077

Prognosis evaluation of liver transplant patients with splenectomy - a meta-analysis

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Background: Researchers have reported beneficial effects of splenectomy on rejection prevention, protection against small-for-size graft syndrome and therapy for hepatitis C virus. However, there are also serious complications of splenectomy in LT, including infection, thrombosis and hemorrhage. Splenectomy is usually avoided in light of these common complications, and indications for splenectomy during LT remain controversial. This meta-analysis aims to assess the prognosis of patients with or without splenectomy during LT.
Methods: We systematically searched for all the studies that compared the outcomes of candidates with splenectomy (SP group) and those without splenectomy (NSP group) in LT using the MEDLINE, Web of Science and Cochrane Library databases. Odds ratio (OR) and 95% confidence intervals (CI) were calculated to compare the pooled data between SP group and NSP group.
Results: Eleven retrospective trials, involving 2012 liver transplant recipients, were included. SP group showed lower rates of acute rejection (AR) and small-for-size syndrome (SFSS) with an OR equal to 0.59 (95% CI = 0.43-0.82, p=0.001) and 0.29 (95% CI = 0.09-0.95, p = 0.004) respectively, compared to the NSP group. Both groups had a similar 1-year patient mortality and infection rates post-transplantation, however, there were poor 1-year graft outcomes (OR=2.25, 95% CI = 1.24-4.09, p=0.008), high rates of veinous thrombosis (OR=5.36, 95% CI =1.66-17.32, p=0.005) and hemorrhage (OR=2.61, 95% CI = 1.51-4.5, p=0.0006) in the SP groups.
Conclusions: Candidates that underwent splenectomy in LT had a decreased risk of suffering from AR and SFSS, but have a higher ratio of veinous thrombosis and post operative hemorrhage, and lower rate of graft survival after LT compared to those who do not undergo splenectomy. Thus, the decision to perform a splenectomy for LT candidates needs to be carefully considered and risk versus benefit should be thoroughly weighed.

P-078

Donor-related risk factors analysis of ischemic type biliary lesion after liver transplantation from organ donation after cardiac death: a single center experience.

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Objective: To investigate the donor-related risk factors for ischemic type biliary lesion (ITBL) after liver transplantation (LT) from organ donation after cardiac death.
Method: Clinical data of 200 donors who donated the organs after cardiac death and the recipients underwent LT in the Third Affiliated Hospital of Sun Yat-sen University between April 2016 and April 2018 were retrospectively analyzed. The incidence of ITBL after LT in the recipients was observed, and the relationship between the incidence and the clinical indexes of the donors was analyzed. The influencing factors for ITBL after LT were analyzed using univariate and multivariate logistic regression analysis.
Results: The incidence of ITBL after LT in the recipients was 11.50%(22/200). Univariate logistic regression analysis revealed the ITBL after LT was related with cerebrovascular accident cause, the warm ischemia time, steatosis of liver, history of cardiopulmonary resuscitation, dosage of dopamine before procurement and hypoproteinemia. Multivariate logistic regression analysis revealed the independent influencing factors for ITBL after LT were the warm ischemia time (OR=1.206, 95%CI: 1.034-1.381; $P< 0.05$), steatosis of liver (OR=5.319, 95%CI: 1.020-27.752; $P< 0.05$) and dosage of dopamine before procurement (OR=1.279, 95%CI: 1.021-1.601; $P< 0.05$).
Conclusion: Postoperative ITBL is one of the major complications after LT. The independent risk factors should be strictly controlled, as the warm ischemia time, steatosis of liver and dosage of dopamine before procurement are contributed to the incidence of ITBL.

P-079

Rendezvous technique can rescue the patients with severe biliary stenosis after liver transplantation: long term follow up results

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Background: To evaluate the long term outcomes of rendezvous technique in patients with severe biliary stenosis after liver transplantation.
Method: We retrospectively analyzed 29 patients who underwent rendezvous due to failure of ERCP after LT.
Results: Of the 959 patients who performed LT from January 2010 to December 2017, 235 (24.5%) performed ERCP because of the structure and leakage. Of the patients who underwent ERCP, 29(13%) patients failed and all attempted rendezvous technique. Of the 29 patients, 10 were removed from the stent, and 19 were currently maintaining the stent. The stenting period of the patient who removed the stent was 14.9 ± 5.6(6.65- 24.14) months and the stenting period of the patient who did not remove the stent was 13.1 ± 8.4 (3.48- 38.61) months. In the case of Lt graft, the stenting period was 27.1 months longer than that of Rt graft(p=0.001).The total follow up periods of all patients were 38.6 ± 24.7 (9.93 - 102.80). Of the patients who had removed the stent, 2(20%) had recurrence. Eight patients achieved stent-free status for a mean of 15(6.7-24.1) months after removal of the stents. Inside stent related sludge or stone was identified in 13(44.8%) patients during follow-up. Other complications were cholangitis, bleeding and ERBD tip perforation in 12 (41.4%), 2 (6.9%) and 1 (3.4%), respectively.
Conclusion: Rendezvous technique in patients with severe stenosis with ERCP failure is not invasive and can increase patient survival. However, in patients with left graft liver transplantation, severe stenosis may require long stenting period.

Patient No	Graft	No. stents	Stone	Interval Rendezous	Stenting period	Maintain stenting period	Total F/U	F/U after stent remove	Current status
1	Rt	2	No	50.2	14.2		102.8	38.4	No stent
2	Rt	2	No	31.0	24.1		76.0	20.9	No stent
3	Rt	2	No	21.2	23.1		74.7	30.4	No stent
4	Rt	2	No	26.4	8.3		72.1	37.4	No stent
5	Rt	2	No	57.9		12.2	70.1		1 stent
6	Rt		No	44.8	6.6		64.9	13.5	No stent
7	Lt	3	Yes	25.2		38.6	63.8		1 stent
8	Rt	2	Yes	43.8		15.6	59.5		No stent
9	Rt	1	Yes	35.3		11.2	46.5		1 stent
10	Rt	3	Yes	9.6	13.9		45.9	22.4	No stent
11	Rt	3	Yes	7.5	16.7		43.7	19.5	Recur
12	Rt	2	Yes	9.1	12.2		42.8	21.5	Recur
13	Rt	1	Yes	32.3		3.5	35.8		1 stent
14	Rt	1	Yes	9.9		24.0	34.0		1 stent
15	Rt	1	No	13.8		15.7	29.5		1 stent
16	Rt	2	No	9.2	13.3		25.1	2.6	No stent
17	Rt	2	No	20.8		5.9	26.7		2 stents
18	Lt	1	No	8.7		15.7	24.4		1 stent
19	Rt	1	Yes	5.1	16.7		23.8	2.1	No stent
20	whole	2	Yes	6.5		15.9	22.4		2 stents
21	Rt	1	Yes	7.9		13.1	21.0		1 stent
22	Rt	2	No	3.9		16.0	19.9		2 stents
23	Rt	2	No	2.2		14.5	16.7		2 stents
24	Rt	2	No	1.6		16.3	17.8		2 stents
25	Rt	1	Yes	6.4		3.6	10.0		1 stent
26	Rt	2	Yes	9.4		4.3	13.8		2 stents
27	Rt	1	No	1.7		11.4	13.1		1 stent
28	Rt	2	No	7.8		5.5	13.3		2 stents
29	Rt	2	No	4.5		5.4	9.9		1 stent

[Details and Outcomes of the Rendezvous Technique in Patients with Biliary Strictures after LT]

P-080

Fatal graft-versus-host disease in liver transplantation. An analysis of UNOS registry

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Purpose: Graft-versus-host disease (GVHD) after liver transplant is a rare complication. This study aimed to analyze the UNOS registry to identify risk factors for fatal GVHD.
Methods: We used the UNOS registry. All adult liver transplant and liver-kidney transplant patients between 2002 and 2018 were analyzed. An endpoint was set as mortality due to GVHD. Multivariate Cox regression model was used to assess risk factors for mortality due to GVHD.
Results: A total of 77295 patients were eligible. There were 121 patients (0.2%) who died of GVHD. Rabbit-anti-thymocyte globulin (rATG) and basiliximab were used as induction in 7488 (9.7%) and 11736 (15.2%). Mycophenolate was used as maintenance in 53309 (68.9%). Donor-to-recipient age discrepancy (recipient age - donor age) was an independent risk factor (HR 1.03 [per year]; P< 0.001). A cut-off value of age discrepancy for prediction was 20 years (Area: 0.65, P< 0.001). Incidence rate of fatal GVHD was 0.3% and 0.1% in the larger and smaller age discrepancy groups, respectively. On a multivariable model, hazard of fatal GVHD in the larger discrepancy group (>20 years) was 2.65 (HR 2.65, P< 0.001). Basiliximab (HR 1.76; P=0.011) remained as independent risk factors, whereas rATG was not associated (HR 1.03; P=0.93). Mycophenolate maintenance showed a protective effect (HR 0.55; P=0.001). A subgroup analysis showed that negative impact of basiliximab and positive impact of mycophenolate were found only in the larger age discrepancy group. In the larger discrepancy group, older recipient age and younger donor age were considered as independent risk factors, whereas neither remained as a risk factor in the smaller discrepancy group.

Recipient to donor age discrepancy >20years or not		P value	Hazard ratio	95.0% CI for hazard ratio	
				Lower	Upper
Smaller discrepancy	rATG	0.572	0.712	0.219	2.317
	Basiliximab	0.152	1.690	0.825	3.461
	Mycophenolate	0.726	0.895	0.482	1.663
	Donor age	0.645	0.994	0.968	1.020
	Recipient age	0.857	1.003	0.973	1.034
	MELD at transplant	0.341	0.986	0.957	1.015
Larger discrepancy	rATG	0.820	1.096	0.498	2.408
	Basiliximab	0.050	1.743	1.000	3.038
	Mycophenolate	<0.001	0.418	0.264	0.662
	Donor age	0.049	0.973	0.946	1.000
	Recipient age	<0.001	1.079	1.041	1.118
	MELD at transplant	0.472	0.992	0.970	1.014

[Risk factors for fatal GVHD]

Conclusions: In cases of large age discrepancy between donor and recipient, avoiding Basiliximab induction and adding Mycophenolate to maintenance may be favorable regimens to decrease a risk of GVHD.

P-081

Liver transplantation in patients with sickle cell disease: Case report and review of the scientific registry of transplant recipients

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Background: Patients with sickle cell disease (SCD) are at risk for liver failure due to iron overload or acquired hepatitis secondary to repeated blood transfusions. There is limited published experience of liver transplantation (LT) or simultaneous liver-kidney transplantation (SLK) in this patient population.
Methods: We identified one patient with SCD from our center. We reviewed the SRTR and identified 22 LT patients with a free text diagnosis of 'sickle cell' and 5 SLK patients with a renal diagnosis of sickle cell anemia. Patient demographics as well as graft and patient survival were analyzed.
Results: Our patient is a 58 y.o. male with cryptogenic cirrhosis complicated by HCC. He also had renal failure secondary to SCD. He was sensitized with a PRA of 34% and multiple red cell antibodies. He received peri-transplant plasmapheresis as well as basiliximab induction. He has done well in the first year post LT with stable allograft function but has been admitted three times with pain crisis. Review of the SRTR revealed 22 patients with SCD who underwent LT. The mean age was 26.3±13.7 years, and they were 59.1% male. The average MELD at transplant was 31.2±8.5. One and five year graft survival was 90.4% and 54.0%, respectively. One and five year patient survival was 90.4% and 76.3%, respectively. There were five patients with SCD who underwent SLK in the SRTR. The mean age was 41.8±7.5 years, and 80% were male. The first two patients had graft and patient survival < 1 year. The three most recent patients have graft and patient survival up to 10 years.
Conclusions: Patients with SCD are medically complex and may require LT. Acceptable graft and patient survival rates can be achieved based on retrospective review of the SRTR, for both LT and possibly for SLK.

P-082

Programmed diagnosis and treatment pattern for hepatic artery thrombosis after orthotopic liver transplantation- a single center experience

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Background: Currently,there is no standard operation procedure that would be achieved early diagnosis and suitable treatment modality selection.
Method: The data of 411 patients who underwent orthotopic liver transplantation (OLT) from December 2011 to July 2018 were retrospectively analysed. Our standard pattern mainly included non-invasive diagnosis stage and minimal invasive treatment stage. Firstly, when hepatic artery resistance index greater than 0.8 or blood flow disappearance was found by ultrasonography, the situation would be immediately confirmed by contrast-enhanced ultrasonography. Secondly, the percutaneous transluminal angiography (PTA) was performed to define the etiology and select the treatment modality to resolve, such as thrombolysis and stent implantation.
Results: HAT was diagnosed in 14 (3.4%) patients and the median time for HAT occurrence was 4.4 days (range 1 to 15 days). All the patients were diagnosed with HAT by contrast-enhanced ultrasonography before the PTA. During the treatment period, the mean dosage of urokinase was 650000U±100000 (range, 250000-1000000U) during thrombolytic therapy and the therapeutic time window required 4-8days after intervention procedure. Stents were implanted during thrombolytic treatment in 3 patients. In one patients with splenic artery steal syndrome, proximal splenic artery embolization was performed during interventional procedure and one patient underwent re-transplantation after the intervention treatment. The technical and clinical success rate was 78.7% (11/14). Hemorrhage was observed in 2 patients and was cured by conservative treatment. No complications associated with the interventional procedures occurred. All patients received anti-platelet therapy for six months or later and underwent follow-up once a month after OLT. Finally, one patient died of multiple organ failure and two patients died of graft dysfunction. The rest of 11 patients still survived until the last follow-up.
Conclusion: Programmed diagnosis and treatment pattern for hepatic artery thrombosis can increase the diagnostic and therapeutic effect and improve the long-term outcome.

P-083

Proximal splenic artery embolization is safe and effective to treat portal hyperperfusion: a 10 years single center experience

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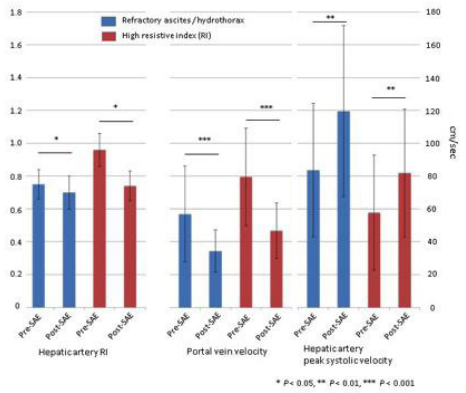
Background: The aim of the present study was to assess the safety and the efficacy of proximal splenic artery embolization (SAE) as treatment of choice for high hepatic artery resistive index (HA RI), refractory ascites (RA) and/or refractory hydrothorax(RH), when clinical manifestations of portal hyperperfusion (PHP).
Method: We conducted a retrospective analysis of all patients who

underwent SAE for PHP between 2007 and 2017 at our center.
Results: Ninety-seven patients were included in the study. The indication was elevated HA RI for 63 patients (65%) and RA and/or RH for the remaining 34 patients (35%). The mean follow-up after SAE was 71 ± 41 months. All patients experienced a decrease in portal vein velocity (PVV) at ultrasounds(Figure1), which resulted in the normalization of the HA RI in the group for which it was elevated and in the resolution of RA and/or/RH in the other group. The time interval between LT and SAE was 3 (0-12) days in the high HA RI group and 38 (7-1675) days in the RA/RH group. The median time between SAE and resolution of clinical manifestation of PHP was 1 (0-13) days in the HA RI group and 34 (3-762) days in the RA/RH group. Overall, the procedure was safe, with minimal incidence of post splenectomy syndrome (3 cases, 3%). Partial and subclinical splenic infarcts were incidentally discovered in 24 patients (24.7%). No cases of splenic abscess or systemic sepsis related to possible hyposplenism occurred.
Conclusions: In our experience SAE was safe and effective in optimizing intrahepatic hemodynamics and for the treatment of PHP after LT. However, the clinical impact of this procedure (i.e. reduction of vascular and biliary complications) needs to be further investigated in future studies.



[Figure 1. Improvement of intrahepatic hemodynamics noticed during ultrasounds evaluations after SAE.]

P-084

Liver transplantation combining partial splenectomy for end-stage liver disease with severe splenomegaly: a single-center experience

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Background: End-stage liver disease (ESLD) are often accompanied by various degrees of splenomegaly, although it can be effectively relieved by liver transplantation (LT), some patients continue suffering with splenomegaly after surgery. Total splenectomy or selective splenic embolization is prone to lead more complications. We retrospectively studied the high risk factors of unrelieved hypersplenism after LT, and then included patients with those high risk factors to perform LT combining partial splenectomy to investigate the safety and effectiveness of the procedure.
Methods: Clinical data of 80 patients with ESLD and splenomegaly had been analyzed retrospectively. Logistic regression analysis was used to screen for high risk factors of unrelieved hypersplenism and established a predictive model. According to the predictive model, 11 high-risk patients were included in this procedure. Safety and efficacy were judged by laboratory tests and imaging examinations post LT.
Results: Multivariate regression analysis showed that platelet count (t=4.277, P< 0.001) and spleen volume (t=6.799, P< 0.001) were independent risk factors for unrelieved hypersplenism after LT. When cut-off values were 50×10^9/L and 1000 cm^3, the sensitivity and specificity were 77.27% and 86.36%, 81.03% and 79.31%, respectively. Eleven patients had been performed combined surgery, and the amount of bleeding from partial spleen removal was 50-100 ml. Platelets returned to normal within 5-10 days, and continuous ultrasound monitoring showed stable blood inflow of all 11 liver grafts. Liver function recovered smoothly in all patients, without complications such as bleeding, infection and thrombosis. CT scan showed a reduction in spleen volume by 39.8%-67.0%.
Conclusions: Platelet count < 50×10^9/L and spleen volume >1000mL are predictors of persistent splenomegaly after LT. Liver transplantation combined with partial splenectomy can effectively prevent the unrelieved hypersplenism in high-risk patients. Satisfactory surgical safety can be achieved through accurate evaluation, careful operation and exact hemostasis.

P-085

Aetiology of delirium post liver transplant: The King´s experience

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Introduction: Delirium post liver transplant (LT) is typically multifactorial with multiple pre-LT and post-LT risk factors. Data suggests that it is associated with increased morbidity and mortality. The aim of this study is to assess the effect of post-LT delirium on patients and identify modifiable risk factors.
Methods: All adult LTs between 08/2012-08/2017 for chronic liver disease performed at King's College Hospital were retrospectively analysed. Laboratory and clinical data from pre- and post-LT were recorded including length of stay (LOS). Inclusion criteria were defined as a documentation of delirium post-LT in the clinical notes. Data was collected, and univariate analysis were performed.
Results: 792 LTs were performed during this time with an incidence of post-LT delirium of 14.3%. ICU LOS was prolonged in patients with post-LT delirium (*Mdn=6.0v3.0,U=21505,n_1=113,n_2=679,p< 0.0001*) as was hospital LOS (*Mdn =14v11,U=29575,n_1=113,n_2=679,p< 0.005*). Patients with delirium post-LT had a higher rate of sepsis (*OR 3.9,CI 2.53-5.85,p< 0.0001*). Patients with pre-LT encephalopathy had a higher risk of post-LT delirium (*OR 2.1,CI 1.3-3.1,p< 0.0005*). Renal-sparing immunosuppression use was associated with a higher rate of post-LT delirium (*OR 2.12,CI 1.42-3.14,p< 0.0005*). Patients with post-LT delirium were older (*Mdn=57v54,U=32,606,n_1=113,n_2=679,p< 0.05*). No significant associations were observed for patients with post-LT delirium and; serum sodium, UKELD or day 5 tacrolimus levels. Patients with NAFLD were more likely to develop post-LT delirium (*OR 1.79, CI 1.03-3,p< 0.05*). No other aetiology was significantly associated with post-LT delirium. Delirium did not affect inpatient survival.
Conclusion: Delirium post-LT is associated with increased hospital LOS. Sepsis is the major risk factor for delirium post-LT. The association of NAFLD with delirium post-LT may be due to a lack of recognition of cerebral small vessel disease pre-LT. The association between the use of renal-sparing immunosuppression and post-LT delirium is unclear and may represent intraoperative factors such as ischaemia-reperfusion injury.

P-086

Prophylaxis for latent tuberculosis in liver transplant recipient: single center experience

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Backgroud: Llatent TB infections (LTBI) in liver transplant (LT) recipients is challenging because hepatotoxicity of Isoniazide (INH) prophylaxis in graft recipients.In our LT center we started to use INH Phx since 2014.In this research we evaluated the efficacy and safety of this prophylaxis schedule in LT recipients comparing them to those subjected transplanted prior of 2014.
Method: From March 2010 to December 2017, we evaluated, on 291 patients who received LT at a single center, isoniazide .we examined the results of tuberculin skin tests and interferon-γ release assays, use of INH, INH-induced hepatotoxicity, and post-LT TB occurrence INH Phx was started prior LT in those having low bilirubin serum level or within 10 days after LT. Close follow-up was managed in those patients.
Results: Among 291 recipients, 127 were those evaluated and followed up prior INH Phx schedule (Group A) while 164 subjects were evaluated for INH Phx according to tuberculosis Lab tests (Group B).No statistically significant differences were found in terms of immunosuppression trough levels or surgical parameters (warm and cold ischemia). 31 patients in Gorup A were found to be positive at TB tests for LTBI while 45 patients in Group B received post-transplant INH Px. No cases of post-transplant TB were detected in both groups. Among INH Px recipients, post-LT TB infection did not occur, however hepatotoxicity after INH Px was present in 6 cases.3 out of six patients undergoing INH Phx after LT required treatment schedule suspension due to significant increase in aspartate aminotransferase (AST) level that was higher than 350 U/L and Total Bilirubin higher than 6.5 mg/dL.
Conclusion: Considering the absence of LTBI in those without any Phx approach, on the basis of adverse effects large multicenter trial, aimed to evaluate the efficacy and safety of INH Phx in real life setting is required.

P-087

Chronic kidney disease in liver transplantation - even early stage disease is associated with post operative renal replacement therapy

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Background: Liver transplant (LT) recipients develop post-operative acute kidney injury (AKI) and require renal replacement therapy (RRT) post-LT, which are associated with worse outcomes. This is a multifactorial process, and underlying chronic kidney disease (CKD) is associated with AKI. Evaluation of renal function is recommended during assessment of LT recipients, however specific diagnostic tools are not defined. We aimed to stratify AKI requiring RRT post-LT by baseline CKD stage.
Method: LT performed at a single institution from 1/1/17 to 31/12/17 were reviewed (aged under 18, multi-organ transplants and acute liver failure were excluded). Clinical and biochemical parameters, and use of RRT were collected from clinical notes. CKD stage at assessment was categorised by eGFR according to KDIGO guidelines.
Results: 164 patients with mean age at transplant 52.9 years. CKD stage 2 or greater at assessment in 42.6% of patients. Incidence of post-LT AKI requiring RRT 22.6%. Lower eGFR at assessment ($p< 0.001$) was associated with RRT post-LT.
Conclusion: Data from our cohort suggests that risk stratification for the development of AKI requiring RRT post-LT can be made by CKD stage at assessment based on eGFR calculation. Even patients with early stage CKD are at increased risk of the requirement for RRT post-LT. Functional tests of renal function and renal biopsy should be considered in patients with more advanced CKD.

CKD stage (eGFR ml/ min/1.73m2	n	RRT (n)	RRT (%)
1 (>90)	94	13	13.8%
2 (60-89)	46	13	28.3%
3 & 4 (15-59)	24	11	45.8%

[CKD stage at assessment for transplantation]

P-088

Strongyloides stercoralis hyperinfection syndrome after liver transplantation: a case report

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Strongyloidiasis is a parasitic intestinal infection produced by the nematode *Strongyloides stercoralis.* Self-infection may result in persistent infection for decades after the original exposure, and in immunocompromised patients it may result in a high severity, with hyperinfection affecting the lungs and gastrointestinal tract, or fulminant dissemination involving organs and tissues outside the natural cycle of the parasite, with fatal cases rates above 70%. The purpose of this poster is to report an unusual case of hyperinfection by *Strongyloides stercoralis* after liver transplantation. A 61-year-old male from Rio de Janeiro, Brazil, with endstage liver disease secondary to hepatitis B and concomitant hepatocellular carcinoma underwent orthotopic liver transplantation in june 2018. Immunosuppressive therapy was based on tacrolimus in combination with high doses of corticosteroids for the induction phase and lower doses of both drugs during the maintenance regimen. Two months after surgery, he presented inappetence and abdominal pain, and CMV screening was performed, with negative PCR. It evolved with diffuse alveolar hemorrhage, respiratory insufficiency and the need for orotracheal intubation. CT scan of the thorax revealed confluent nodules, ground glass and consolidations. The possibility of fungal infection was suggested. Because of the severity of the condition, treatment with tazocin and amphotericin B, associated with ganciclovir, was prescribed. Bronchoscopy with bronchoalveolar lavage was performed identifying *Strongyloides stercoralis,* despite the prophylaxis was performed pretransplant. Ivermectin treatment was instituted 18g each day by enteral catheter, with later association of albendazol 400 mg every 12 hours. He presented hemodynamic instability with need for vasoactive drugs and acute renal failure. After clinical and laboratory worsening, meropenem and polymyxin B were initiated to treat a new infectious process by *Pseudomonas aeruginosa* identified in tracheal secretion. Patient evolved to death due to refractory sepsis after 20 days of hospitalization.

P-089

The role of sarcopenia in predicting outcomes after orthotopic liver transplantation

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Background: Sarcopenia has shown to be predictive of outcomes in orthotopic liver transplant (OLT) recipients. We aimed to investigate if sarcopenia was comparably predictive in our cohort of patients receiving an OLT.
Methods: An IRB-approved study was performed examining evaluable patients who received an OLT from January 2015 through August 2017. We compared clinical outcomes of sarcopenic and non-sarcopenic patients stratified by gender. Outcomes of interest were hospital LOS (hLOS), ICU LOS, number of ventilator hours (VH), blood products administered in the operating room, complications and death within 90 days and death within one year.
Results: A total of 257 patients were evaluated and 61 (23.7%) were considered sarcopenic. Of the total cohort, the median age was 58.1 [50.8-62.6] and MELD scores were 19 [13-25], respectively. The etiology of end-stage liver disease between the two groups were comparable. Stratified by gender, sarcopenic women had statistically significant longer hLOS and ICU LOS, 14.2 [10.7-35.2] days and 3.57 [1.8-7.4] versus 8.7 [6.6-16.0] days and 2.0 [1.5-3.4] days in non-sarcopenic women (p= 0.0036 and p=0.0205). Also, sarcopenic women required longer ventilator support with 31.3 [21.6-92.8] hours than non-sarcopenic women 17.0 [13.8-32.8] hours (p=0.0034). Men deemed sarcopenic required more blood products intra-operatively (19 [11-34.5]) than non-sarcopenic men (8 [2-18]) (p-value< 0.0001). There was not a statistically significant relationship between sarcopenic patients and complications or death within 90 days or one year after surgery.
Conclusions: In our patient population, we found that sarcopenic women had a significantly longer hLOS and ICU LOS and significantly more ventilator hours compared to non-sarcopenic women. Sarcopenic men had a significantly higher number of blood products administered. But, men nor women did not have a significantly different rate of death at one year after surgery.

P-090

Redefining cirrhotic cardiomyopathy: a shifting paradigm

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Background: Diastolic dysfunction (DD) is the hallmark of cirrhotic cardiomyopathy (CCM) which criteria were established in 2005. The prevalence of CCM was accordingly thought to approach 50%. Since then, substantial advancement in the techniques of Echocardiography have occurred prompting American and European cardiac societies to set new diastolic dysfunction criteria in 2016. In this study, we evaluate the prevalence of DD among patients with decompensated cirrhosis according to the new criteria.
Methods: This is a retrospective chart review of patients who underwent liver transplant for decompensated cirrhosis at a North American center between 01/2008 and 11/2017. Only patients with complete echocardiographic data were included. Descriptive analysis was performed to compare pre-transplant diastolic dysfunction prevalence according to 2005 criteria with that according to 2016 criteria. In a subset with post transplant echocardiography, post transplant measurements were compared to those pre-transplant.
Results: There were 158 patients of whom 59 were women. Mean age at transplant was 58 (±8) years. When the DD criteria from 2005 were applied, 117/158 patients (74 %) fulfilled the criteria. With the 2016 DD criteria applied, the overall prevalence of DD in the cohort was 12.6% (20/158 patients); 14.5% of patients with NASH-related cirrhosis and 12.7% of patients with alcohol-related cirrhosis compared with 11.1 % of patients with other disease etiologies (p=0.47). 10 of the 20 patients with pre-transplant DD had repeat echocardiography after transplant (median 539 days) and there were no significant changes in the means of new diastolic dysfunction surrogates after transplant (Table 1).
Conclusion: The new diastolic dysfunction criteria suggest that CCM is less common than previously believed. This may explain the relative lack of predictive value of prior CCM criteria on clinical outcomes. Post transplant improvement cannot be assumed.

Diastolic Dysfunction Surrogate	Mean Septal e' cm/sec	Mean Lateral e' cm/sec	Mean E/e' ratio	Mean Tricuspid regurgitation velocity m/sec	Mean Left atrial volume index mL/m2
Pre-Transplant (N=10)	6.6	7.4	17.7	2.764	42.5
Post-Transplant (N=10)	5.7	8	18.9	2.83	41.9

[Changes in Diastolic Dysfunction Post Transplant]

P-091

Reoperation in the early period after adult living donor liver transplantation is poor

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Background: Reoperation after liver transplantation was considered as poor outcomes. However, The effect of reoperation due to gastrointestinal (GI) tract related complications after adult living donor liver transplantation (LDLT) was not known to the prognosis. The aim of present study is to identify the relevance between the cause and the outcome of reoperation after LDLT and classify the risk group after LDLT.
Method: A retrospective analysis of 506 cases of reoperation within 30 days after adult LDLT which was performed in Samsung Medical Center from 2010 to 2015.
Results: Among 506 adult LDLT recipients, 98 patients(19.4%) were underwent reoperation. The causes for reoperation were bleeding (n=39, 39.8%), vascular complications (n=26, 26.5%), wound complications (n=12, 12.2%), bile leakage (n=7, 7.1%), GI tract complication (n=6, 6.1%), and others (n=8, 8.1%). A multivariate analysis revealed that postoperative long intensive care unit stay, increased recipient operation time, and red blood cells transfusion within one week after LDLT were independent risk factors for reoperation. The patient survival rate at 1-, 3-, and 5-year was 90.7%, 83.8%, and 82.1% in the non-reoperation group and 82.7%, 73.5% and 71.4% in the reoperation group, respectively. The patient survival curve in the reoperation group was significantly lower than in the non-reoperation group (P=0.019).
In reoperation group, The survival rates of GI tract-related complication group, included bile leakage and GI tract complications(71.4% and 66.4%) were significantly worse than those of non-GI tract-related group included vascular complications, bleeding, and wound complications. (30.8%, 20.5% and 16.7%)
Conclusion: Present study shows that reoperation after adult LDLT is poor and GI tract-related complications are considered as high risk group of patient survival in the patients who underwent reoperation.

P-092

Relationship between ecocardiographic alterations and NT-proBNP plasmatic levels in cirrhotic patients

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Aims: To establish a relationship between NT-proBNP plasmatic levels and parameters of cardiac function determined by Doppler echocardiography in cirrhotic patients candidates to a liver transplantation.
Methods: A group of 81 cirrhotic patient (63 male and 18 female) candidates for a liver transplantation was selected for the study. A two-dimensional transthoracic echocardiography in M mode and Doppler was performed for each patient participating in the study. Parameters determined were: diastolic enlargement of interventricular wall thickness (IVW), diastolic enlargement of left ventricular posterior wall thickness (PW), diastolic left ventricular diameter (LVD), sistolic left ventricular volume (LVV), left ventricular mass (LVM), left auricular diameter (LAD), left ventricular ejection fraction and left ventricular diastolic function. NT-proBNP plasmatic levels were determined in plasma samples obtained from each patient . NT-proBNP values were determined using an electrochemiluminescence immunoassay in an Elecsys-2010 equipment (Roche Diagnostics, Germany). A group of twelve healthy volunteers with similar age to the patients of the study collaborated to establish normal (basal) values of NT-proBNP.
Results: NT-proBNP mean values in cirrhotic patients were 216.04 ± 3.76 pg/mL in male, significantly enhanced compared with healthy volunteers group values (p< 0.005). NT-proBNP mean values in cirrhotic female were 92.79 ± 85.80 pg/mL being this value no significantly enhanced compared to healthy volunteers. There were no significant differences in male in relation to LAD, LVD, PW or DD presence, although a no significant enhancement in NT-proBNP values was related to an IVW increase (p>0.005). In female, a significant enhancement in NT-proBNP was related with an increase in IVW values (p=0.041). There were no significant differences in relation to other parameters of the study.
Conclusion: The results must be an indication of a major incidence of cardiomyopathy in these patients in relation to cirrhotic patients with a normal interventricular wall thickness.

P-093

Biliary stricture after liver transplantation: Reappraisal of long-term outcomes

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Biliary strictures (BS) remain a major source of morbidity after liver transplantation. BS are categorized as anastomotic strictures (AS) or non-anastomotic strictures (NAS), which are associated with opposed prognoses. While BS were traditionally treated surgically, the widespread development of conservative treatments (interventional radiology and endoscopy) has dramatically modified the management of these patients. Yet, the value of these conservative treatments on a long-term perspective remains poorly described.

Methods: All patients undergoing liver transplantation between 2010 and 2016 at a single center were analyzed retrospectively. BS was divided into AS and NAS. Controls (no BSs) were used for comparison. Survival outcomes were compared in two separated propensity-score matched models (model 1: AS vs. Controls, ratio 1:1; model 2: NAS vs. Controls, ratio 1:3).

Results: Of 513 eligible patients, 112 patients (21.8%) experienced BSs (AS, n=97 and NAS, n=15). In the AS group, conservative treatments were undertaken for 96 patients (99.0%) and were successful for 95. In the NAS group, 7 patients were initially managed conservatively but eventually required retransplantation in 1 case. The remaining 8 patients underwent retranspantation in 3 cases and palliative therapy in 5 cases. Median follow-up was 48.3 months. In model 1 (97 patients of each), patient (95.0 and 85.5% vs. 88.8% and 86.5%, AS vs. Controls, P=0.862) and graft survival (88.8 and 80.0% vs. 86.1 and 83.8%, P=0.699) at 3 and 5 years were comparable between the two groups. In model 2 (NAS, n=15 and Controls, n=45), graft survival at 3 and 5 years was significantly lower in the NAS group (92.7% and 89.4% vs. 60.0% and 53.3%, P=0.004), while patient survival was similar between both groups (92.7% and 65.6% vs. 73.3% and 62.9%, P=0.174).

Conclusions: AS can be managed conservatively in the vast majority of the cases, while NAS remains an independent risk of graft loss.

P-094

De novo hepatitis B virus infection after pediatric living donor liver transplantation: risk factors, recognition and prevention strategies

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Purpose: To evaluate the risk factors of De novo Hepatitis B, especially the Hepatitis B serotype of both doners and recipients in pediatric living donor liver transplantation (LDLT). The effectiveness of prophylactic Lamivudine and the subgroups more responsive to Lamivudine are also defined among patients from anti-HBc-positive liver doners.

Methods: We collected the data of 990 pediatric living donor liver transplant recipients from June 2008 to December 2017 in Shanghai Ren ji Hospital. The preoperative (pre-OT) serum test for Hepatitis B antigen and antibody, pre-OT liver function and other characteristics of both doners and recipients were compared.

Results: 46 (4.88%) cases infected De novo Hepatitis B among 942 recipients underwent LDLT, and the mortality was 29 (10.47 %) for patients from anti-HBc-positive doners. Two important determinants for De novo Hepatitis B, anti-HBs negativity for recipient (P=0.010) and anti-HBc positivity for doners (P=0.001) were defined. Meanwhile, there were no difference in other clinical features of both recipients and doners (P >0.05). The incidence of De novo Hepatitis B among recipients from HBsAg(-)anti-HBs(-) anti-HBc(+)anti-HBe(-) HBeAg(-) doners or HBsAg (-) anti-HBs(-) anti-HBc(+) HBeAg(-) recipients was 7(33.33%)/4(19.05%), which is higher compared to other serotypes (P=0.000). Among patients from anti-HBc positive doners, prophylactic lamivudine could reduce the morbidity of De novo HBV infection significantly (P=0.000). According to the subgroup analysis, Lamivudine could be used to precisely prevent De novo Hepatitis B in recipients age ≥6 months, graft recipient weight ratio (GRWR) ≥3 and anti-HBc-negative (P< 0.05).

Conclusions: The anti-HBc -positive doners and anti-HBs-negative recipients are at high risk for De novo Hepatitis B. Lamivudine, as prophylactics, has statistical effect among recipients from anti-HBc-positive doners and is especially effective among those recipients age ≥6 months, GRWR≥3 and anti-HBc-negative.

P-095

Long-term results in comparative analysis of merits in using Polypropylene and Polydioxanone for microsurgical biliary reconstruction in LDLT

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Purposes: There is a high propensity of biliary complications in LDLT. Complications result in pronounced morbidity and occasionally compromised graft function. The success of biliary reconstruction is multi-factorial and no one can ignore the importance of suture material. The aim of this single centre retrospective study was to compare the results of biliary reconstruction using 6-0 Polypropylene and 6-0 Polydioxanone.
Materials and methods: 133 patients who underwent biliary reconstruction during LDLT from Nov 2014 to Dec 2015 were included. Prolene and PDS were randomly used for biliary reconstruction in 80 and 53 cases respectively. Right lobe graft was mainly used in two groups. Duct to duct reconstruction was done in majority of patients in both groups.
Results: The overall biliary complication rate was 10.0% in Prolene group including 1 patient with bile leak, 6 with stricture and 1 with leak followed by stricture. Whereas 11.3% patients in PDS group had complications including 2 with bile leak, 3 with stricture and 1 with leak followed by stricture. All biliary complications managed successfully and no mortality observed. There was no statistically significant difference in biliary complications between two groups (P=0.715).
Conclusions: The theoretical advantages of PDS over Prolene in biliary reconstruction couldn't be explained with this study.

P-096

Assessing frequency and risk factors for post-operative cardiac arrhythmias in patients undergoing liver transplantation

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Background: Acute cardiac events, including arrhythmias, are a major cause of mortality in end-stage liver disease (ESLD) patients following liver transplantation (LT). Post-operative atrial fibrillation in particular has been associated with increased mortality, graft failure, acute kidney injury, and prolonged hospital stay. Previous studies have suggested that pre-transplant renal impairment and prolonged QTc interval are independent predictors of post-transplant cardiac events. Currently, there are no specific stratification guidelines available to determine risk of post-transplant arrhythmia. The aim of this study was to assess the frequency and correlates of post-LT arrhythmias.
Method: Adult patients with ESLD undergoing LT between 2014 and 2016 at a single institution were retrospectively evaluated (n=72). Patient demographics, medical and social history, results of cardiac preoperative work-up, MELD score at time of transplant and development of cardiac arrhythmias were recorded. Standardized odds ratios for risk factors of post-transplant arrhythmias were calculated.
Results: The average MELD score across all patients was 23.1. Of 72 patients who underwent LT, 11 developed post-transplant arrhythmias (15.3%). Obesity (defined as BMI greater than 25) (odds ratio 5.079; 95% confidence interval 1.276-18.73), MELD score greater than 25 (OR 6.48; CI 1.412-31.18) and left ventricular hypertrophy (OR 7.891; CI 4.421-76.61) were found to be significant predictors of post-transplant arrhythmias. Gender, smoking status, coronary artery disease, diabetes, and chronic kidney disease were not significantly associated with increased risk of post-transplant arrhythmias.
Conclusion: Obesity, pre-LT MELD score greater than 25, and left ventricular hypertrophy, are associated with increased risk of post-LT arrhythmias and identify patients who may require enhanced vigilance for cardiac events in the post-operative setting.

P-097

Long term co-morbidity profile and outcomes of obese recipients undergoing liver transplantation - winning a battle, losing the war

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Background: Obesity is affecting more than 60% of adults in UK, contributing to an increasing prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD). Our aim was to compare the co-morbidity profile pre and post liver transplantation among the obese patients.
Methods: A retrospective single center study of all patients with

Body Mass Index (BMI) greater than 30 who underwent primary liver transplantation from September 2009 to August 2015 were analysed. Co-morbidities assessed were Hypertension (HTN), diabetes, serum triglyceride levels and weight pre and post transplantation.
Results: 957 patients underwent liver transplantation during the study period. Among those, 174 patients were obese with a mean value BMI of 33.6 (range 30-42) with a median follow up period of 61 months. Most common aetiology was NAFLD (39%) followed by hepatocellular carcinoma (28%). There was no difference in the weight pre and post transplant (p=0.24). New onset of diabetes was seen in 57% of the patients, while the diabetic control was significantly worse among those patients that were diabetic prior to transplant measured by the level of HbA1c (p=0.02). Serum triglyceride levels as well as the incidence of hypertension post-transplant increased significantly (p=0.04 and p< 0.01 respectively). The incidence of cardio-vascular events after transplant was 12% accounting for 21% of the overall mortality. Only 23% of the patients were involved in mild intensity regular exercise post liver transplant.
Conclusion: Co-morbidities of obese patients worsen following liver transplantation. Aggressive treatment of co-morbidities using a multidisciplinary approach, including improvement of diet and exercise routines for all pre-and post-transplant patients is imperative in order to improve the outcomes and the survival in obese transplant recipients and help reduce the risk of re-transplantation for NAFLD in the future.

P-098

The clinical course of biliary complications after adult to adult living donor liver transplantation: when does the achilles' heel heal?

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Background: Biliary complications (BC) is one of the most common complications after living donor liver transplantation (LDLT). Therefore, achieving complete resolution (CR) of BC is essential and associated with better long-term outcomes. We aimed to study the clinical course of LDLT recipients with BC, from its onset to CR and identify risk factors for its' non-resolution (NR).
Methods: A retrospective study of adult LDLT recipients from June 2006 to December 2016 with BC was done. Patients with ABO-incompatibility, transient early leak and malignant biliary stricture were excluded. CR was defined as the time when all abdominal drains (leak cases) and biliary stents were removed (stricture cases).
Results: We included 133 recipients. Median time to develop BC was 4.5 [interquartile range (IQR):0.9-15.3) months. Most common BC were strictures (n:84, 63%). CR was achieved in 80 (60%) patients after a median duration of 16.9 (IQR:7-26)months. Overall, the most common treatment modality was endoscopic biliary stenting (n:81, 61%), with a CR rate of 68%. Patients with NR of BC had longer median time to develop BC (7 vs 2.7 months; *p*0.041) and was treated more using PTCD (40% vs 8%, *p*< 0.001). Overall, PTCD treatment was the only independent risk factor for NR [OR:7.7 (CI95%:1.5-40.5) *p*0.016]. In patients with strictures, GRWR >0.96 [OR:0.22 (95%CI:0.05-0.95) *p*0.042] and complex stricture angulation [OR:10.5 (95%CI:2.5-44.7) *p*0.001] were the independent risk factors for NR. Two-year overall survival (OS) of patients in the NR group was 88% (CR:100%; Log-Rank test *p*< 0.001).
Conclusion: Patients with NR of BC is associated with worse OS. Endoscopic biliary stenting can address most BC cases with a high CR rate. Patients with GRWR of >0.96 may decrease the risk of NR by 78%. Patients with complex angled strictures and had used PTCD had a significant 10-fold and 7-fold increased risk of NR, respectively.

P-099

Pretransplant protein profiles predict acute kidney injury following liver transplantation from donation after circulatory death

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Background: Acute kidney injury (AKI) occurs frequently following liver transplantation (LT) and it essentially impairs the posttransplant outcomes. However, little is known about clinical risk factors of AKI following LT from donation after circulatory death (DCD), and intragraft molecular events responsible for the development of AKI remain largely unknown. The objects of this study are to identify clinical risk factors of AKI following DCD LT, and to investigate the potential relationship between protein profiles of pretransplant graft and the onset of AKI.
Methods: Relevant clinical data of 113 consecutive DCD LT procedures at authors' center was retrospectively collected and analyzed. The expression patterns of nine putative proteins were determined by immunochemistry examination.
Results: AKI patients displayed early continuously higher postoperative creatinine levels and consequently a markedly

increased possibility of renal replacement therapy, as well as a higher incidence of early allograft dysfunction. In univariate analysis, old donor age and intragraft high expressions of VEGF and NOX-1, were found to be associated with the development of AKI. Multivariate analysis identified donor age and NOX-1 expression as two independent predictors.
Conclusions: Old donor age and NOX-1 overexpression contribute to the development of AKI following LT from DCD.

	Leak	Stricture	Overall Biliary Complication
Single BD 22 (38.6%)	0	2	2 patients (9%)
Multiple BD 35 (61.4%)	4	3	5 patients (14%)
TOTAL 57	4 (7%)	5 (8.8%)	

[Biliary complications of grafts with single and multiple bile ducts after LDLT]

P-100

Microsurgical biliary reconstruction of multiple bile ducts reduce biliary anastomotic complications in living donor liver transplantation

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Introduction: Complications of Biliary reconstruction (BR) in complex biliary anatomy in living donor liver transplantation (LDLT) has negative impact on outcomes. In order to decrease complication rate in this setting, use of operating microscope (OM) for BR has been advocated. Here we present our 2 centers experience in BR with OM and its impact on biliary complication rate after LDLT.
Patients and methods: From Oct. 2015 to Nov 2018, 57 duct-to-duct BR using OM included in the analysis. All procedures were performed by a single transplant surgeon from each center. All BRs were performed inserting transanastomotic external drainage stents.
Results: There were 22 (38.6%) grafts with a single, 28 (49.1%) grafts with two, 6 (10.5%) grafts with three and one (1.8%) graft with 4 bile duct orifices that were reconstructed using OM. The mean bile duct diameter was 3.4mm. The mean time for BR using MT was 52.86 (23-123) minutes. There were 4 (7.0%) bile leak, 5 (8.8%) biliary strictures within a mean 15.9 (1-38) months follow-up. 2 patients experienced both leak and stricture. In total, 7 (12.3%) of 57 patients had biliary complications after LDLT. Complications occurred after a mean time period of 3.58 months(1-13 months). Only 1 patient had late biliary stricture after 1 year. Overall biliary complication rate was not significantly different comparing single bile duct to multiple bile duct reconstructions (p>0.05).
Conclusion: Using OM in complex biliary anatomy with multiple bile ducts reduces complication rate comparable to single bile duct grafts. Further studies with more patients and longer follow up are required in this setting.

P-101

Hepatic artery reconstruction is a risk factor for arterial thrombosis after liver transplantation

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Background: Aberrant anatomy in deceased donors has always been a challenge to the transplant community. Anatomical variations of the hepatic artery in donor often necessitates reconstruction on the back bench. The aim of this study was to determine the influence of hepatic artery reconstruction on hepatic artery thrombosis after liver transplantation and subsequent recipient morbidity and mortality.
Methods: We studied 244 consecutive deceased donor orthotropic liver transplants performed at our centre between October 2014-October 2017 by interrogating a prospectively maintained electronic database. Outcomes were compared in recipients with and without hepatic artery reconstructions using by 2-tailed t tests and chi-squared tests on continuous and categorical data respectively. Donor, recipient and operative risk factors for hepatic artery thrombosis (HAT) were identified using multivariate cox regression analysis.
Results: Liver transplants with and without hepatic artery reconstruction were largely comparable in terms of donor and recipient characteristics. HAT was significantly more common in the hepatic artery reconstruction group (18.75% vs. 5.6%; p=0.0076), although this did not increase morbidity (ITU/hospital stay, re-operation, bile leak) or mortality(both 30-day and 1 year). Overall, 20 out of 244 patients had Hepatic artery thrombosis (8.19%; 13 of which were early, occurring within 4 weeks and 7 were late, occurring after 4 weeks of transplantation). Multivariate regression analysis revealed donor age (p=0.0397) and hepatic artery reconstruction (p=0.0071) as risk factors for HAT. 9 out of these 20 patients required re-transplantation. However, there was no short-term (30 day) mortality amongst the HAT cohort.

Conclusion: Hepatic artery reconstruction is a risk factor for causing HAT in the recipient post liver transplantation. However, with better management strategies, this does not adversely affect the patient survival.

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Successful treatment of hepatic vein occlusive disease after liver transplantation using defibrotide

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Hepatic vein occlusive disease (HVOD) is a rare complication after liver transplantation but it often takes a life-threatening course. HVOD is characterized by nonthrombotic, fibrous obliteration of the small centrilobular hepatic veins by connective tissue and centrilobular necrosis in zone 3 of the acini. We describe, for the first time, our experience with defibrotide administered to HVOD after living donor liver transplantation.
A 39 years old female patient was diagnosed as primary biliary cirrhosis (PBC). PBC was managed with several medications including azathioprine. Liver transplantation was considered as her condition was getting worse. And she was taking azathioprine just before operation. Her elder sister donated liver and living donor liver transplantation was performed on December 6, 2017. The liver enzyme and total bilirubin were gradually increasing from post operation day 4 (POD). When we checked CT abdomen, hepatic veins size were decreased and perivascular low density. We considered to clinical acute rejection and started to steroid pulse therapy. She presented with ascites, jaundice, weight gain, and recurrent RUQ pain. We performed transjugular liver biopsy and transferred to ICU for management of fluid retention at POD 14. A liver biopsy was confirmed the diagnosis of HVOD. Histologic result showed perivenular inflammation, congestion, and hemorrhage. We started to conservative management such as low-molecular weighted heparin, PEG E1, antithrombin III, and diuretics. However, there was no reduction in the patient's weight, no improvement in the amount of ascites fluid, and liver enzyme, total bilirubin. We administered intravenously to defibrotied, 6.25mg/kg every 6 hours in a day, for 21 days. The patient was slowly recovered from jaundice and elevated liver enzyme was also slowly normalized.
Defibrotide is a promising drug for the treatment of HVOD after liver transplantation and warrants further evaluation in large, prospective studies.

P-103

Posttransplant lymphoproliferative disorder after liver transplantation: report of 17 cases among 735 liver transplants in single center

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Background: Posttransplant lymphoproliferative disease (PTLD) refers to lymphadenopathy or lymphadenia occurred in a group of patients with solid organ transplantation and hematopoietic cell transplantation under continuously immunosuppressive state. We report our experience with PTLD following liver transplantation in Beijing Friendship hospital.
Methods: We retrospectively analyzed 16 patients diagnosed with PTLD among 735 liver transplants between 2014 and 2018 in our center, the clinical and laboratory data of them were reviewed.
Results: The total incidence of PTLD was 2.2%. In these cases, 3 were adults and 13 were pediatric patients. One adult patient underwent combined liver-kidney transplantation, 2 adults and 4 children underwent OLT and the other underwent LDLT. The primary disease of pediatric patients were Biliary atresia, Ornithine transcarbamylase deficiency and Glycogen storage disease type III. The primary diseases of adult-patients were respectively Polycystic liver and kidney disease, Hepatitis B cirrhosis and Alcoholic cirrhosis. The immunosuppressive therapies in our center were the combination of calcineurin inhibitor with or without prednisolone and mycophenolate mofetil. The primary symptom of PTLD was variable: fever, EB-viremia, enlarged lymph nodes, abdomen pain with diarrhea, transplanted graft failure. 13 patients diagnosed PTLD in one year after liver transplantation. Patients were diagnosed as early lesions, polymorphic PTLD, monomorphic PTLD and classical Hodgkin lymphoma-type PTLD. Treatment involved reduction in immune-suppression (RIS) in 15. 6 patients were treated with Rituximab alone, 3 patients were treated with Rituximab and chemotherapy. Besides, we also used surgery and radiology to treat the enlarged lymph nodes. Except for one dropped case, all the patients were alive and 6 patients achieved full remission, while one relapsed.
Conclusion: PTLD is a complicated life-threatening complication of liver transplantation. The incidence of PTLD in our center is approximately same with previous studies, while prognosis is much better.

Table1. characteristics of 16 patients diagnosed with PTLD following LT

Patient No.	Age (m/y)	Sex	Primary disease	Type of surgery	Immunosuppressive regimen	Months after transplant to PTLD	Site of lymphoma	Liver function	EBV status of PTLD	PTLD type	Treatment	Prognosis
1	19 m	M	Glycogen storage disease type III	LDLT	Tacrolimus	8	Mesenteric and cervical lymph nodes	Normal	Positive	PTLD, early lesion	RIS, Rituximab	Clinical remission
2	29 m	M	OTCD	LDLT	Tacrolimus	6	Mesenteric and cervical lymph nodes	Normal	Positive	PTLD, early lesion	RIS, Rituximab	Clinical remission
3	8 m	F	Biliary atresia	OLT	Tacrolimus	16	Porta, mesenteric and cervical lymph nodes	Normal	Positive	Monomorphic PTLD, T cell type	RIS	Follow up
4	6 m	F	Biliary atresia	LDLT	Tacrolimus	9	Mesenteric lymph nodes	Abnormal	Positive	Polymorphic PTLD	RIS, Rituximab	Clinical remission
5	46 y	M	Alcoholic cirrhosis	OLT	Tacrolimus, prednisolone, Cellcept	7	Liver and retroperitoneal lymph nodes	Abnormal	Positive	Polymorphic PTLD	RIS, Rituximab, Chemotherapy	Clinical remission
6	17 m	F	Biliary atresia	OLT	Tacrolimus	46	Cervical lymph nodes	Normal	Negative	PTLD, early lesion	RIS	Follow up
7	7 m	F	Biliary atresia	LDLT	Tacrolimus	11	Cervical lymph nodes	Normal	Positive	Early lesion, infectious mononucleosis PTLD	RIS, Rituximab	Follow up
8	13 m	F	Biliary atresia	LDLT	Tacrolimus	7	Small intestine, mesenteric lymph nodes	Normal	Positive	Monomorphic PTLD, diffuse large B cell lymphoma	RIS, Rituximab, Chemotherapy	Clinical remission
9	9 m	M	Biliary atresia	LDLT	Tacrolimus	7	Mesenteric and cervical lymph nodes	Normal	Negative	PTLD, unclassified	RIS	Follow up
10	6 m	M	Biliary atresia	LDLT	Tacrolimus	9	Porta and inguinal lymph nodes	Normal	Unknown	PTLD, unclassified	RIS	Follow up
11	5 m	M	Biliary atresia	OLT	Tacrolimus, prednisolone	10	Mesenteric and cervical lymph nodes	Normal	Unknown	PTLD, unclassified	RIS	Follow up
12	13 m	M	Biliary atresia	LDLT	Tacrolimus, prednisolone	5	Cervical lymph nodes	Abnormal	Positive	PTLD, early lesion	RIS, Rituximab	Relapse after treatment and follow up
13	46 y	M	Hepatitis B cirrhosis	OLT	Tacrolimus, prednisolone, Sirolimus	11	Retroperitoneal lymph nodes	Abnormal	Negative	Monomorphic PTLD, diffuse large B cell lymphoma	RIS, Rituximab, chemotherapy	Follow up
14	32 m	M	Biliary atresia	OLT	Tacrolimus	36	Mesenteric lymph nodes	Abnormal	Positive	PTLD, unclassified	RIS	Follow up
15	53 y	F	Polycystic liver and kidney disease	Combined liver-kidney transplantation	Tacrolimus, prednisolone, Cellcept	3	Kidney and porta lymph nodes	Abnormal	Positive	Polymorphic PTLD	RIS, Rituximab, Chemotherapy	Clinical remission
16	8 m	M	Biliary atresia	LDLT	Tacrolimus, prednisolone	4	Cervical lymph nodes	Normal	Positive	PTLD, unclassified	/	Lost to follow up

m: month; y: year; M: Male; F: Female; OLT: Orthotopic liver transplantation; LDLT: Living donor liver transplantation; OTCD Ornithine transcarbamylase deficiency

[Characteristics of 16 patients diagnosed with PTLD following liver transplantation]

precluded reconstruction. Hence, PVA was done by anastomising the recipient replaced RHA to the portal vein (end to side). Biliary anastomosis was dismantled and Roux-en-Y hepaticojejunostomy was performed. There was improvement in LFT and in the affected areas of the graft (imaging). He developed 3 episodes cholangitis during follow-up which were managed conservatively. At 32 months after LDLT; LFT is normal; imaging showed normal graft with portal venous inflow, outflow, patent arterio-portal anastomosis, mild splenomegaly, no biliary abnormality or ascites. Endoscopy showed grade2 esophageal varices. He is on low dose of beta-blockers and being monitored for portal hypertension (PHT).

PVA is a salvage technique to re-establish arterial inflow to the LDLT graft, when re-LT, surgical or endovascular revascularization isn't possible. Conversion of biliary anastomosis to RYHJ is likely to help with additional arterial flow to the biliary ducts. Strict surveillance for PHT complications is recommended.

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Portal vein arterialization as a salvage procedure in hepatic artery thrombosis following LDLT

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Early hepatic artery thrombosis (HAT) post living donor liver transplant (LDLT) is an emergency; it de-arterializes the graft, causing parenchymal necrosis, dysfunction and biliary complications. Early intervention limits morbidity. We used portal vein arterialization (PVA) as a rescue technique in HAT, in the 3rd week post LDLT, when other options to restore arterial flow failed. 34 year old male, with auto immune hepatitis related chronic liver disease, underwent a modified right lobe LDLT (with reconstruction of anterior sector veins; single arterial anastomosis - graft right hepatic artery (RHA) to replaced RHA of recipient; single duct to duct biliary anastomosis). Post-operative period was uneventful; he was discharged on POD15, on low dose aspirin as per protocol. Raised transaminases on POD18 led to Doppler ultrasound, followed by contrast enhanced CT scan. Intrahepatic arterial flow was absent and neo-MHV was thrombosed, with areas of anterior sectoral congestion. Failed endovascular re-vascularization necessitated surgical re-exploration. Extensive thrombosis of graft artery

P-106

The role of frailty in predicting outcomes after orthotopic liver transplantation

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Background: In previous studies, frailty has shown to be predictive of outcomes in orthotopic liver transplant (OLT) recipients. Therefore, we aimed to investigate if frailty in our liver transplant patients was comparably predictive.

Methods: An IRB-approved study was performed evaluating patients who received an OLT from January 2015 through August 2017. We compared frail and non-frail patients as defined by the Karnofsky Performance Status Scale in terms of hospital LOS (hLOS), ICU LOS, number of ventilator hours, blood products (BPs) administered in the operating room, complications and death within 90 days and death within one year.

Results: A total of 257 patients were evaluated and 111 (43%) were frail. The median age of frail patients was 55.7 [47.8-61.9] years and 58.8 [52.5-63.5] years for non-frail (p-value=0.012). The median MELD for frail patients was 24 [18-31] and 15 [10-20] (p=< 0.001) for non-frail patients. HLOS and ICU LOS was 11.5 days [8.1-21.0] and 2.8 days [1.8-6.2] for frail vs 8.2 days [6.4-13.1] and 2.2 days [1.5-3.4] for non-frail patients (p < 0.0001 and p < 0.0001). Median ventilator hours were 23.7 [15.0-52.3] hours for frail versus 15.8 [12.0-24.7] hours for non-frail patients (p< 0.0001). Median number of complications per patient at 90 days was 2 [1-3] for frail vs 1 [0-2] for non-frail patients (p< 0.0001). The number of blood products administered in the operating room

was 17 [1-27] for frail vs 6 [2-16] for non-frail patients (p= < 0.0001). Death at 90 days and one year was not significantly different between the 2 groups.
Conclusions: In our patient population, we found that frail patients had both a significantly longer hLOS, ICU LOS, ventilator hours, and number of complications within 90 days as well as an increased number of blood products administered in the operating room.

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Hemodynamic changes with autologous flushing of donor graft during orthotopic liver transplantation

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Background: Reperfusion syndrome (RPS) is a known challenge during reperfusion of the donor graft during orthotopic liver transplantation and can result in cardiopulmonary arrest and death. Our liver transplant service instituted a flushing method of the donor graft with autologous blood to reduce the severity of RPS.
Methods: An IRB-approved study was performed evaluating the effectiveness of this flushing method that was started at our institution in 2015. A retrospective evaluation of intraoperative records were evaluated for cardiopulmonary arrest and death after reperfusion as well as changes in heart rate(HR), blood pressure(BP), pulmonary artery pressures(PAPs), cardiac output (CO), central venous pressure (CVP), systemic vascular resistance (SVR) and finally vasopressor (VP) consumption.
Results: There were 300 control vs 328 study patients. Pre-operative variables of MELD, age, gender, and etiology of cirrhosis were comparable. There were 7 cardiopulmonary arrests resulting in 4 deaths in the control group while there were 2 cardiopulmonary arrests resulting in no deaths in the study group. 5 minute HR showed significantly less % change in the study group -7.7 [-14.4–1.3] versus the control group -10 [-16.0–3.2] (p=0.0278). At 10 minutes, % VP reduction was more significant in the study group -53.6 [100.2-0] vs the control group at -25.0 [-80.16-0] (p= 0.0001). % SVR showed significantly less reduction in the study group at 10 minutes with -1.8% [-16.2-+12.6] vs the control group with-10.9% [-24.7-+3.9] (p=< 0.0001).
Conclusions: In this retrospective study, cardiopulmonary arrest and death was significantly decreased in the study group. In addition, the study group had a significantly lower consumption of. vasopressors as well as a significantly reduced decrease in systemic vascular resistance. These findings suggest that this autologous flushing of a donor graft may decrease the severity of RPS.

P-108

Liver transplantation without antifungal prophylaxis - incidence and outcome: single center experience

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Although widely practiced, there is no universal standard prophylaxis regimen among transplant centers in managing invasive fungal infections (IFI) after LT. In Europe, antifungal prophylaxis was administered in 35% of centers in all LT recipients, in 53% of centers in patients at risk, and in 12% of centers not at all. Here, we aimed to analyze the incidence and outcome of invasive fungal infection in our adult LT recipients who received no systemic antifungal prophylaxis.
Material and method: 131 LTs in 125 adult patients were retrospectively reviewed.The median follow-up time was 725 days (range 5 - 2182 days). 112 (85,4%) LTs were performed using right liver grafts from living donors. Low-dose tacrolimus (Tac) based triple regimen were used. No antifungal prophylaxis were employed in the patients. In the management of infectious episodes, empirical broad-spectrum antimicrobial treatment was initiated after appropriate cultures were taken. Treatment was adjusted shortly after the identification of the specific etiological agent and its relevant antibiotic susceptibility pattern.
Results: Twenty-eight (20%) recipients received empirical broad-spectrum antimicrobial treatment including fluconazole with a median of 8 days (range 2-448 days) after LT for suspected infection from undetermined origin. Fungal infection was detected in 10 (8%) recipients. Of these, 2 (%1.6) were accepted as IFIs since Aspergillus spp. was isolated from cerebrospinal fluid (CSF) in one and pathological examination of specimen from paranasal sinus revealed hyphae confirming Aspergillus spp. infection in another. In latter two, fluconazole was switched to voriconazole and posaconazole following the identification of infective pathogen, respectively. Nine recipients including those with IFIs were recovered after treatment and survived. One recipient was declared as brain death 6 days after re-LT done for delayed primary non-function
Conclusion: Institutional variability in incidence of IFI is likely due to variability in surgical techniques and differences in donor selection (living) and immunosuppressive regimens.

P-109

Successful treatment for end-stage hepatic alveolar echinococcosis with ex-vivo liver resection and autologous liver transplantation: a case report

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Objective: To explore the surgical process of *ex-vivo* liver resection and autologous liver transplantation (ERAT) for end-stage hepatic alveolar echinococcosis (HAE) and evaluate the therapeutic effect and surgical benefit.
Methods: The clinical data of one end-stage HAE patient treated with ERAT combined complicated hepatic vein reconstructionwas analyzed retrospectively. Preoperative examination and intraoperative exploration revealed the second hepatic portal was involved. We successfully initiated an operation through *ex-vivo* liver resection, hepatic vein reconstruction with the autogenous saphenous vein, and subsequent piggyback autologous liver transplantation by wide-mouth hepatic vein-artificial inferior vena cava anastomosis (end to side).
Results: This patient discharged uneventfully 14 days after the operation. The injection of low-molecular-weight heparin sodium and consequent oral warfarin sodium tablets were administered for anticoagulant therapy. Regular autograft ultrasound examination revealed no tarombokinesis in autologous liver and inferior vena cava.
Conclusion: ERAT is an ideal surgical method for end-stage HAE. Wide-mouth hepatic vein reconstruction using an autogenous saphenous vein is the key procedure. Postoperative anticoagulant therapy is significant for the improvement of transplanted liver function.

P-110

Risk factors for acute kidney injury in the postoperative phase after herniorraphy in patients with cirrhosis

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The incidence of abdominal hernia in cirrhotic patients is as higher 20% and in cases of major ascites the incidence may increase up to 40%.One of the main and most serious complications in the postoperative period of cirrhotic patients is acute renal failure, known as acute kidney injury (AKI).
Objectives: The objective of this study is to analyze the renal function of cirrhotic patients undergoing hernia surgery in our service, and compare the patients who presented AKI postoperative (PO) with the others, to determine the factors related to their occurrence.
Methods: Follow-up of cirrhotic patients who underwent hernia surgery between 2001 and 2014. Laboratory tests were routinely collected in the PO period. AKI was defined based on the consensus of the ascite´s club in 2015.
Results: Of 174 patients included, the primary outcome of AKI occurred in 58 (34.9%) patients. We observed that there was a significant difference between the groups in the variables: initial MELD, basal creatinine, and creatinine POI, the group with AKI PO had averages higher than the group that did not have AKI PO. In the AKI PO group, we observed that 74.1% of the patients had emergency surgery, whereas in the group without AKI PO, we had 34.6%. In the group with AKI PO, we observed that 90.4% of the individuals had complications in the PO, whereas in the group without AKI PO, we had 29.9%. We observed that the variables Age, Initial MELD, Baseline Creatinine, and Creatinine POI were statistically significant for survival.
Conclusions: There is an association between AKI PO and emergency surgery and also between AKI PO and complications after surgery.The factors related to higher occurrence of AKI PO in cirrhotic patients underwent hernia surgery are initial MELD, basal Cr, Cr Poi. We believe that cirrhotic patients must be well prepared before surgery because they present high incidence of AKIPO.

P-111

Effect of preoperative splenectomy on the prognosis after liver transplantation: a single center experience

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Objective: To investigate the influence of preoperative splenectomy on the prognosis after liver transplantation(LT).
Method: The retrospective cohort study was conducted. The clinical data of 120 patients who underwent liver transplantation in the Third Affiliated Hospital of Sun Yat-sen University between January 2006 and January 2016 were collected. 40 patients undergoing preoperative splenectomy and 80 undergoing spleen-preserving LT were allocated into the study and control group. All patients received modified piggyback LT by the same team. Observation indicators:
1) intra- and post-operative situations;
2) follow-up and survival. The follow-up includes routine blood test, concentration of immunosuppresants, function of liver and kidney, ultrasound and abdominal CT scan.
Results:
1) Intra- and post-operative situations: The operation time, volume of intraoperative blood loss and blood transfusion were (483±136) minutes, (5683±2950) ml, (4887±3682) ml in the study group and (392±103) minutes, (3522±1885) ml, (3455±2630) ml in the control group, respectively, with statistically significant differences (t=3.683, 4.358, 2.202, P< 0.05). 6 patients in the study group had introperative portal vein thrombosis(PVT), while no patient with PVT in control group, showing a statistically significant differences (χ^2=1.979, P< 0.05). The cases with postoperative infection, acute rejection, new-onset PVT and PV stenosis were 26,0,2,2 respectively in the study group and 46,1,2,1 in the control group, with no statistically significant differences (χ^2=1.171, 0.590, 0.547, 1.184, P>0.05).
2) Follow-up and survival: 120 patients were followed up for 3-24months, with an average time of 18 months. The rate of chronic rejection, the 1- and 2-year accumulative survival rates were 5.0%(2/40) vs. 6.25%(5/80), 90.0%(36/40) vs. 92.5%(74/80), 82.5%(33/40) vs. 78.8%(63/80) in the study and control groups respectively, with no statistically significant differences (χ^2=0.325, 0.780, 0.987, P>0.05).
Conclusion: The splenectomy before LT is easy to form PVT, increase time and difficulty of transplant surgery, however, it doesn´t increase complication risk after transplantation and affect postoperative survival.

P-112

Comparison of tacrolimus and cyclosporine combined with methotrexate for graft-versus-host disease prophylaxis after allogeneic hematopoietic cell transplantation: a meta-analysis

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Background: After patients received hematopoietic stem cell transplantation (HSCT), both cyclosporine (CsA) and tacrolimus (TAC) in combination with methotrexate (MTX) have been recommended as standard prophylaxis strategy for GVHD by European Group of Blood and Marrow Transplantation (EBMT). However, the advantage of TAC combined with MTX lacks conclusive evidence.
Methods: We searched online databases for studies on the comparsion of CsA+MTX and TAC+MTX on patients received HSCT. Odds ratio (OR) and 95% confidence interval (CI) was applied to compare the pooled data.
Results: We found that there is a significant reduction of Grade II to IV aGVHD (OR 0.42; [CI], 0.28-0.61; p< 0.00001), Grade III to IV aGVHD (OR 0.59; [CI], 0.38-0.92; p=0.02), chronic GVHD (OR 0.79; [CI], 0.62-1.00; p=0.05) and non-relapse mortality (OR 0.62; [CI], 0.40-0.95; p=0.03), and increased OS rate (only in those received from unrelated donor) (OR 1.30; [CI], 1.15-1.48; p< 0.0001) in TAC+MTX group. And similar outcomes occurred in relapse rate and disease free survival rate in both groups.
Conclusion: We conclude that TAC+MTX is superior to CsA+MTX on the prevention aGVHD in patients received HSCT, which further prolongs OS in some specific populations. Further studies are still required to evaluate effect of TAC or CsA combined with other suppressors in the therapy of HSCT.

P-113

Pure red cell aplasia(PRCA) due to mycoplasma pneumonia infection in adult recipient after liver transplantation: a case report and review of the literature

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Background: Mycoplasma pneumonia infection is rare among adult after liver tranplantation.To our knowledge, this is the first reported case of pure red cell aplasia (PRCA) due to mycoplasma pneumonia infection in adult recipient after liver transplantation.
Method: We described and analysed the clinical manifestation, diagnosis, treatment and prognosis of the one liver transplant recipients confirmed to have PRCA induced by Mycoplasma pneumonia.
Results: The patient had fever one month after liver tranplantation and had a gradual decline of haemoglobin levels within 2 months posttransplantation. The diagnosis was confirmed by several tests including bone marrow aspiration and enzyme linked immunosorbent assay (ELISA). The recipient achieved remission using symptomatic treatment that included intravenous immunoglobulins (IVIG), immunosuppressive regimen switch,anti-infection and blood transfusion.
Conclusion: Pure red cell aplasia induced by mycoplasma pneumonia infection is a disease with a favourable prognosis after symptomatic and supportive treatment.(i) ELISA technology combined with bone marrow aspiration and other laboratory examinations will meet the requirement for the diagnosis.(ii) IVIG is recommended as the first regimen for the treatment of PRCA induced by mycoplasma pneumonia infection in liver transplant recipients. IVIG can be repeated if the patient has a relapse.(iii) A switch of the baseline immunosuppressive regimen may achieve a favourable curative effect.

P-114

The tacrolimus-induced abnormal lipid metabolism through circRNAs/miR-33/FASN in terms of the liver

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Backgrounds: Immunosuppressant such as tacrolimus (TAC) is considered as a major contributor of post-transplant metabolic syndrome. Previous studies investigating the role of TAC in post-transplant diabetes mellitus. Here, we uncover a mechanism of TAC in dyslipidemia through a circRNA/miRNA/mRNA pathway.
Methods: Mice were treated with TAC under a chow-fed diet for 12 weeks. A set of tests (e.g., Oil Red O staining and lipid metabolism assays) and transgenic models were performed both *in vivo* and *in vitro*.
Results: Overexpression of miR-33 by transfecting liver cell lines HepG2 and Huh7 with miRNA mimics induced triglyceride accumulation through SREBP1 and FASN, miR-33 is a potential target of has-circ-0046327 (FASN), has-circ-0018811 (ppp3cb) and has-circ-0070511 (ppp3ca) predicted by starBase (http://starbase.sysu.edu.cn) and verified in vitro. TAC influenced the expression of circRNAs and miR-33 in vivo and vitro, followed up with accumulation of triglyceride.
Conclusions: TAC is more likely to induce abnormal lipid metabolism through a circRNAs/miR-33/FASN pathway. Gene targeted management may contribute to prevent or heal TAC-associated dyslipidemia after liver transplantation.

P-115

Predictors of alcohol o substance relapse in liver transplantation

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Background: Substance's addiction are one of the most common factor in patients that need organ transplantation; addiction's history could be a risk factor and could be linked with some psychological and physical recidivism. This clinical study focuses on alcohol and substance recidivism in patients after liver transplantation. The study's aim is analyze psychological and socioeconomic factors that could impact after liver transplant and lead into alcohol and drug relapse.
Method: We evaluated a sample of 119 liver-transplanted patients, 63 patients (52,9%) didn't report any drug or alcohol use or abuse while 56 patients (47,1%) reported clinical history of alcohol and/or substance abuse (abuse history (AH). In the AH group we analyzed their histories through clinical observations and psychological interviews during five years. We focused on different clinical and psychological indeces. After liver transplantation the patients with abuse history that relapsed into drug or alcohol abuse are n=15 (26,7%) and the patients without addiction relapse are n=41 (73,3%).
Results: The analysis found that 50% of AH patients with alcohol or drug relapse after liver transplantation, shows experiences and feelings of anger and hostility; more than 42% reported several antisocial practices and a cynical attitude towards the authorities. In patients that relapsed into drugs or alcohol, in over 64% we deduced a low self-esteem feeling and negative thoughts: very often this characteristic is linked with hypersensitivity to criticism and rejection. Despite the presence of these clinical elements just reported, over 70% of patients with alcohol or drug relapse after transplantation, seems to be willing to admit the problems of abuse.

Conclusions: From these results it seems very important a follow-up after liver transplantation, in which psychologist could plan clinical treatments to reduce the relapse's risk. Despite of little sample analyzed, we believe that this study can be the basis for further researches.

P-116

Post liver transplant delirium in alcoholic cirrhotic patients

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Background: Post liver transplant delirium is a common condition that has found to be associated with high morbidity and mortality within the first 6 months after transplant. In our previous study, history of alcohol abuse was found as a predictive factor of developing delirium in the ICU following liver transplant surgery. We aimed to find the risk factors of delirium and the impact on outcomes in alcoholic cirrhotic recipients undergoing liver transplant.
Methods: We reviewed 65 alcoholic cirrhotic recipients, whom were free from hepatitis B or C liver disease, and underwent liver transplant from January 2014 to August 2018 in our hospital, a medical center in Taiwan. We grouped them based on whether the patients had post liver transplant delirium. Parameters such as patient demographics, pre-operative laboratory data, hepatic encephalopathy, esophageal varices bleeding, MELD score, in-hospital mortality, major complications, length of ICU stay, length of intubation, and length of hospital stay were taken into consideration.
Results: Incidence of posttransplant delirium in alcoholic cirrhotic patient is 54% (37 of 69 recipients) in our series. In preoperative and clinical risk factors analysis, there were significantly higher preoperative hepatic encephalopathy rate (64% vs. 31%; p=0.009), higher MELD Score (27.5 vs. 18.7; p=0.005), and more intraoperative blood loss (4483 vs. 2393 ml; p=0.002). The delirium group also had significantly longer length of ICU stay (12.2 vs. 9.2 days; p=0.008), length of intubation (7.1 vs. 2.5 days; p< 0.001) and hospital stay (37.4 vs. 27.2 days; p=0.014).
Conclusion: Alcoholic cirrhotic recipients with posttransplant delirium were associated with preoperative hepatic encephalopathy, high MELD scores and increased intraoperative blood loss. Alcoholic cirrhotic recipients who experienced post-operative delirium also had prolonged hospital course, including length of ICU stay and endotracheal intubation after the transplant and overall hospital stay.

P-117

Rescue the intimal injury of graft hepatic artery by intraoperative fluorescence vascular stenting

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We present a new idea with rescuing the intimal injury of graft hepatic artery by intraoperative fluorescence vascular stenting. In one case with a hard hepatic artery thrombosis and the radiologist could not pass the guide wire through it, an intimal injury on both the graft and the donor side of the hepatic artery (HA) was found after a thrombectomy; this condition lead to increase frequency of arterial anastomosis, percutaneous transluminal angioplasty procedure, and prolongation of arterial thrombosis. We performed an anastomosis between unhealthy graft vessels and a healthy recipient vessel. The flow of the anastomosis region was patent initially by an ultrasound color Doppler examination but disappeared quickly due to thrombus formation. An intraoperative fluorescence vascular angiography was applied immediately since a fresh thrombosis is easier to pass through by angioplasty guide wire. A long endovascular stent was inserted to the injured vessels and the proper HA was reconstructed under microscopy. On the 3rd day after reconstruction, the post-angioplasty HA showed no dissection, stenosis, or pseudoaneurysm. Unexpectedly, the patient recovers well with acceptable graft function under 8 months follow up, respectively.

P-118

Incidentally diagnosed abdominal tuberculosis in liver transplant recipients during living donor liver transplantation (LDLT)

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Background: Active tuberculosis(TB) infection is considered to be a contraindication for liver transplantation. Literature on incidentally detected tuberculosis intraoperatively during LDLT is scanty. The aims of this study are to describe the prevalence of incidental TB in LDLT from endemic area and to analyze the outcomes in such rare presentation.
Methods: This is a retrospective study of LDLT recipients with incidentally detected tuberculosis between Feb 2016 and June 2018. All the prospective recipients were screened for tuberculosis. Intraoperative diagnosis of suspicious cases with peritoneal nodules or abdominal lymph nodes was confirmed by frozen section/histopathological examination/tissue PCR analysis. All of them were started on POD 3 with modified Antitubercular drugs (isoniazid, rifabutin, ethambutol & levofloxacin for 4 months followed by isoniazid and rifabutin for 5months) for a total of 9 months. Immunosuppression protocol was standard.
Results: 7 of 490 LDLT recipients(1.4%) had incidentally diagnosed tuberculosis. Explantation was difficult requiring relatively more blood transfusions and longer operative times. Drains were removed between 3 and 10 days (median 6 days). 2 patients required percutaneous drain reinsertion for massive ascites. None of them had worsening or dissemination of TB after introduction of immunosuppression.1 out of 7 patients died on postoperative day 30, due to fungal sepsis. No significant drug related hepatotoxicity or graft dysfunction was observed in surviving patients. Post operative median hospital stay was 30 days(19 to 80 days). None of the patients were lost to follow up and median follow up was 14 months (9 to 32 months). No active TB was diagnosed in the surviving patients after completion of ATT.
Conclusion: Abdominal tuberculosis diagnosed intraoperatively is not rare and it's not a contraindication for liver transplantation. Modified antitubercular drugs don't cause major hepatotoxicity or graft dysfunction. Prognosis and outcomes for tubercular patients are comparable to non infected patients.

P-119

Liver transplantation for severe portopulmonary hypertension: a report of 3 cases and literature review

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Objective: Portopulmonary hypertension(POPH) is a disease characterized by pulmonary hypertension on the basis of portal hypertension. Perioperative mortality in patients with severe POPH was so significantly increased that severe POPH was once considered a contraindication of liver transplantation. The perioperative treatments of severe POPH patients undergoing liver transplantation are sorted out and analyzed.
Method: The clinical data of 3 patients with severe POPH who underwent liver transplantation from June 2013 to June 2018 in our center were retrospectively analyzed. Combined with relevant literature, the effect and prognosis of perioperative medication for severe POPH were analyzed.
Result: Among the 3 patients with severe POPH, there were 2 female and 1 male, aged 31, 40 and 39 years respectively. The primary diseases were drug-induced liver failure, Caroli's Disease and hepatitis B virus-related cirrhosis. The preoperative mean pulmonary artery pressure (mPAP) was 58 mmHg, 50 mmHg and 49 mmHg, with an average of 52.33 ± 4.03 mmHg, respectively. All of them were diagnosed with severe pulmonary hypertension. After the treatment of treprostinil, sildenafil, tadalafil and ambrisentan, mPAP decreased to 32 mmHg, 37 mmHg and 34 mmHg before liver transplantation, with an average of 34.33 ± 2.05 mmHg. The duration of treatment was 9 months, 6 months and 5 months, respectively. All 3 cases were treated with cadaveric liver transplantation. One patient developed antibody-mediated rejection (AMR) and died of acute heart failure after re-transplantation. The remaining two cases recovered well after operation. Pulmonary artery pressure (PAP) was steadily lowered by Echocardiographic monitoring after the operation.
Conclusion: Liver transplantation with severe POPH has a very high perioperative mortality rate. It is still considered as a contraindication of liver transplantation. However, the safety of liver transplantation can be greatly improved by reducing mPAP to less than 40 mmHg by pharmacotherapy before operation.

P-120

Incidence and predictors of post-transplant diabetes mellitus in liver transplantation: a systematic review and meta-analysis

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Background and aims: Post-Transplant Diabetes Mellitus (PTDM) compromises overall survival in the long term due to cardiovascular risk, infection and graft failure. The study of PTDM in liver transplantation (LT) has been limited, without clear consensus regarding diagnosis and management.
This meta-analysis aims to review the incidence of PTDM in LT and identify its predictors, in comparison to other solid organ transplant (SOT) groups.
Methods: Literature search was conducted in databases of Medline, EMBASE, CDSR and CCRCCT from January 1995 to January 2017. Two independent reviewers screened the studies and extracted data. Incidence and predictors were then analyzed by means of meta-analysis.
Results: 350 eligible studies (38 LT studies) involving 151318 post-transplant patients were included in the meta-analysis. The incidence of PTDM by immunosuppression medication was 13% in cyclosporine and 19% in tacrolimus and sirolimus cohort across SOT (incidence at 1 year post-transplant was 11%, 16% and 12% respectively). The incidence in LT at year 1 post-transplant was 20% in cyclosporine and 14% in tacrolimus and sirolimus cohorts. Incidence by organ cohorts at post-transplant year 1 and years 2-3 is as shown in the table 1.
Conclusions: This represents the first meta-analysis of PTDM in LT. PTDM has an incidence of 19.6% in LT at 3 years, which is comparable to its incidence in other SOT groups. Significant predictors specific to LT include age, body mass index, hepatitis C, tacrolimus use and male sex.

Organ	Post-transplant year	Studies	Incidence	CI	I^2
Liver	1	11	13.6	7.9-22.4	88.0
Liver	2-3	20	19.6	14.6-26	95.8
Kidney	1	119	12.5	10.8-14.4	95.2
Kidney	2-3	77	17.1	14.9-19.5	98.2
Heart	1	3	29.3	9.5-62	84.9
Heart	2-3	10	22.4	17.1-28.8	93.6
Lung	1	4	8.1	2.4-24.1	87.0
Lung	2-3	5	18.8	8.6-36.3	96.8

[Table 1: Number of studies, prevalence by organ systems and year]

P-121

The "rule of number 5" to define primary non-function following liver transplantation: a single center experience trasplanting of liver grafts with severe ischemia-reperfusion injury

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Background: Primary non-function (PNF) of the liver graft is the most severe manifestation of graft dysfunction and represents the need of early emergency re-transplantation or patient death within the first week of liver transplantation (LT). However, there is not a objective universally accepted definition for PNF.
Methods: A consecutive series of recipients of LT between 2006 and 2018 was analyzed from our prospective collected database. Patients receiving partial liver grafts were excluded. We divided the cohort according to the occurrence of postoperative 30-days death in "Alive" or "Death" patients. Preoperative status, donor condition, graft quality, and intra and postoperative variables were analyzed to predict factors for post-transplant 30-days mortality.
Results: We identified 237 recipients: Alive 206 and Death 31. Preoperative, donor and graft variables were similar in two groups. The need of intra-operative ≥5 Red-Blood-Packed Cells (RBC) transfusion (p< 0.01), and number of patients with postoperative AST level peak >5000 mg/dl (p< 0.01), prothrombin concentration < 50% (p< 0.01), bilirubin level peak (p< 0.01) during the first 5 postoperative days were higher in the Death group. Multivariate analysis revealed that requirement of ≥5 RBC packs intraoperative transfusion and the presence of AST peak >5000 mg/dl, prothrombin < 50% within the first 5 post-operative days are predictive factors for 30-days postoperative mortality.
Conclusions: The occurrence of the"Rule of Number 5" (i.e.: AST peak >5000 mg/dl plus prothrombin < 50% within the first 5 post-operative days in patients requiring ≥5 RBC packs intraoperative transfusion) could be helpful for listing patients early for liver re-transplantation. International validation in larger series is urgently need to better define PNF following LT.

P-122

Impact of organ procurement team arrival time on pre- and intra-operative outcomes in liver transplantation

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Background: In low- and middle-income countries, hospital workforce, including surgical staff, decreases significantly during night shift (20:30-07:30 hrs). It is unknown if this has an impact on intraoperative outcomes when performing complex surgeries, such as liver transplantation. We aimed to evaluate whether organ procurement team (OPT) arrival at the receptor institution during night shift increases intraoperative adverse events or the time lapse between OPT arrival and start of recipient surgery.
Method: This was a cross-sectional study in a single center in Mexico. Arrival times and intraoperative data were retrieved from a prospectively collected database at the Department of Transplant Surgery. Patients transplanted for the first time between February 2017 and June 2018 were included. Retransplantation and combined liver-kidney transplants were excluded.
Results: A total of 56 liver transplants were included. Recipients had a mean age of 49.8±11.8 years, and 37(66%) were female. OPT arrived during daytime in 40 (71.4%) procedures and during night shift in 16(21.8%). There were no statistically significant differences in intraoperative adverse events (iAE) (10% vs 6.4%, p=0.657), length of surgery (387.9±81.5 vs 372.2±60.0 min, p=0.490) and bleeding (3731±3167 vs 3503±4045 mL, p=0.823) when comparing daytime surgeries to night shift procedures. On average, time lapse between OPT arrival and start of surgery was 69 minutes longer when arriving at night shift compared to arriving during daytime (95% CI: 12.5-125.5 min; p=0.018).
Conclusions: Liver transplants performed during night shift do not appear to increase the length of surgery, bleeding or incidence of iAE. However, arrival of the OPT during night shift increases the time lapse between arrival and start of surgery. These results demonstrate that there is room for improvement during the critical pathway of liver transplantation at night shift that should be addressed by our institutional policy makers.

P-123

Passenger lymphocyte syndrome after liver transplantation in a case of minor ABO mismatched donation

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Background: Passenger lymphocyte syndrome (PLS), a subtype of graft-versus-host disease, occurs when donor lymphocytes are transplanted with a solid organ and produce alloantibodies that react with antigens on the recipient´s red blood cells (RBCs). We report a case of PLS in liver transplantation (LTx) and describing the successful management of PLS in a deceased donor LTx.
Methods: A 64-year-old male sufferred from decompensated hepatitis B related cirrhosis received a LTx from a donation after cardiac death. OLT was performed successfully using the piggyback technique with 5 minutes of warm ischemia time in August 2018. The donor was ABO group O+ and the recipient was A+. Tacrolimus, mycophenolate mofetil and basiliximab were used as immunosuppressive regimen.
Results: On post-operative days (POD) 12, anemia was confirmed since the hemoglobin (Hb) fell to 5.9 g/dL. And group A packed RBCs were transfused. However, an ABO discrepancy was found in the ABO blood group matching: the forward type was A, but the reverse type demonstrated O with anti-A antibody. Positive direct anti-globulin test, negative indirect anti-globulin test and positive irregular antibody screening provided a prompt to the diagnosis of PLS. O+ washed RBCs transfusion, prednisone and gamma globulin pulse therapy, and tacrolimus transfer to cyclosporin protocol were adopted for treatment. Eventually, anemia was resolved; however, a positive direct antiglobulin test persisted to the last follow-up date (POD 92).
Conclusion: In the event of severe hemolysis and anemia after ABO non-identical LTx, PLS should be considered. Transfusion of compatible RBCs, utilization of steroid and alteration of immunosuppressor provided much help for the control of PLS.

P-124

The management of portal vein thrombosis after adult liver transplantation: a case series and review of the literature

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Portal vein thrombosis (PVT) after adult liver transplantation (LT) is a rare but serious complication with no consensus on the ideal treatment. We report a case series and a comprehensive review of the literature on PVT after LT to discuss the therapeutic options. The clinical data of 360 adult patients (≥18 years of age) that underwent LT from January 2015 to January 2018 were reviewed, and a comprehensive search of PubMed and Web of Science was conducted. Patients diagnosed with PVT after LT were identified, and relevant risk factors and therapies were analyzed. Among the 360 patients, seven (2.69%) developed PVT after LT. The onset of PVT within one week after LT was found in six patients (85.71%). Four of these seven patients with PVT received systemic anticoagulation (low molecular weight heparin and warfarin) therapy. Minimally invasive interventional therapies combined with systemic anticoagulation (heparin and warfarin) were applied to three patients, two of whom died because of severe abdominal hemorrhage and liver failure. In the 29 cases reported in the literature, minimally invasive interventional therapy combined with systematic anticoagulation or sclerotherapy were the most used methods (19/29). Systemic anticoagulation was administered to three patients, surgical operation (thrombectomy; portosystemic shunt and retransplantation) was performed for seven patients. Among these 29 patients, four eventually died. In conclusion, interventional therapy combined with systemic anticoagulation is a good choice for the management of PVT after LT, and in our experience, good result could also be achieved by systemic anticoagulation for early PVT patients.

P-125

Early vascular complications after liver transplantation

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Purpose: If vascular complications occur during the early post- liver transplantation (LT) period (esp., within 1 month after transplantation), it can be catastrophic. The aim of this study was to introduce our experience of treatments of patients suffered early vascular complications after LT.
Materials and methods: From November 2009 to August 2018, 60 adult patients underwent 61 LTs at our institution consecutively. Clinical liver function tests and imaging modalities were used to diagnose these vascular complications following LTs.
Results: Two patients (3.3%), one e deceased donor liver transplantation(DDLT) patient and one right lobe living donor liver transplantation (LDLT) patient, suffered hepatic artery stricture within two weeks after LTs. The first patient survived after receiving emergent revasculization, but he suffered subsequent biliary tract stricture. The other patient died in spite of receiving endovascular treatment for her hepatic artery thrombosis. There were 6 patients, including 5 DDLT patients and 1 LDLT patient, suffered portal vein stenosis (PVS) within 1 month after LTs. Primary percutaneous transhepatic portal vein stents (PTPS) were used in these patients. Technical success was achieved in all 6 patients. Clinical success was obtained in 4 patients. Another 39-year-old female left lobe LDLT patient suffered left hepatic vein stenosis 12 days after operation. Unfortunately, migration of inferior vena cava stent into right antrum was encountered during endovascular procedure. This migrated metallic stent was extracted from heart by open heart surgery 40 days after her initial procedure. All surviving PVS and hepatic vein stenosis patients had good liver grafts and patent stents.
Conclusion: TAE-related intima injury of hepatic artery was a risk for hepatic artery complications after LTs. The PTPS is a feasible alternative rescue procedure for patients with symptomatic early PVS. Surgical removal instead of endovascular removal of migrated metallic stent in heart was suggested to prevent rupture of heart.

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Relationship between NT-proBNP plasmatic levels and cirrhosis ethiology in cirrhotic patients candidates to a liver transplantation

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Aim: To evaluate preoperative plasma values of NT-proBNP among patients with hepatic cirrhosis, included in an active waiting list for liver transplantation, to establish a possible correlation with cirrhosis etiology.
Methods: Natriuretic peptide-B plasmatic levels were studied in 81 cirrhotic patients candidates for liver transplantation. The patients were distributed into three groups: group 1, alcoholic cirrhotic patients (n=40, 26 male and 4 female); group 2, viral cirrhotic patients (hepatitis C or B viruses; n=35, 27 male and 8 female); and group 3, patients with primary biliary cirrhosis (n= 6,6 female). Hepatic cirrhosis status was estimated by Child-Pugh and MELD scores. Body Mass Index (BMI) was also estimated as well as ascites presence.
A group of twelve healthy volunteers with similar age to the patients of the study collaborated to establish normal (basal) values of NT-proBNP.
NT-proBNP values were measured in plasma samples.
Results: Control group of healthy volunteers showed a NT-proBNP plasma levels of 21.82 ± 25.97 pg/mL for male and 66.11± 55.71 pg/mL for female. The results of the study showed no significant differences between groups concerning sex, age, cirrhosis status, body mass index, presence of ascites, Child-Pugh or MELD scores. NT-proBNP plasmatic levels were significantly enhanced in male of groups 1 and 2 compared with male of control group (p< 0.005). A significant enhancement in NT-proBNP values was detected in male of group 1 compared with male of group 2 (p< 0.005). On the other hand, NT-proBNP plasmatic values in female of all studied groups were enhanced compared with female of control group although that enhancement was not statistically significant. There were no significant differences in NT-proBNP female values among the three groups of the study.
Conclusion: Our results show a relationship between the elevation of NT-proBNP plasma levels and the severity of liver cirrhosis.

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Surgical complications requiring an early relaparotomy in HIV infected liver transplanted patients: risk factors and impact on survival

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Background: HIV infected patients with liver cirrhosis represent a superselected category of liver transplant recipients with possibly a different susceptibility to major transplant-related complications. The aim of the present study was to analyze the risk factors for early complications requiring relaparotomy and the related impact on overall survival (OS) in HIV infected liver transplanted patients.
Methods: retrospective study on a nationwide multicenter cohort of 157 HIV infected patients submitted to liver transplantation in 6 Italian Transplant Units between 2004-2014.
Results: Median preoperative MELD score was 18 (IQR 12-26.5). An early relaparotomy was performed in 24.8% of cases and the underlying clinical causes were biliary leak (8.2%), bleeding (8.2%), intestinal perforation (4.5%) and suspect of vascular complications (3.8%). The OS at 1, 3, 5 years was 74.3%, 68.0% and 60.0% respectively and an early relaparotomy was not a prognostic factors itself but increasing number of relaparotomies was associated with decreased survival (p=0.011). At univariate analysis, preoperative refractory ascites (OR 3.32, p< 0.01) and Roux-en-Y choledochojejunostomy reconstruction (OR 16.15, p< 0.01) resulted significant risk factors for early relaparotomy. Both variables maintained significance even at multivariate analysis.
Conclusions: In HIV infected liver transplanted patients, increasing number of early relaparotomies due to surgical complications did negatively affect the OS. Preoperative refractory ascites reflecting a severe portal hypertension and a difficult biliary tract reconstruction requiring a Roux-en-Y choledochojejunostomy were associated with increased risk of early relaparotomy.

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DLQI and impact of comorbidity among chronic alcoholic liver diseases in developing countries

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Objective: To study DLQI and Impact of care among chronic alcoholic liver diseases
Methods and materials: The retrospective data study with 91 patients: 51 men (82,4%) and 40 women(17,6%), aged 75 to 93 yrs (mean age 80 yrs). The Dermatology Life Quality Index(DLQI), WHO ICD-10 codes, Hospital Anxiety (A) and Depression (D) Scale (HADS) was taken for validation. Cases were evaluated with clinical, Lab and Biopsy wherever needed.
Results: Skin disorders like Fungal diseases(n=6), benign skin tumors and xerosis (seborrhoeic keratosis, papilloma) in 90% of cases; rosacea(n=2); herpes zoster(n=7); eczema(n=22); seborrheic dermatitis(n=24); recurrent chronic urticaria(n=9), allergic contact dermatitis(ACD) (n=7), dyshidrotic eczema on the hands(n=14). Systemic disorders as cardiovascular disorders(n=11) , Endocrine disorders(n=10) urogenital (n=20): GI(n=27), neurological disorders (n=15) pulmonary disorders (n=3), rheumatoid arthritis(n=3), others(n=2). In this study for HADS, the anxiety level (A) was from 2 to 16 points(mean=6.94). Depression level(D) from 2 to 20 points(mean=7.35). Cardiovascular disordersA:D= 11.2:9 Endocrine disordersA:D=10:6.2,urogenital disorders A:D=7.2:9.2, GI disorders A:D=7.3:5:3, neurological disordersA:D=11:6.3, pulmonary disorders A:D=5.6:2.3, rheumatoid arthritis A:D=7.3:5.2, Skin disorders A:D=6.3:7.1. Stigma and discrimination about the social-security and marriage of their off-springs.
Conclusions: In this study, Both having subclinical levels of anxiety,depression. Patients are more anxious with Skin disorders, pulmonary and rheumatic disorders than depression in neurological, urogenital and GI disorders. Caregiver of own family facing more stigma, discrimination due to poverty, illiteracy, migration, health disparity, gender inequalities and lack of government policy. Marriage, fear of rejection by neighbor, and the need to hide the fact from others were some of the more stigmatizing aspects. Many caregivers reported feelings of depression and sorrow. The relevance of stigma in the cultural context is increasing due to illiteracy, poverty, superstition, lack of awareness in developing countries like Nepal and India. Comorbidities among alcoholic with dementia, Alzheimer´s disease related neurological disorders impact can minimize with trained caregiver

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Prevention and treatment of cytomegalovirus after solid organ transplantation: a Bayesian network analysis

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Purpose: Cytomegalovirus infection is one of the most common complications after solid organ transplantation. Clinically, there have been several kinds of antiviral drugs for the prevention and treatment of cytomegalovirus, such as acyclovir, valacyclovir, ganciclovir and valganciclovir. We performed a network meta-analysis to evaluate their efficacy and safety.
Methods: We searched relevant prospective and multi-armed studies on PubMed up to Mar.2018. The primary outcome is the occurrence of cytomegalovirus infection and cytomegalovirus disease after solid organ transplantation.
Results: 17 prospective studies involving 2062 patients were included in our analysis. In the case of cytomegalovirus infection, the ganciclovir group (OR= 0.24 95% CI: 0.09-0.57) and the valacyclovir group (OR=0.20 95% CI: 0.04-0.69) is significantly better than the control group. The ganciclovir (OR=0.37 95% CI: 0.13-0.86) and valacyclovir groups (OR=0.31 95% CI: 0.07-0.98) showed moderate superiority compared to the acyclovir group. As for cytomegalovirus disease, the ganciclovir group, the valacyclovir group and the valganciclovir group showed significant advantages compared with the control group (ganciclovir group: OR=0.17 95% CI: 0.07-0.31, valacyclovir group: OR=0.08 95% CI: 0.01-0.33, valganciclovir group: OR=0.14 95% CI: 0.02-0.45). Similarly, the ganciclovir group (OR=0.38 95% CI: 0.12-0.71) and the valacyclovir group (OR=0.17 95% CI: 0.03-0.72) is better than the acyclovir group.
Conclusions: valacyclovir might be the most efficient in the prevention and treatment of cytomegalovirus infection and disease. Finally, however, it is also likely to induce leukopenia. Acyclovir may have the weakest therapeutic effect, while the possibility of leukopenia is also minimal.

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Fecal microbiota transplantation for refractory antibiotic-associated diarrhea secondary to severe complicated sepsis after liver transplantation

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Background: Severe complicated sepsis is the leading cause of infection related death after liver transplantation (LT), which requires multiple antibiotics. One of the most common toxicities is antibiotic-associated diarrhea. Fecal microbiota transplantation (FMT) can be a safe and highly efficacious therapy. However, approaches incorporating modulation of the microbiome to treat therapy-refractory diarrhea have not yet been explored in LT patients.
Method: We enrolled two patients onto this treatment protocol. Fecal microbiota was prepared from healthy donor and was delivered via the nasojejunal feeding tube.
Results: The first patient was a 66 yo male with hepatocellular carcinoma and liver cirrhosis. He suffered severe aspiratory pneumonia 5 days post-LT, and then developed refractory hyoxemia. Extracorporeal memberane exygenator (ECMO), continuous renal replacement therapy (CRRT), bronchoscope and multiple antibiotics (*Ceftazidime Averbatan*) were administrated. Hyoxemia and pneumonia significantly improved after 5 days. However, antibiotic-associated diarrhea was developed and refractory to standard therapy. After receiving FMT for 7 days, significant and rapid improvement occurred, with no diarrhea, no fever and abdominal distention. Importantly, stool samples were collected prior to FMT and following FMT to assess the diversity and composition of the microbiome before and after intervention. Results demonstrated more diversity microbiome and B/E value of ten-fold increased. The second patient was a 59 yo male with acute liver failure. Two weeks after LT, he developed severe complicated sepsis, with multidrug-resistant *Klebsiella pneumonia* detected in blood, sputum, stool, bile and urine. Diarrhea was occurred after 3 weeks of antibiotics (*Tegocycline*) administration. After receiving FMT for 7 days, the patient experienced partial improvement of gastrointestinal symptoms and complete resolution after a second FMT treatment for 14 days.
Conclusion: We report the first LT case series of refractory antibiotic-associated diarrhea, secondary to severe complicated sepsis, successfully treated with fecal microbiota transplantation via reconstitution of the gut microbiome.

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The efficacy and outcome of simultaneous proximal ligation of splenic artery and glue embolization of splenic artery aneurysm during living donor liver transplantation

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Background: The natural history of untreated Splenic-Artery-Aneurysms (SAAs) in transplant patients remains poorly understood. The clinical significance of SAAs is due to the fact that although SAAs are rare, the complication of rupturing is often fatal. There is some evidence to suggest repair of SAAs regardless of its size at the time of Liver-Transplantation given the propensity of these to rupture. Only Proximal Ligation of Splenic-Artery (SA) often results in treatment failure, therefore we combined it with Glue-Embolization of SAAs during Living-Donor-Liver-Transplantation (LDLT). We report the Efficacy and Outcome of this procedure.
Method: Of 192 LDLTs during the study period from September 2015 to November 2018, 05 (2.6%) were found to have SSAs on pre-operative imaging. All five underwent Simultaneous Proximal Ligation of SA and Glue-Embolization of SAAs after direct puncture of SA during LDLT. The recorded variables were the patients' demographic profile, pre-operative diagnosis, characteristics of SAAs and the post-operative outcomes.
Results: Of the five patients with SAAs, four were females. The mean age was 37.6±7.63 years. The cause of cirrhosis in four patients was Hepatitis B Virus and in one was Veno-Occlusive Disease. The number of SAAs were 2 in two patients and multiple in 3. All the patients had atleast one SAA located at the hilum or distal one-third of the SA. All the patients had atleast one SAA of size more than 25 mm. Post LDLT, no patient had SAA rupture or severe postembolization syndrome except one patient developed Splenic Abscess that was managed with percutaneous drainage on Out-patient-basis. All the patients are alive and well at present.
Conclusion: Simultaneous Proximal Ligation of SA and Glue-Embolization of SAAs during LDLT showed excellent efficacy and outcome. We recommend it regardless of the size of SAAs in order to avoid severe morbidity and mortality related to SAA rupture.

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Extra-anatomic bypass for the treatment of a mycotic pseudoaneurism after liver transplantation for hilar cholangiocarcinoma

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Liver transplantation (LT) for hilar cholangiocarcinoma after neoadyuvant chemo-radiotherapy is associated with arterial complications. Herein we report the case of a patient that had a mycotic pseudoaneurism of the celiac trunk graft, that was solved with an extra-anatomic bypass.
Clinical case: 47 years old man, diagnosed of a Bismuth IV unresectable hilar cholangiocarcinoma. After biliary drainage and neoadyuvant chemotherapy and radioteraphy, a LT was performed. The arterial anastomosis was done directly between the donor celiac trunk and the supraceliac aorta.
Two motnhs after LT, during a routinely performed computed tomography, a mycotic pseudoaneurism of the arterial anastomosis to the aorta was observed. An endovascular stent was placed, and antibiotic an antifungal treatment was initiated. 48 hours after the first stent, persistent leakage was observed, and surgical treatment was indicated.
The retroperitoneum was accessed via a toraco-phreno laparotomy. After controling the infrarenal aorta, a T-L anastomosis with a Rifampicine impregnated Dacron phrostesis was performed. Proximally, the phrostesis was anastomosed at the thoracic aorta, proximal to the pseudoaneurism. The aortic pseudoaurism was partially resected, and the hepatic artery sutured.
Postoperative outcome was uneventful, with normal hepatic and renal function. No medullary events were observed. Pseudoaneurism culture confirmed candida infection. In the present time, 6 months after the procedure, the patient is alive and without complications.
Conclusion: The use of an extra-anatomic bypass is a new option for the management of patients with mycotic pseudoaneurism. This access avoids the previous surgical field, affected by radiotherapy and infection.

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Mucormycosis in the liver allograft after liver transplantation for secondary biliary cirrhosis due to bile duct injury

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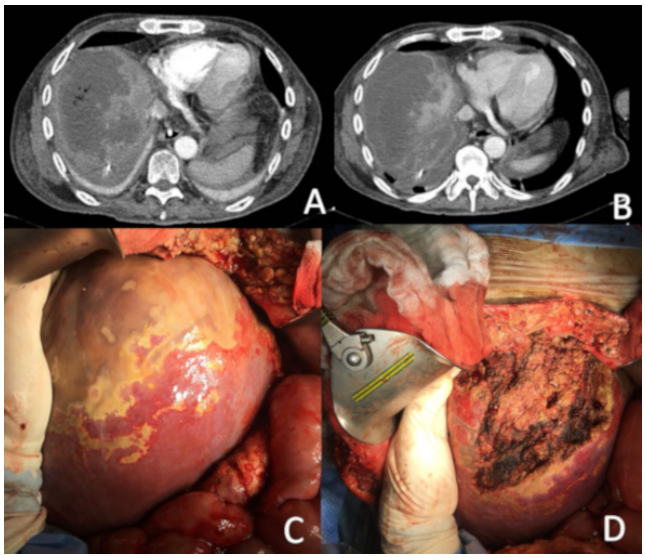
Introduction: Mucormycosis refers to a group of opportunistic mycoses that occur generally in immunocompromised patients and are caused by Mucorales.
Case report: A 57-year-old man with a history of secondary biliary cirrhosis due to bile duct injury during cholecystectomy and underwent a Y-en-Roux hepaticojejunostomy. Posteriorly, he presented multiple episodes of cholangitis that required long stay hospitalizations. He was referred to our center and underwent LT on June 2018 (17 y/o Male DBD, CIT 10 hrs, WIT 39 min, 6 PRBC, induction with basiliximab). Due to severe coagulopathy he underwent exploratory laparotomy and abdominal packing for 48 hours. He recovered with good liver function and LFT´s with a tendency towards normalization. On postop day 8 the patient presented fever and a CT scan was performed showing a large zone of hypoperfusion with bubbles of gas in the liver dome (Figure A). A percutaneous biopsy was taken for cultures. Preliminary results reported a filamentous fungus and liposomal amphotericin b was initiated with the suspicion of mucormycosis. The patient remained afebrile and asymptomatic. After 5 days of treatment a new image was performed, and progression of the lesion was noticed, due to these findings the patient was taken to the OR for surgical debridement (Figure B and C) Involvement of the liver dome was noticed and a non-anatomic hepatectomy (Figure D). After surgery the patient required increasing amounts of vasopressors. Despite all the support he progressed to multiple organic failure and finally expired. The product of hepatectomy confirmed the diagnosis of mucormycosis (Rhizopus sp).
Discussion: Mucormycosis represents a 2 to 4% of fungal infections. Despite all the efforts the patients' clinical condition deteriorated after surgery showing the high mortality rate in liver transplant recipients that has been reported of 50 to 100%.



[Liver Allograft]

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Nursing care of patients with end-stage cirrhosis complicated with portal vein thrombosis

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Objective: To investigate the nursing points of liver transplantation in patients with end-stage cirrhosis with portal vein thrombosis (PVT).
Methods: The clinical data of 152 patients with end-stage cirrhosis who underwent liver transplantation at the Organ Transplantation Center of the First Affiliated Hospital of Sun Yat-sen University from January 2010 to January 2016 were retrospectively analyzed. Thirty-two patients with PVT were included in the PVT group, and the remaining 120 patients without PVT were used as controls.
Results: The proportion of preoperative splenectomy in the PVT group was significantly higher than that in the control group (46.8% vs 18.3%, $P < 0.05$). The difference was statistically significant. There were no significant differences in the intraoperative blood loss, ICU stay, postoperative complication rate, perioperative mortality, 1-year and 3-year survival rates between the two groups ($P>0.05$). The re-embolization rate in the PVT group was higher than that in the control group (9.4% vs 1.7%, $P< 0.05$).
Conclusion: We should be fully aware of the patient´s condition. For patients with a history of preoperative splenectomy and a history of PVT, special attention should be paid to the observation of portal vein thrombosis in order to achieve more predictive observation and care.

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Analysis of risk factors of primary nonfunction after liver transplantation: report of four cases

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Background: Primary nonfunction(PNF) after liver transplantation(LT) poses a life-threatening situation for the recipient. 243 adult cadeveric LTs from February 2016 to August 2017 were reviewed retrospectively, 4 (1.6%) patients developed PNF and were analyzed to identify risk factors contributing to PNF following LT.
Case presentation:
Case 1: A 47-year-old male received emergent ABO-incompatible LT for HBV-related acute-on-chronic liver failure and severe degree hepatic encephalopathy. The DBD donor had 9h11m cold ischemia time. The operation lasted for 6h13m with the estimated blood loss 4800ml. He had profound coagulopathy and survived for 2 days post-LT.
Case 2: A 58-year-old female underwent LT for HBV-related liver cirrhosis and hepatocellular carcinoma(HCC). She had splenic embolization before. She received laparotomy post-LT due to low portal venous velocity, and later developed portal vein thrombosis(PVTT) and she was implanted portal vein stent. Her coagulation function deteriorated and she survived for 9 days-post-LT.
Case 3: A 51-year-old male underwent LT for HBV-related liver cirrhosis and HCC with PVTT. He had splenectomy before. The DBD donor was a 35-year-old male(height 165cm, weight 80kg) with cardiopulmonary resuscitation before harvesting. The donor liver weighted 2500mg and had macrosteatosis(25%). During the operation, severe abdominal adhesions and total PVTT, so portal vain was reconstructed. He had coagulopathy and survived for 3 days.
Case 4: A 54-year-old male patient underwent LT for HCC. The DBD donor liver was harvested under ECMO(extracorporeal membrane oxygenation) support. The donor liver had hepatocyte ischemic change (10%) with macrosteatosis(10%). The CIT was 13h15m. He developed graft failure and received re-LT 4 days post-LT. He was recovered and now he lives well.
Conclusions: PNF is uncommon but serious and life-threatening condition post-LT. Severe preoperative condition, ABO-incompatible LT, donor quality(prolonged CIT, macrosteatosis, large graft,cardiopulmonary resuscitation history) and complications post-LT are all risk factors contributing to development of PNF.

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Liver transplantation for Infrahepatic interruption of the inferior vena cava with azygos substitution - a case report

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Infrahepatic interruption of the inferior vena cava (IVC) is a congenital anomaly. The existence Interruption of the IVC is of particular interest to the liver transplant surgeon for surgical programming, because the hepatic vein may drain directly into the right atrium rather than into the suprahepatic vena cava. In this present study we report a case of orthoptic liver transplantation in a male pacient with a infrahepatic interruption of the inferior vena cava with azygos or hemiazygos substitution. 67-year-old man with a history of non-alcoholic steatohepatitis cirrhosis, Child pugg-A, and hepatocellular carcinoma (HCC), despite several comorbidities. The donor liver was prepared and the infrahepatic vena cava was oversewn. The suprahepatic vena cava anastomosis of the new liver was performed as usual. The operative time was 3hours and 35minutes with a warm ischemic time of 20minutes. No blood transfusions were given. The patient had an uncomplicated evoluation.

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Operation opportunity for renal transplant recipients who need liver transplantation: a single center experience in China

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Background: With the improvement of kidney transplantation, more and more patients have a long survival outcome; among them, some recipients would develop liver dysfunction because of previous hepatic diseases, autoimmune disorders and immunosuppressant toxicity, which, meanwhile, could rapidly cause renal allograft loss. These recipients had to undertake liver transplantation (LT) or even combined liver and kidney transplantation (CLKT). We aim to discuss the operation-related indications, timing, methods choice, treatment and risk factors, and to improve these patients' survival rate.

Methods: The clinical information and materials of 10 renal transplant recipients in our center from 2013 to 2016 who undertook LT or CLKT were retro-prospectively analyzed.
Results: All the 10 patients had viral hepatitis before retransplantation. The prognosis nutrition indexes (PNI) of all the 10 patients were less than 50. The MELD scores for all the 10 patients were over 20. Before retransplantation, 6 patients had dialysis for 2-3 times a week and over 3 months. 4 of them undertook synchronous CLKT, of which one died of severe infection a month after transplantation with good organ function, two of them only undertook LT and were still on dialysis and waiting for kidney transplantation. The other 4 patients had residual renal function, and they all only undertook LT, and 2 recovered renal function gradually after LT; the other 2 of them recovered with azotemia, but do not need dialysis.
Conclusions: The renal recipients with liver dysfunction receiving LT or CLKT can promote their prognosis. The risk factors which influence the successful rate of retransplantation are related to the nutrition condition (PNI), renal function, MELD scores, the frequency and lasting period of dialysis before LT or CLKT. Therefore, the choice and adjustment of operative timing and methods of LT or CLKT is pivotal.

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Anastomosis site stenosis after portal vein reconstruction through a pparacholedocal vein in cavernous transformation of recipient portal vein: a case report

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Introduction: Diffuse thrombosis of the entire portal vein (PVT) and cavernous transformation of the portal vein (CTPV) represents a demanding challenge in liver transplantation. We present the case of a patient with hepatocellular carcinoma and alcoholic liver cirrhosis concomitant with CTPV. We successfully treated with orthotopic deceased donor liver transplantation.
Case: A 50-year-old man with alcoholic liver cirrhosis and hepatocellular carcinoma was referred for liver transplantation. We found the cavernous transformation and complete thrombosis of the portal vein in the hepatic hilar area by preoperative Computed Tomography. From the deceased donor, the liver transplantation has been performed. The portal inflow to the graft was performed through paracholedochal collateral vein, obtaining good early graft function. During the follow-up, he diagnosed with portal vein stenosis after the first 3 months of the LT. This patient with PV stenosis did not show the portal hypertension symptom as melena

and hematemesis and he had normal liver function. After balloon angioplasty was done, he alive after these procedures and currently under close follows up.
Conclusion: This alternative is considered one of the useful methods to use in the cases of diffuse thrombosis and cavernous transformation of portal vein. We need to observe by regularly follow up Doppler ultrasonography for detecting PVC as early as possible.

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A case of unexpected sclerosing encapsulated peritonitis in deceased donor liver transplantation

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Sclerosing encapsulated peritonitis (SEP) is most commonly associated with CAPD and describes a fibrous peel that encompasses the peritoneal surfaces, bowel obstruction, malnutrition and eventually poor prognosis. It also has been rarely reported in end-stage liver disease complicated by ascites and SBP. Here we report a case of SEP found during DDLT. The fifty years old male patient who had HBV related liver cirrhosis, was ignored previous episodes of abdominal obstruction and evidence of peritoneal peel. We have to decide to perform or not. After several hours struggling with obscure anatomic structure, we exposed liver and finally finished total hepatectomy. Although very shallow space for whole liver graft, fortunately we got small graft and then completed DDLT.
The patient recovered uneventfully and still had good graft function in postoperative 1 year, even though there were many pessimistic reports.
We think that there was no evidence of aborting liver transplantation due to SEP and hope to discuss this uncommon difficult case.

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Management of cytomegaloviral esophagitis after liver transplantation: from nursing care perspective

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Background: Cytomegalovirus (CMV) is a common viral pathogen that affects the outcome of liver transplantation. Esophagitis is a common gastrointestinal (GI) manifestation during CMV infection.
Methods: Herein, we described a patient presented with significant gastrointestinal symptoms after liver transplantation. Endoscopy found active esophagitis with ulceration and granulation proliferation as well as local inclusion bodies. Immunohistochemistry observed positive cytomegalovirus staining. This patients was therefore diagnosed as cytomegaloviral esophagitis.
Results: Antiviral treatment (intravenous ganciclovir) was prescribed to the patient. Of note, comprehensive nutritional support were applied as well, including analgesia, acid suppression, gastric mucosa protection, soft food, appropriate food temperature, enteral nutrition with supplementary parental nutrition, and psychological support. Eventually, this patient recovered and were discharged from hospital.
Conclusions: Particular attention should be paid to cytomegaloviral esophagitis in patients receiving liver transplation. Comprehensive nutritional support from nursing care is helpful to accelerate the recovery of these patients.

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Neutrophil count of ascites will predict an occurrence of peritonitis after liver transplantation

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Background: An occurrence of a peritonitis after living donor liver transplantation is sometimes needs to emergency operation, and sometimes leads to death. So that we needs to detect an occurrence of peritonitis before the patient's condition become severe. We examined that what factor can predict an occurrence of peritonitis after liver transplantation.
Method: 60 patients who underwent liver transplantation (include both living donor and deceased donor) in our hospital were examined. The periods were between September 2011 to May 2017. We examined multiple factors such as age of recipient, gender, primary disease of transplantation, ABO compatibility, DSA titer, neutrophil count of ascites, type of liver graft (right lobe, left lobe, whole liver), and GRWR.
We used tacrolimus and MMF and steroid as immunosuppressive agents. We used rituximab more than two weeks before transplantation if the patient has a DSA, or ABO incompatible case.
Results: 10 patients had a peritonitis after transplantation. Only neutrophil count of ascites had a significant difference between peritonitis group and non-peritonitis group. Usually, neutrophil count of ascites decreased after transplantation, but when the peritonitis was occurred, neutrophil count rose again, even if there was no clinical sign of peritonitis.
Conclusion: The neutrophil count of ascites has a possibility of predictable factor for occurrence of peritonitis after liver ransplantation.

Poster Round I, Session 1, 2, 3: Donation after Cardiac Death

P-142

Changes of cytokines in rat donor liver during functional warm ischemia

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Background: Using donors after cardiac death is an effective method to ameliorate the shortage of donor livers. Cytokines are the key of reperfusion injury. However, little research has been done about the changes of cytokines during ischemia, especially functional warm ischemia.
Methods: A rat model about donors after cardiac undergo functional warm ischemia was established. Four groups were set up according to different time points of functional warm ischemia, including Sham group, 0 min group, 15 min group and 30 min group. Luminex high-throughput technique was used to detect the changes of 23 inflammatory-related cytokines in rat liver and serum, including G-CSF, GM-CSF, GRO/KC, M-CSF, IFN-gamma, IL-1a, IL-1beta, IL-2, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12 (p70), IL-13, IL-17A, IL-18, MCP-1, MIP-1a, MIP-3a. RANTES, TNF-alpha and VEGF. Meanwhile, the changes of AST and ALT in serum, SOD and MDA in tissues were detected, and the degree of pathological damage in liver tissues was assessed by H&E staining.
Results: The serum IFN-g showed statistical difference, showing a gradual upward trend, while the other indicators had no statistical difference. In liver tissue, there were 17 cytokines, including IL-1b, IL-2, IL-4, IL-7, IL-10, IL-12, IL-13, IL-17, G-CSF, GM-CSF, IFN-g, M-CSF, MIP-3a, TNF-a, VEGF and MCP-1 showed statistical difference. The most significant cytokines were IL-2, IFN-g, TNF-a.
Conclusion: With the prolongation of functional warm ischemia time, inflammatory-related cytokines in liver tissue have a significant change trend, which can be used to evaluate the quality of donor liver.

P-143

Recipients' gender and BMI are related to early acute rejection in donation after cardiac death liver transplantation

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Background/aim: Early acute rejection (EAR) is a common complication after liver transplantation (LT). The purpose of this study was to evaluate the incidence and risk factors of EAR in donation after cardiac death (DCD) liver transplantation recipients.
Method: We retrospectively analyzed the data of 461 DCD liver transplants performed during the period from January 2010 to June 2016 to study the relationship between EAR and various clinical factors. EAR was defined as histologically proven acute cellular rejection occurring less than 90 days after transplantation.
Result: The median follow-up time for this study was 33.1 months (range, 0.03-92.8months). Thirty-two (6.9%) patients developed EAR with a median period of 20.5 days (5-88 days) after transplantation. A multivariate analysis revealed that female recipient (hazard ratio, 2.801; P = 0.024) and high recipient body mass index (BMI) (hazard ratio, 1.005; P = 0.049) were two independent risk factors for early acute rejection. A multivariate analysis was performed in order to evaluate the factors that influenced the overall survival, the result revealed that HCC (hazard ratio, 2.308 ; P < 0.001), ABO-incompatibility (hazard ratio, 1.793 ; P =0.001) and operation time≥360 minutes (hazard ratio, 1.627; P = 0.012) were the independent prognostic factors for overall survival after liver transplantation.
Conclusions: Recipients' gender and BMI are related to early acute rejection in DCD liver transplant. HCC, ABO-incompatibility and OT ≥360 minutes are the independent prognostic factors for overall survival.

P-144

Femoral artery isolation to enhance efficiency and safety in liver donation after circulatory death: the University of Wisconsin approach

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Background: Liver procurement from deceased after circulatory death (DCD) is time-sensitive. Every minute of functional warm ischemic time (FWIT; time from oxygen saturation < 70% or SBP < 70mmHg to declaration of death) carries risk of biliary and non-biliary complications. Therefore, the procurement team is under pressure to operate quickly, which increases potential for sharps injuries. To optimize time constraints and improve operator safety, we have developed a method of femoral artery isolation prior to life support withdrawal.
Methods: Informed consent for the intervention is discussed with the potential donor's substitute decision maker. The potential donor is brought to the operating room and prepared for groin dissection and laparotomy. Lidocaine is used for analgesia while physical and vital signs are monitored for pain responses. The common femoral artery is isolated. The procurement team then leaves, and the patient's loved ones are brought to the bedside during withdrawal of life support. FWIT is limited to under 30 minutes. During the five-minute "hands-off" period, the family leaves. After final declaration of death, femoral cannulation is performed, systemic cold flush is initiated, and the laparotomy is performed. If the potential donor does not progress, the groin incision is closed and dressed appropriately.
Results: The femoral artery isolation technique has been used routinely for the last 15 years and DCD donors comprise about 10% of our total liver transplant volume. There have been no concerns raised regarding the procedure and no complaints about the groin incision should the donor not progress.
Conclusion: Performing femoral isolation in a controlled fashion in potential DCD donors establishes an environment in which safety and time efficiency are maximized. This technique has potential to decrease the time from declaration to cold flush by 2-4 minutes. Larger studies are required to determine the incidence of sharps injuries during DCD recoveries.

Poster Round I, Session 1, 2, 3: Donor Selection Criteria/Patient Selection/ Organ Allocation

P-145

Toronto validation of a machine-learning algorithm to predict liver transplant waitlist drop-out for non-hepatocellular carcinoma candidates

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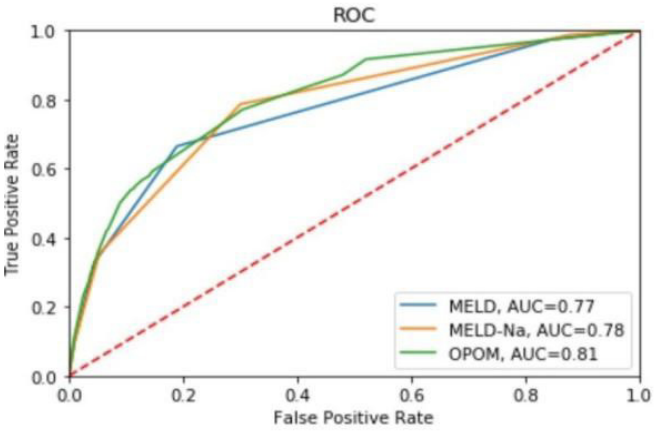

[Figure: ROC curves for 3-month waitlist dropout (OPOM, MELD, MELD-Na)]

Background: Currently the Model for End-Stage Liver Disease (MELD) is used to rank candidates for liver transplant in Canada. However, MELD does not provide equitable organ allocation to all waitlisted candidates. Recently, the Optimized of Mortality (OPOM) model was developed to predict 3 month waitlist mortality or drop-out, calibrated on the SRTR dataset. OPOM is an Optimal Classification Tree (OCT) machine-learning model which considers 28 dynamic variables and was previously shown to be superior to MELD-based allocation in simulation models. It is uncertain whether this model is valid in other patient populations.
Methods: From 2003-2018, 3142 non-HCC patients were waitlisted and 2056 patients were transplanted at University of Toronto. This time-stamped dataset prospectively captured all candidate details used in OPOM. Each valid candidate timepoint was evaluated using the previously calibrated OPOM classification tree to categorize the 3-month drop-out status at each leaf node. Using a rounding threshold of 0.5, the classification of Toronto data was compared to the risk prediction of OPOM. The AUC of OPOM was calculated and compared to MELD and MELD-Na.
Results: 22,111 discrete candidate timepoints in 2376 patients were assessed. The data was coded into the 5th layer of the OPOM decision tree model with 32 leaf nodes. The differences between the actual and predicted outcomes were assessed at each leaf node. The predictive accuracy of OPOM on Toronto data is 90.0%. The model had a positive predictive value of 39.6% and a sensitivity of 34.6%. The OPOM had an AUC of 0.81 for 3-month waitlist drop-out, compared to MELD(0.77) and MELD-NA(0.78)(Figure).
Conclusion: The OPOM model was validated on a large cohort of Canadian liver transplant candidates. These results suggest that a machine-learning approach may be valuable to stratify the sickest patients for future waitlist prioritization.

P-146

Predicting successful use of livers from deceased organ donors using UNOS Donor Management Goals Registry and a machine learning model

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Background: Artificial Intelligence is increasingly used to improve outcomes in healthcare. Understanding the likelihood of a particular organ being transplanted from a deceased donor may allow for better resource allocation during donor management and organ allocation. The national Donor Management Goals Registry (DMG) gathers data from 16 organ procurement organizations (OPO) and currently contains physiologic critical care data over the time course of donor management. We use machine learning on this dataset to predict whether a donor liver will be transplanted.
Methods: We included 188 variables for 12,194 potential deceased donors from April 2012 to November 2018 in the DMG dataset. Variables included vital signs, medication doses, lab values, diagnoses, and demographics. Three time points per temporal

variable were included: referral to the organ procurement organization (OPO), time of authorization of organ donation, and 12-18 hours after the OPO had taken over donor care. Data collected immediately prior to organ retrieval and variables revealing outcome (e.g. cross clamp time) were excluded. Outcome was defined as successful transplant of donor liver. The data were separated into training (64%), validation (16%), and test sets (20%). A gradient boosting machine (GBM) model was trained using the python package XGBoost with the default package parameters for binary classification. The GBM performed better than logistic regression, random forest, and neural network on the validation set.
Results: Of 12,194 total donors in the dataset, 8,805 (72%) livers were transplanted. We achieved accuracy of 78.99% and ROC-AUC of 0.791 on the test set. The most predictive factors in order of importance were: weight, age, BMI, and pO2 at time of authorization.
Conclusion: Machine learning can be used to make accurate predictions about whether a particular organ will be transplanted. Such predictions could be updated in real-time as a clinical decision support tool in organ donor management.

P-147

Benefits of an organ procurement organization (OPO) donor surgeon: reduced discards and improved utilization of marginal liver donors

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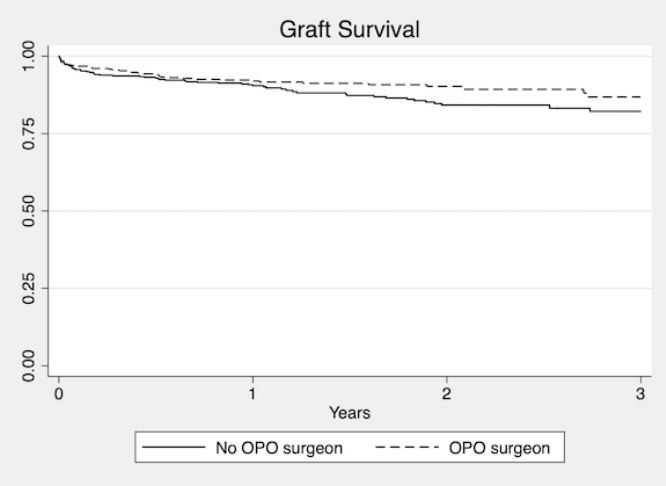
Introduction: In 2014, the OPO in North Texas hired a full-time donor surgeon. The intent was to enhance the organ donation process and increase organ use. The aim of our study was to investigate the impact of the OPO surgeon on rates and patterns of liver allograft utilization.
Methods: A retrospective review of the TXSB OPO liver procurement activity between January 2014 and November 2017 was performed. Two groups: (NO-OPO) OPO surgeon not involved in procurement and (OPO) OPO surgeon present at procurement were compared. Basic donor demographic data, serologies, marginal donor characteristics and intraoperative donor variables were collected. Donor risk index was calculated. Marginal liver characteristics were collected for all potential donors. Organ disposition codes and sharing codes were obtained to evaluate patterns of utilization. Recipient characteristics and outcomes were also compared.
Results: Discard rates were lower within the OPO group (5.8% v 7.4%). This was especially noteworthy when considering that the OPO group had significantly higher donor risk index scores (1.39 v 1.49, p< 0.0001) and had significantly greater frequency of donors with two or more marginal characteristics (34 v 14, p< 0.002). The OPO group had much greater frequencies of sharing both regionally (28% v 23%, p< 0.05) and nationally (16% v 6%, p< 0.0001). Importantly, when recipient outcomes were compared, there were no differences in patient or allograft survival between livers from the OPO and NO-OPO groups despite these higher risk organs (Figure 1).
Conclusion: The addition of a dedicated full-time OPO surgeon has improved the utilization rates of livers and reduced discards. Sharing opportunities appear to be enhanced by the presence of the OPO surgeon and promote excellent outcomes.



[Liver allograft survival is equivalent from organs procured with OPO surgeon present or absent]

P-148

Share 21 rather than share 15: balancing transplant opportunity without compromising waitlist outcomes

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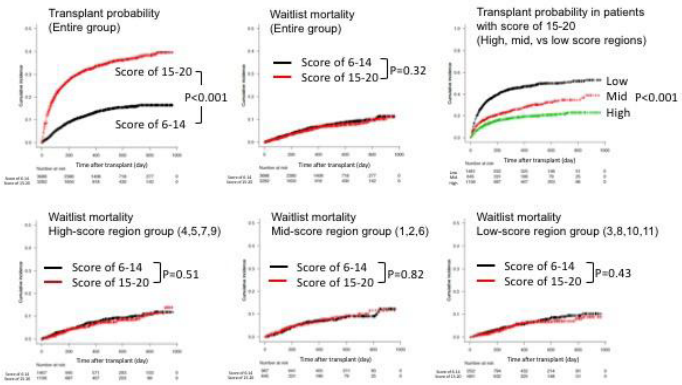
Purpose: We recently reported that, with the introduction of MELD-Na liver allocation, the score at which patients benefit from liver transplant as opposed to remaining on the waitlist, has shifted from MELD of 15 to MELD-Na of 21 (Gastroenterology2018;155). The aim of this study was to evaluate waitlist outcomes in patients with MELD-Na scores < 21 and explore the possibility of replacing “Share 15” with “Share 21”.

Methods: The study used data from the OPTN/UNOS registry. All adult patients who were registered for liver alone or liver-kidney transplant after implementation of the MELD-Na based allocation were evaluated. Waitlisted patients with initial and final scores < 21 were eligible. Patients with exception scores were excluded. Waitlist outcomes were compared between patients with an initial score of 6-14 and those with a score of 15-20. As a subgroup analysis, UNOS regions were categorized into high, mid, and low transplant score groups and waitlist outcomes were compared. Gray and Fine-Gray models were used to consider effects of competing risk events.
Results: There were 3686 patients with an initial score of 6-14 (group 1) and 3282 with a score of 15-20 (group 2). 444 and 1034 patients in groups 1 and 2 received transplant. Overall waitlist mortality rates were similar between groups 1 and 2 (P=0.32), whereas transplant probability was significantly higher in group 2 (P< 0.001). Similar waitlist mortality rates between groups 1 and 2 were observed in high (Regions 4,5,7,9), mid (Regions 1,2,6), and low (Regions 3,8,10,11) score regions. In group 2, transplant probability in the low score group was 3-fold higher than in the high score group (HR 3.00, P< 0.001), and mortality risk was comparable.



[Comparisons of waitlist outcomes in patients with low MELD-Na scores]

Conclusions: Share 21 may balance transplant opportunity between geographic regions without compromising waitlist outcomes nationwide.

P-149

Revised allocation policy to improve utilization of split-liver grafts to lower the waitlist mortality for young children and women candidates

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Young children and small statured candidates are dying on liver candidate waiting lists. This study evaluated the US experience of splitting donor livers to propose changes to liver allocation policy. A total of 935 donors were used for split-liver grafts and transplanted into 1870 recipients from 2002 to 2016. Controlling for recipient factors, a multivariable Cox hazard model for graft survival revealed donor age 3-10 had a RR of 3.27 (1.8-5.48) and donor age >30 had a RR of 1.76 (1.30-2.33) of graft failure. The CIT had a RR of 1.05 (1.02-1.08). In addition, the donor to recipient body surface area ratio (D/R BSA) of < 0.9 had a RR of 1.49(1.01-1.24). A donor availability review focused on the 11-17 year-old donors since by US policy this age group is favored to be transplanted in the < 18 year candidates. Of these donors 57.8% of larger split-grafts go into women as opposed to 44.3% of the whole grafts going into women. We propose an allocation policy change for mandatory splitting of any 11-17 year-old donor meeting criteria to be split and after meeting criteria for pediatric and adult status 1 allocation. A 0-5 year-old candidate meeting the D/R BSA criteria ≥ 0.90 would be needed in a location not unduly prolonging the CIT before splitting the 11-17 year-old donor. The remaining graft would be allocated according to the policies for adult allocation but with the criteria of meeting the D/R BSA ≥0.90. With these policy changes, the waiting list deaths for 0-5 year-old children can be drastically reduced and more small statured candidates including women would receive more liver transplants.

P-150

Are we prepared for social media altruism in living donor liver transplant - still a *terra incognita*!

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Introduction: To address organ scarcity in living donor liver transplant (LDLT), tech-savvy patients are turning to social media (SM) when there is no suitable donor from first-degree relatives (FDR) or distant relatives (DR). We report the changing trends in altruistic donation and analyze the demographics and outcomes of SM donors since the inception of our LDLT program.
Methods: 189 LDLT recipients and donors were retrospectively reviewed. SM was defined as LDLT from any form of electronic/ internet-based content sharing or communication channels. Demographic and clinical data were analyzed using SPSS v.20.

Results: Between Time-period 1 (1996-2008) and 2 (2009-2018), the rate of LDLTs from DRs (2.1% to 26.8%, p< 0.001) and SM (0% to 8.5%, p=0.040) have increased significantly. 12 SM-LDLTs came about by different platforms including Facebook™ (5/12), Instagram™ (1/12), Whatsapp™ group-chats (1/12) and newspapers/electronic media (5/12). SM donors were more likely to be Chinese (%Chinese, FDR:59.7%, DR:48.1%, SM:100%, p=0.017) and unmarried (%Unmarried, FDR:20.6%, DR:44.0%, SM:41.7%, p=0.019) compared to the other groups. Religious beliefs were also different between the groups. (FDR:31.3% no religious beliefs, DR:40.7% Buddhist, SM:50% Christian, p=0.033).
No difference in other demographic, socioeconomic factors or indication for transplant was demonstrated between groups. Operative data such as blood loss, duration of operation, length of hospitalization and complication rates appeared similar between the groups. The median referral-to-transplant time was shorter in the SM group but did not reach statistical significance. (days (IQR), FDR:125days (61-253), DR:92days (41-204), SM:67days (7-739), p=0.186)
Conclusion: SM donation in LDLT is likely to continue increasing in the near future, has the same safety profile as FDR and DR-LDLT and may help to shorten the waiting time for an organ. Culture-specific ethical guidelines can help to navigate this *terra incognita*. LDLT programs can tailor support for SM donors based on their unique demographic profile, which appears to be significantly different from the conventional donor.

P-151

Liver transplant candidate attitudes towards organs from increased risk donors: a single center survey

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Background: Increased Risk Donors (IRDs) are a significant proportion of the deceased organ donor pool but may be declined by patients on the liver transplant waiting list due to various factors. We conducted a survey of patients with end-stage liver disease awaiting a liver transplant in order to determine the factors leading to the acceptance of an IRD organ, and what strategies we could use to better inform and increase this rate of acceptance.
Methods: Adult liver transplant candidates who were outpatients completed a survey consisting of 51 questions on a 5-point Likert scale, with categories related to demographics, knowledge of IRDs, and likelihood of acceptance.
Results: A total of 150 transplant candidates completed the survey (age 19-80 years), with the majority (84.0%) being on the waiting list for less than 3 months. Male patients constituted 67.3%. Many patients (58.7%) had post-secondary education. Only 23.3% of patients already had a potential living donor and 58/144 (40.3%) were not optimistic to receive an organ in the next 3 months. Overall IRD organ acceptability was 41.1% whereas 26.2% would decline an IRD organ. Women were more likely to accept an IRD organ than men (54.3% vs. 34.7%, p=0.02). Those who had college education or higher tended to have lower IRD organ acceptability (28.3% vs. 47.4%, p=0.07). Acceptability of an IRD organ also increased as the specified transmission risk of HIV or HCV decreased (p< 0.001). Patients were also more likely to accept an IRD organ if they were educated on benefits of IRD organs eg, knowledge that an IRD organ was better quality than non-IRD increased overall acceptance from 41.1% to 63.3% (p< 0.001).
Conclusions: Our survey provides insight into liver transplant candidates that would benefit from greater education on IRD organs. Strategies targeting specific educational points are likely to increase acceptability.

P-152

Waitlist dynamics in adolescents and adult patients with below average bodyweight listed for liver transplantation, results from the Eurotransplant database

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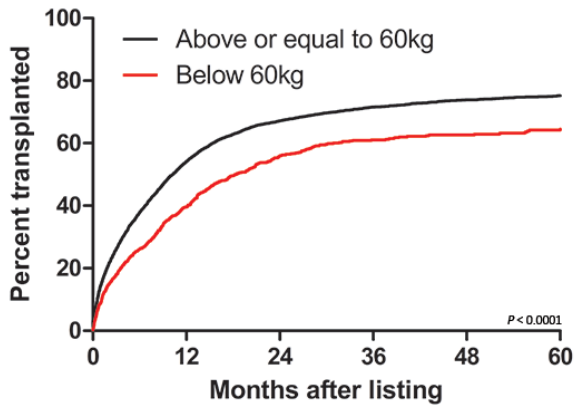
Background: Adult patients with below-average bodyweight waitlisted for liver transplantation (LT) may face a shortage of size-matched liver grafts. Objective of this study was to compare time to transplantation in adult patients with a bodyweight < 60kg (BW< 60kg) to patients with a bodyweight ≥60kg (BW≥60kg).
Methods: The prospective Eurotransplant (ET) database was used, 11,686 patients listed for LT between 2010 and 2015 were included. Paediatric recipients, recipients of living donor liver transplantation (LDLT), re-LT or approved organ combinations, and patients with an initial high urgency status were excluded. Time to transplantation for patients with BW< 60kg was compared to patients with BW≥60kg. Time to transplantation was compared with use of a cox proportional-hazards model controlling for recipient sex, recipient age, country of listing, year of listing, listing MELD-score and listing

for kidney transplantation.
Results: In total, 1,296 patients with BW< 60kg were compared to 10,390 patients with a BW≥60kg. In multivariate analysis BW< 60kg was associated with a lower chance for LT (HR: 0.82, 95%CI:0.75-0.90, P< 0.0001). At 12, 24 and 36 months after listing transplant rates were respectively 34%, 45% and 48% for patients with BW< 60kg *versus* 48%, 56% and 58% for patients with BW≥60kg. Median waiting time was 548 days for patients with BW< 60kg and 307 days for patients with BW≥60kg. At the end of follow-up waitlist mortality was 23.5% for patients with BW< 60kg *versus* 18.8% for patients with BW≥60kg. Patients with BW< 60kg received a split LT near three times more often (BW< 60kg: 3.4% *versus* BW≥60kg 1.2%).
Conclusion: Small adults are disadvantaged for receiving a size-matched liver graft in the ET region. These patients may benefit from intention-to-split policy, LDLT or assignment of exceptional MELD points.



[Kaplan-Meier curve of time to LT]

P-153

Von Willebrand factor independently predicts mortality on the waitlist for liver transplantation and facilitates additional risk stratification in low MELD patients

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Background and aims: MELD score is primarily used for decision making in organ allocation for liver transplantation (oLT). Still, MELD score was shown to underestimate complications resulting from portal hypertension and infection. vWF-Ag was recently found to not only be associated with portal hypertension but also to be a pleiotropic predictor for outcome in patients with end-stage liver disease. Accordingly, this study aimed to evaluate the predictive potential of vWF-Ag for outcome on the waitlist for oLT.
Methods: VWF-Ag at time of listing was assessed in 269 patients. Mortality on the waitlist and overall survival were documented.
Results: Patients dying within 3 months on the waitlist displayed elevated levels of vWF-Ag (p< 0.001). Indeed, MELD and vWF-Ag were comparable and independent in their predictive potential for 3 month mortality on the waitlist (AUCvWF-Ag=0.739,AUCMELD=0.770). A cut-off at 413% for vWF-Ag was found to identify patients at risk for early death on the waitlist. Strikingly, when incorporating vWF-Ag into the MELD score, predictive potential substantially improved (AUCvWF-Ag+MELD=0.836).
Conclusion: The present study identifies a single measurement of vWF-Ag at listing for oLT as an easily assessable marker to predict early mortality. VWF-Ag allows risk stratification even in patients with low MELD score and does hence give additional information for clinical decision making.vWF-Ag could therefore facilitate improved prioritizing of organ allocation and concomitantly decrease wait list mortality.

P-154

Graft TO recipient weight ratio: How low can we go?

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Background: The graft-to-recipient weight ratio (GRWR) in adult-to-adult living donor liver transplantation (LDLT) is one of the major risk factors affecting survival. Smaller size grafts (GRWR < 0.8%) can expand the living donor pool. This study investigated the outcome of LDLTs with grafts having GRWR < 0.8% and studied the role of portal flow modulation in these grafts.
Method: We included 730 adult patients undergoing LDLT between December 2011 and June 2018 in this study. All LDLTs were divided into 2 groups based on GRWR: Standard (S) with GRWR ≥ 0.8% and Low (L) GRWR < 0.8%. Patients in low GRWR group were further subdivided into those with and without portal flow modulation. Donor and recipient factors, portal vein pressure (PVP), pressure gradient between PVP and central venous pressure (CVP), occurrence of small for size syndrome (SFSS), ascites, and posttransplant laboratory data were compared. Patient and graft survival were compared using Kaplan-Meier methods.
Results: Demographic data was comparable between the two

groups. The two groups showed similar patient and graft survival at 1 and 6 months. There was no difference in amount of ascites posttransplant and correction of International Normalized Ratio were similar between the groups studied. Left lobe grafts with a smaller GRWR required portal flow modulation more often than right lobe grafts. Low patient MELD was another favourable factor when using grafts with lower GRWR.
Conclusion: GRWR < 0.8% is safe in adult-to-adult LDLT even without portal flow modulation in selected cases (low MELD of the recipient, right lobe graft). Patients undergoing LDLT with right lobe grafts have favourable outcomes even with GRWR < 0.65.

P-155

Liver transplantation from octogenarian donors: a single center propensity score analysis

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Background: Interest in the older donors, in order to expand the donors pool, has grown in the past few years.
While this strategy had been slowed down by the concern of sub-optimal outcomes and higher rate of complications, the use of elderly donors is now an accepted practice.
However, conclusive results are lacking and the use of organs from octogenarian donors is still controversial.
We aim to analyze the outcomes and the complications of LT with octogenarian donors and compare them with those of LT with younger donors.
Methods: Included in our study were all LTs (577) consecutively performed in adult cirrhotic patients since 2010 at the Padua Transplantations unit.
Survival rates and complications were analyzed for the 577 before and after the propensity score matching (PSM).
Results: Before PSM survivals at 1, 3 and 5 years were respectively 85.2%, 76.0% and 72.3% for the < 80 years old donor group and 90.9%, 76.9%, 72.3% for the ≥80 years old donor group.
Also, statistically significant differences were found between median MELD scores at LT for the < 80 and ≥80 years old donor groups, respectively 18 and 14 (P =0.001), and number of patients transplanted with a MELD>20 (43.5% vs 18.3%, P< 0.001) and >30 (16.2% vs 4.2%, P= 0.006).
After PSM survivals at 1, 3 and 5 years were respectively 86.6%, 82.0% and 78.4% for the < 80 years old donor group and 89.3%, 75.5%, 70.1% for the ≥80 years old donor group.
Survival rates and risk of complications were comparable among the two groups (respectively P= 0.49 and P> 0.3).
Conclusions: Even though donor's age is a relevant prognostic factor, LT with an octogenarian donor is safe and efficient as long as the patient is accurately selected and a division-of-risk MELD based policy is applied.

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Amyotrophic lateral sclerosis and organ donation: The University of Wisconsin experience.

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Background: Amyotrophic Lateral Sclerosis (ALS) is a terminal neurologic disease with an estimated prevalence of over 12,000 patients in the US. There are few documented cases of ALS patients proceeding to organ donation; however, media reports and neurology surveys indicate that many patients are interested in donation. We examined our experience with these patients and their recipient outcomes.
Methods: Donor charts were examined through the United Network for Organ Sharing portal. Retrospective review of recipient charts was performed to evaluate outcomes.
Results: Of six patients identified with ALS, all proceeded to donation. Three signed their own consent form. Average donor age was 57(45-69). Five donors underwent deceased after circulatory death(DCD) donation with mean warm ischemic time 68.8 minutes(21-140). Median KDPI was 59%(50-88%, 4/6< 85%) and mean creatinine 0.67mg/dL(0.4-0.97mg/dL). Liver function tests were normal on all donors. None had diabetes or hypertension. Fourteen organs were transplanted into 13 recipients. Table 1 details 1- and 5-year outcomes in 9 recipients (3 lost to follow-up, 1 transplanted < 1 year ago.) No recipients developed ALS. All families and surrogates expressed satisfaction with the donation process.
Conclusion: We present the largest series of ALS patients proceeding to organ donation in the literature. Many ALS patients have a unique opportunity to consent to donation until the moment of death, and some have expressed interest in donation prior to their terminal admission. All patients with ALS proceeded to donation. Outcomes were consistent with DCD organs. Surrogate and family feedback was favorable. Patients with ALS and their families are frequently amenable to donation and their quality of life may be improved with improved access to donation options.

Organ Type	1-year Graft Survival	5-year Graft Survival	1-year Patient Survival	5-year Patient Survival
Kidney	6/7 (85.7%)	4/7 (57.1%)	6/7 (85.7%)	5/7 (71.4%)
Liver	2/2 (100%)	2/2 (100%)	2/2 (100%)	2/2 (100%)

[Mean 1- and 5-year graft and patient survival.]

Conclusions: Gamma-MELD is a score ranging 6-40, based only on variables available before organ procurement. This score efficaciously predicted early graft and patient survival, being able to stratify the population of transplanted patients in risk-classes. External validation of the score is on the way.

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Gamma-meld: a new predictor of early patient and graft survival after liver transplantation

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Background: The combination of donor-, transplant- and recipient-related features has been proposed with the intent to optimize the selection of patients at high-risk for poor clinical course after liver transplantation (LT). However, many of them have shown unfair prediction performances. Furthermore, these scores are typically based on features obtainable only during the LT process (i.e., cold ischemia time).
The present study aimed at identifying a score composed by the combination of donor- and recipient-related features, all of them available before organ procurement, and at comparing it with other previously proposed scoring systems in terms of early (3-month) patient and graft survival.
Methods: 988 adult (≥18 years) first LT were consecutively performed during the period January 2004-September 2018 in the University Centres of Rome.
Results: At multivariable Cox regression analysis, seven independent variables were identified for the risk of 90-day graft loss: MELD score (hazard ratio, HR=1.05; p< 0.001), procurement distance (HR=1.22; p< 0.001), split-liver (HR=3.50; p=0.001), donor age (HR=1.16; p=0.002), hemodynamic instability (HR=1.58; p=0.02), use of airplane for procurement (HR=0.44; p=0.03), and donor gamma-GT (HR=1.01; p=0.04). Using these variables, the new Gamma-MELD score was created. Gamma-MELD had the best diagnostic ability when compared with other scores (MELD, BAR, DRI, ET-DRI), with areas under the curve of 68.2% and 69.1% for the risk of 3-month graft loss and patient death, respectively. Stratifying the entire population in risk-classes, the lower-risk subgroup (Gamma-MELD=6-19) had a 3-month graft loss rate of 8.0% respect to 16.6% and 42.6% in the corresponding medium- (Gamma-MELD=20-29) and higher-risk (Gamma-MELD=30-40) subgroups, respectively (log-rank p< 0.001).

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System usability and workload of searching for information of waitlisted liver transplant patients: does the transplant community need an innovative solution?

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Introduction: While reviewing an institution's liver transplant waitlist for organ acceptance, surgeons must make timely decisions regarding patient selection at the time of an organ offer. As electronic medical records (EMR) are designed to evaluate one patient at a time, many centers utilize a spreadsheet system (SS) to facilitate simultaneous review of pertinent clinical information for groups of patients. However, the usability and workload of the SS remain unknown.
Methods: Surveys were administered to transplant surgeons at an urban academic center. The System Usability Scale (SUS) and the National Aeronautics and Space Administration Task Load Index Scale (NASA-TLX) were used to assess the perceived usability and workload of the SS, respectively. The NASA-TLX weighted score accounts for individualized perception of the importance of mental demand, physical demand, temporal demand, performance, effort, and frustration regarding the task. A weighted NASA-TLX score greater than 50 indicates a task is burdensome. A SUS score less than 68 indicates a system is difficult to use.
Results: 6 surgeons completed surveys (100% response rate). Overall, the SS scored poorly on the SUS (47.5, IQR: 43.8-55.0) and NASA-TLX (54.7, IQR: 49.3-68.8) (Table 1). The SS was reported to be mentally demanding and the pace of the work was felt to be rushed. Using the SS made respondents feel frustrated and respondents did not feel they performed well in accomplishing the task.
Conclusions: The SS evolved as a workaround to the inability of EMRs to review information of multiple patients simultaneously. While the SS is easy to create, it exacerbates workload and is not easy-to-use. Therefore, we are developing digital health technology in the form of a mobile application that solves clinical pain points associated with searching for information of patients waitlisted for liver transplant.

Table 1. System Usability and Surgeon Workload of Searching for Information of Waitlisted Liver Transplant Patients

Measurement Tool to Assess the Spreadsheet System	Median Score for Transplant Surgeons (N=6)
System Usability Scale	47.5 (43.8–55.0) [a]
NASA-Task Load Index Weighted Score [b]	54.7 (12.2–49.3) [c]
NASA-Task Load Index Component Score	
Performance	67.5 (36.3–80.0)
Effort	60.0 (47.5–68.8)
Mental Demand	57.5 (46.3–80.0)
Temporal Demand	57.5 (45.0–73.8)
Frustration	57.5 (37.5–70.0)
Physical Demand	40.0 (35.0–45.0)

[a] System Usability Scale ranges from 0 to 100; a score < 68 indicates a system is difficult to use

[b] The NASA-TLX weighted score accounts for individualized perception of the importance of mental demand, physical demand, temporal demand, performance, effort, and frustration regarding the task.

[c] NASA-TLX ranges from 0 to 100; a score > 50 indicates a burdensome task load

[Table]

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The impact of the opioid epidemic on the risk of graft failure in liver transplantation

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Background: An increase in the rate of deaths due to opioid and other respiratory depressant overdoses over the past several years has potential implications for transplantation. Although many of the organs from opioid overdose mortalities are currently being transplanted, it remains unclear whether these organs pose any increased risk of graft failure.
Methods: We used national data from the Scientific Registry of Transplant Recipients to estimate the cumulative incidence of graft failure for recipients of deceased donor liver grafts, comparing the risk amongst donors who died from anoxic drug overdose and those who died of other causes.
Results: The risk of graft failure or patient death at 5-years was similar for recipients of anoxic drug overdose donor grafts (24.0% [95% CI, 21.9 to 26.0%]) and recipients of other grafts (24.9% [95% CI, 24.4 to 25.4%); risk difference: 1.0% [95% CI, -0.9 to 2.7%] for donation after brain death. Similar results were seen for donation after cardiac death donor grafts (risk difference: 1.8% [95% CI, -7.8 to 11.8%]). Utilization of anoxic drug overdose donor grafts from brain dead donor was similar to utilization of grafts from other donors, but grafts from anoxic drug overdose cardiac death donors (DCD) were less frequently utilized compared to non-drug overdosed DCD grafts (25.9% vs. 29.6%, 95% CI for difference, -6.7 to -0.7%).
Conclusions: Recipients of liver grafts from HIV, hepatitis B, and hepatitis C seronegative drug overdosed donation after brain death and donation after cardiac death donors did not have an increased risk of graft failure compared to recipients of non-overdose donor grafts. Given the rising incidence of opioid overdose mortalities, efforts to increase the conversion rate of these potential donors as well as the utilization of their grafts by transplant centers could help to address transplant waitlist demands.

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In LDLT scenario barring stage 5 CKD sequential and simultaneous kidney transplant approach have comparable outcomes in CLD with CKD cohorts

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Introduction: In present day scenario the gold standard for chronic liver disease(CLD) chronic kidney disease (CKD) is combined liver kidney transplantation(CLKT). This is based on DDLT data. However, in LDLT scenario based on our clinical experience we felt that the above statement may not be true. Because even today with so many biomarkers available to assess the renal functions it is difficult to differentiate CKD from HRS. Moreover, it is difficult to find 2 donors for 2 for 2 organs at a short notice. Hence we decided to analyze our data on this cohort of patients.
Materials and Method: Retrospective analysis of prospectively maintained data from August 2006 to October 2018 were analyzed. All CLD with CKD patients were included in the study. Some underwent CLKT and others underwent LT alone(LTA) with intention of sequential kidney transplant later on if needed. Primary outcome was mortality. Secondary outcome was Native kidney function in the LT alone group. Subgroup Analysis was done based on the grades of CKD.
Results: A total of 105 cases out of 2482 adult LDLTs performed in our institute were found to have CKD with decompensated CLD. **82 underwent LTA (Study Group N=82) and 23 underwent CLKT (Control Group N=23)**. Patient survival, Liver graft survival, Kidney graft/Native kidney survival were compared between two groups. Subgroup analysis was done based on the CKD stage. **On statistical analysis the study group had significantly lower serum creatinine , GFR (P< 0.001) and higher „Day of Peak bilirubin“ (P< 0.05)**. On subgroup analysis patient survival, liver graft survival, kidney/kidney graft survival were comparable between both groups unto stage 4 CKD. **Only in stage 5 CKD Patient survival was significantly better (Kaplan Meir P < 0.05).**
Conclusion: In LDLT scenario barring stage 5 CKD sequential kidney transplant and CLKT have comparable outcomes.

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Liver transplantation for ALD: characteristics associated with ETOH recidivism post liver transplant

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Introduction: Liver transplant for alcoholic liver disease (ALD) continues to be a challenge for transplant centers. We sought to identify risk factors for alcohol (ETOH) recidivism and its impact on survival in liver transplant recipients.
Methods: Demographic, clinical, social and psychosocial characteristics were retrieved from EMR in 241 LT recipients with ALD. We focus in factors specially associated towards harmful recidivism. Harmful recidivism was defined as alcohol consumption causing liver injury, cirrhosis or frequent readmissions.
Results: 18-20% of patients with ALD have some type of recidivism. However, harmful recidivism as defined above was noted in 25 (10.4%) patients. On univariate analysis pre-transplant pre transplant criminal history, duration of alcohol abstinence < /= 6 months, younger age at transplant were significant predictors for post-transplant recidivism. On multivariate analysis, younger age (OR 0.931; 95% CI: 0.885-0.980, 0=0.0060), and criminal history (OR 2.885; 95% CI 1.050-7.923, P=0.0398) were significantly associated with increased hazard of graft loss. There was a trend for increased risk for recidivism with duration of alcohol abstinence < /= 6 months (OR 2.181; 95% CI 0.916-5.194, P=0.0781). Based on univariate analysis using Cox proportional hazard model, education (OR 0.554; 95% CI 0.307-1.000, P=0.0498), employment type (OR 0.429; 95% CI 0.203-0.905; P= 0.0264), and duration of alcohol abstinence (< /= 6 months (OR 2.517; 95% CI 1.409-4.497, P= 0.0018) were identified as significant predictors for graft survival. Multivariate analysis, only duration of alcohol abstinence < /= 6 months predicted significant increase in the hazard of graft loss [OR: 2.517; 95% CI (1.409-4.497]. Outcome was significantly impacted by recidivism.
Conclusions: Alcohol recidivism post transplantation occur in around 20% of patients. Armful ETOH in half of them. Factors such as young age, previous criminal history, and pre LT alcohol abstinence are associated with harmful ETOH recidivism and worse outcomes post transplantation.

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Positive Chagas donors: continues to be a limitation?

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Background: The low availability of donor graft is the main limitation for transplantation globally and Argentina is not the exception to the rule. As a consequence, the number of patients on the waiting list is constantly increasing, leading to an increase in drop-out rates. One of the options to face this problem arose under the concept of donors with expanded criteria, which includes, among other possibilities, the use of donors with infectious risk and with it the possibility of using donor grafts with positive serology for Chagas. In the literature there are reported 40 cases of donors with positive serology for Chagas with recipients with negative serology, and the results are encouraging.
Methods: We evaluated the cases of liver transplantation using cadaveric donors Chagas positive in negative recipients on a total of 262 transplants performed between January 2013 and December 2018, and their results.
Results: In the period between January 2013 and December 2018, 262 liver transplants were performed at the El Cruce hospital, of which 8 were donors with positive serology for Chagas with recipients with negative serology. The average MELD score was 26.9 (r 20-44) and the average waitlist position was 20.6 (r 1-59) with an average waiting list time of 399.5 days (r 12-1404). A strict follow-up was carried out for at least one year in each case. Out of the total of 8 transplanted under these conditions, seroconversion occurred at 120 days in 3 cases confirmed by PCR and Strout technique. Benznidazole treatment was indicated for 60 days in all cases. None of the patients developed Chagas disease. One patient died of sepsis with KPC isolation, unrelated to Chagas.
Conclusion: The use of grafts from positive Chagas donors in negative recipients can be used safely if a strict serological follow-up is performed and eventually timely treatment.

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Nonagenarian grafts for liver transplantation: a comparison with ideal young donors

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Background: Use of very old donors in liver transplantation (LT) is showing favorable results and is growing worldwide. However, this practice is not yet universally implemented.
Materials and methods: This was a retrospective analysis on whole-size, primary, ABO-compatible, adult LT from donors after brain death (DBD) between January 2014 and September 2018. Recipients of DBD graft ≥90 years were compared to patients transplanted with donors aged 18-39 years.
Results: A total of 16 DBD transplants from nonagenarian donors was compared to 37 recipients of younger grafts. The two groups were overall comparable in terms of indication for LT, HCV serology and pre-LT MELD score. The median (IQR) follow-up was 16 (6-33) months for older grafts versus 25 (15-36) for younger grafts (p=0.23). No graft loss or patient death was observed in the elderly graft group versus 3 cases among younger graft recipients. There were no cases of early allograft dysfunction (EAD) in the older group vs 4 cases in the younger group (p=0.42). Three cases of post reperfusion syndrome (PRS) were observed in the older group vs 8 in the younger one (p=0.89). Post-LT ALT peak value was lower in older graft group (367 vs 593; p=0.03), but the latter had better post-LT INR peak value (1.3 vs 1.4; p=0.01). The median interval to return to normal range was 7.5 versus 6 days for AST (p=0.08); 14.5 versus 13.5 days for ALT (p=0.72); 6.5 vs 5 days for total bilirubin (p=0.07), and 4 vs 3 for INR (p=0.25) in older and younger grafts, respectively. The median (IQR) hospital stay was 15 (11-16) days for older grafts versus 11 (9-15) for younger grafts (p=0.71).
Conclusion: Our preliminary experience shows that no age should preclude consideration of any donor for liver transplantation.

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Assessment of Canadian policies regarding liver transplant (LT) Candidacy on alcohol, tobacco, marijuana and opiates: a national survey

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Background: When last assessed in 2013, all liver transplant (LT) programs in Canada required 6-months of abstinence from alcohol and excluded patients with acute alcoholic hepatitis (AH). New studies have questioned the validity of these policies. Traditionally, tobacco and marijuana have been discouraged although there is a trend in the US to become more permissive; furthermore marijuana was legalised in October 2018 in Canada. Given these changes, our objective was to obtain an understanding of current practices of LT programs in Canada regarding addiction, restrictions regarding using alcohol, tobacco, marijuana or opiates, as well as any period of abstinence required.
Methods: Surveys were sent out to the medical directors of all seven adult LT programs in
Canada. Data was aggregated to provide a national perspective on this topic.
Results: To date, data has been collected from 5/7 Canadian LT programs. 40% of programs ‚always' require 6-month abstinence from alcohol, 40% ‚usually' require it, and 20% ‚sometimes' require it. Formal alcohol rehabilitation is mandatory in 20% with the other programs usually/sometimes requiring completion. 60% of programs ‚never' or ‚rarely' consider patients with acute alcoholic hepatitis (AH) as candidates. 40% of programs require smoking cessation before a patient can be considered a transplant candidate. 80% of programs had no formal policy on marijuana use before transplantation but 60% of programs felt that marijuana use is ‚rarely' or ‚never' a contraindication to LT. Opioid taper/ discontinuation is mandatory in one program while 60% ‚sometimes' requires it.
Conclusion: Significantly more Canadian programs perform LT for patients who have not been abstinent of alcohol for 6 months and AH is no longer an absolute contraindication in Canada. National LT program policies on smoking and opiates are quite variable. The vast majority of programs do not have a formal policy regarding marijuana use before transplantation.

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Potential expansion of deceased donors including anti-HCV+: a population based cross-sectional study from Argentina

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With the advent of new direct-acting antiviral agents (DAAs) for the treatment of hepatitis C (HCV), the pool of cadaveric donors could potentially be expanded with the use of anti-HCV+ donors. We sought to evaluate the prevalence of anti-HCV+ in all deceased donors from 2006 to 2017 in Argentina.
A cross sectional study from Argentina analyzing official data from the National Procurement of Transplantation (INCUCAI) was performed. Data from all type of donors was analyzed. Viral serologic tests were done in all donors during the procurement process, including anti-HCV, hepatitis B virus antigen (HBsAg), core antigen antibody (HBc IgG), anti-HBs. A stratified analysis according to the type of donor and anti-HCV, HBsAg and HBc IgG serologic status was done. Chagas disease and HIV serologic status were also included in the analysis. We searched donor rates per million population per year and overall population/year from official National reports.
From 2006 to 2017, 11,421 deceased donors were included. Serologic tests were positive as follows: anti-HCV 1.12%, HBsAg in 0.4% HBc IgG 2.6%, HIV 0.26% and Chagas disease 3.7%. Prevalence ratio per periods among anti-HCV+ showed the highest prevalence was observed in 2007 and the lowest prevalence in the last 2 years 0.57% in 2016 and 0.79% in 2017. Prevalence for anti-HCV+ among type of donors was significantly higher in non-effective donors 6.46%, followed by tissue donors only 1.31% and lower in effective donors 0.41% *P*< 0.0001. Among HBV tests, the highest and lowest HBsAg prevalence were observed in 2007 (0.67%) and in 2017 (0.30%), whereas the highest HBc IgG prevalence was observed in 2007 (4.2%) and the lowest prevalence in 2017 (1.45%) HBc IgG,
The prevalence of anti-HCV in donors in Argentina is declining. The use of these donors, would not significantly increase the donors pool.

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ABO incompatible living donor liver transplant: result from a single institution

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Background: Donor shortage is biggest hurdle to save patients requiring liver transplant. ABO incompatible liver transplant is important to increase donor pool.
Methods: From SEP 2015 to DEC 2018, out of 195 LDLTs, 11 (5.64%) ABO-I LDLTs performed. Right lobes graft without MHV with single bile duct, used in all patients. Rituximab (375mg/m^2) was given intravenously 2-3 weeks before liver transplantation. The IA titres and CD 19/CD 20 levels were monitored. IA titres >1:32 required plasmapheresis . MMF and tacrolimus was started preoperatively. Postoperative immunosuppression was achieved with MMF, Tacrolimus, and steroids.
Results: Median age was 44 years (range (r)= 59-33). The median CTP and MELD were 10 (R= 7-13) and 17 (r=13-30). The aetiology of liver diseases included alcohol (n= 6,54.5%), hepatitis B(n=2, 18.18%), NASH (n=2, 18.18%) & Cryptogenic (n=1, .%) respectively. The median graft-to-recipient weight ratio (GRWR) was 0.90% (r= 0.72%-1.46%). All possible combination of donor to recipient mismatch of blood type was done. The initial median titre of the IA was 64 (r= 1024-64) and initial CD19/20 counts were 32% (r=90-1.5) and 37% (r=90-0). Following Rituximab administration it decreased to a median of 0.3% & 0% respectively. The median number of sessions of plasmapheresis was 1 (r=0-4), leading to decreased IA titre of 16 (r= 2-32). Only 1 patient (09%) had higher IA titres after transplantation than at transplantation, which required postoperative plasmapheresis. Two weeks after transplantation, the median IA titre was 4 (r=2-16) and median CD19/CD20 counts were 0% & 0% respectively. There was no re-transplantation and one patient (09%) died after six months of transplant due to severe sepsis. No antibody mediated rejection or ischemic biliary stricture with cholangitis was observed. Biliary complications was observed in one patient(09%).
Conclusion: In a selected group of patients, excellent outcomes can be achieved for ABO I LDLTs.

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Phenotype of Non-Val30Met mutations in Familial Amyloidotic Polyneuropathy (FAP) in a liver transplantation center in Brazil

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Introduction: FAP is a rare disease endemic in Brazil probably due the Portuguese colonization. More than 130 mutations were described worldwide, but the most prevalent is Val30Met, corresponding to more than 90% of the case in our country.
Objective: We described the phenotypic findings in non-Val30Met mutation cases.
Casuistic results: We found 5 different genotypes in 14 patients, six women (Phe64Ser, Gly67Glu, Glu109Lys, Val142Ile, Ala101Val) in Hospital Israelita Albert Einstein in Sao Paulo Brazil. The findings are described in Table 1.

LT: liver transplantation;
LTWL: liver transplantation waiting list;
CLT: combined cardiac and liver transplantation;
CLTWL: combined cardiac and liver transplantation waiting list.
Conclusion: The increasing of availability of genetic tests permits the diagnosis of non-common mutations in the set of FAP. The identification of these patients is important to define the best treatment and outcome. The use of PAF donor grafts with non-Val30Met mutations should be discussed.

Mutation	Age of onset	Familial history	PNP	Cardiac symptoms	Autonomic disfunction	Weight loss	Outcome
Phe64Ser	37	yes	yes	no	yes	yes	LT
Gly67Glu	36	yes	yes	yes	yes	yes	Death
Gly67Glu	37	yes	yes	no	yes	yes	LT
Gly67Glu	36	yes	yes	no	yes	yes	LTWL
Gly67Glu	36	yes	yes	no	yes	yes	LT
Gly67Glu	31	yes	no	yes	yes	yes	CLTWL
Gly67Glu	-	yes	no	no	no	no	Follow up
Glu109Lys	54	no	no	yes	yes	no	CLT
Glu109Lys	34	yes	yes	no	yes	no	Tafamidis
Glu109Lys	-	yes	no	no	no	no	Follow up
Ala101Val	70	yes	no	yes	no	no	Tafamidis
Val142Ile	-	no	no	no	no	no	Follow up
Val142Ile	-	no	no	no	no	no	Follow up
Val142Ile	58	no	no	yes	no	no	CLTWL

LT: liver transplantation; LTWL: liver transplantation waiting list; CLT: combined cardiac and liver transplantation; CLTWL: combined cardiac and liver transplantation waiting list.

[Phenotype profile of Non-Val30Met mutations patients]

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Clinical analysis of emergency liver transplantation in patients with high MELD score

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Background: In general, patients with a high model for end-stage liver disease (MELD) score have a poor prognosis before and after liver transplantation. The mortality rate after liver transplantation in high MELD patients is an important consideration in future liver allocation system. This study was performed to identify poor prognostic factors and mortality rates in patients with high MELD score.
Method: From September 2001 to December 2017, living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT) were performed in 851 and 157 patients in our center, respectively. The 81 patients with MELD score of 35 or more were analyzed. We divided 81 patients into survival group and mortality group. To assess the risks associated with high MELD score, we evaluated various preoperative and operative factors.
Results: Of the 81 patients, LDLT was performed in 49 (60.5%) patients and DDLT in 32 (39.5%) patients. Overall survival rates at 1, 3, and 5 years in 81 patients were 72.4%, 67.3%, and 67.3%, respectively. The survival group was 63 (77.8%) and the mortality group was 18 (22.2%). In univariate analysis, the mean age of the mortality group was higher ($p = 0.028$), the mean MELD score was higher ($p = 0.045$), the proportion of intubated patients was higher ($p < 0.001$) and the proportion of positive culture was higher ($p = 0.042$). There were more patients with mental status above stupor ($p = 0.014$). In multivariate analysis, age [$p = 0.006$, Exp(B) = 1.118], intubation status [$p = 0.042$, Exp(B) = 6.073], and culture positive [$p = 0.036$, Exp(B) = 5.218] were significant.
Conclusion: In patients with high MELD score, the 3-year and 5-year survival rates are not significantly deteriorated unless initial post-operative mortality is achieved. And the prognosis was poor in patients with old age, preoperative intubation or positive culture.

P-169

Impact of a temporary cardiac arrest in a brain dead liver donor on liver transplantation results

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Background: The use of hepatic allografts from donors who have suffered a temporary cardiac arrest (TCA) may be considered as a risk factor of liver failure following liver transplantation (LT) because it could lead to graft dysfunction. Conversely, some studies suggested a protective effect.
The objective of this work is to study the influence of TCA in brain dead donors on LT outcome.
Methods: Single institutional retrospective study on 429 consecutive LT (01/2008-06/2017). Exclusion criteria: retransplantation, multiorgan transplantation, splits and domino grafts, controlled cardiac dead donors. A group of LT from TCA donor (n=111) was compared to a group of no TCA (n=318). Primary end point: arteriobiliary complications free survival (ABC free survival) during the first year post-LT.
Results: patients from the TCA group were younger than patients from the no-TCA group. Main cause of death was anoxia in the TCA group and vascular in the no-TCA group. The following donor's characteristics were higher in the TCA group: AST and ALT levels (peak), µGT and ALP at day 1 after ICU admission, creatinine, PT and peak of lactate and bilirubin. Patient survival, graft survival and

Early Graft Dysfunction were not different between the 2 groups. AST and ALT level at postoperative day 2 were lower in the TCA group. The ABC free survival was significantly higher in the TCA group compared to the no-TCA group (81% versus 70% at 1 year, p=0,044) at univariate analysis. However, this difference disappeared at multivariate analysis.
Conclusion: We failed to observe any deleterious effect of a TCA in brain dead donors on LT outcome. On the contrary, some results were suggestive of a protective influence.

P-170

Orthotopic liver transplantation using HCV-viremic donor organs for HCV-nonviremic recipients, a single center experience

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Background: Direct-acting antiviral (DAA) therapy has hepatitis C virus (HCV) cure rates over 95%. With the success of DAAs, orthotopic liver transplantation (OLT) using HCV-viremic organs for HCV-nonviremic recipients has been proposed but little published data exists on its efficacy. Our institution developed a clinical program employing this strategy for patients whose illness was not accurately reflected by their MELD-Na scores.
Method: HCV-nonviremic patients listed for OLT whose disease burden was poorly reflected by their MELD-Na score were identified. Suitable adult patients underwent a detailed informed consent process. Donor organs were HCV seropositive or viremic as confirmed by nucleic acid testing (NAT). Organs were excluded if they were not otherwise suitable for OLT. No organs were obtained from prisoners or institutionalized persons. Post-operative HCV NAT was performed serially up to 24 weeks or until positive. DAA therapy was initiated as soon as possible once patients became HCV-viremic. Post-operative care, including immunosuppressive regimen, was otherwise unchanged.
Results: Fifteen HCV-nonviremic patients enrolled in our program underwent OLT, of which eleven patients received an HCV seropositive, NAT positive organ. All eleven of these patients developed viremia. All patients were approved for DAA therapy, with a median DAA start time of 23 days from viremia. Nine of eleven patients have completed treatment, with all nine having non-detectable HCV RNA at end of therapy. Six patients have attained sustained virologic response 12 weeks (SVR12) after DAA therapy and one patient has reached SVR at 4 weeks. Genotypes 1a (n=7), 2 (n=1), 3 (n=2) and 4 (n=1) were represented in this cohort. There were no appreciable differences in allograft function or rejection rates compared to our institutional standards.
Conclusion: Donor pool expansion using HCV-viremic livers is safe and can be considered for HCV-nonviremic patients. Additional research exploring cost-effectiveness and long-term allograft survival is needed.

P-171

Liver from prostate cancer positive donors - option for recipients from higher MELD score

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Introduction: The use of organs from deceasad donors with prostate cancer (PC) is widely discussed. This particularly applies to early forms of PC with the lowest transmission rate from the donor to the recipient
Aim: A proposal to use organs from deceased donors with prostate cancer
Material and methods: From September 2014 to August 2018 in Department of General, Transplant and Liver Surgery Medical University of Warsaw, 601 liver transplantations from deceased liver donors were performed. In this group, 9(1,5%) recipients received an organ from PC positive donors . The recipients were subject to active surveillance. The material was retrospectively analised.
Results: In 8/9 (88.90%) cases, the diagnosis of PC was made in routine histopathological examination, in 1/9 case (1.10%) the diagnosis of PC was made in a frozen biopsy.
In all cases, an early PC was diagnosed, it means a single leasion of 1 mm - 8 mm in diameter with a low malignancy - Gleason score ≤6 points (3 + 3). Median donors´ age was 63 years (58-69). Median PSA concentration in the donors' serum of 11,4ng / dl (2,71-67). The livers were transplanted 9 recipients (3 women and 6 men) qualified for transplantation due to acute (1) and acute-on-chronic liver disease (8).
The median MELD score was 19 (7-33). During the observation period - median 442 days (1-1038) there were no symptoms of PC transmission from donors.
Patient transplanted due to acute liver failure died on the first day after surgery due to multiorgan failure.
Conclusions: The possibility of liver transplantation from deceased donors with Gleason ≤6 points (3 + 3) PC should be considered. The allocation of these organs should primarily concern recipients with high MELD score. It is necessary to set up a multidisciplinary team to establish precise recommendations.

P-172

Clinical efficacy of liver transplantation using aged liver grafts from donation after citizen´s death: a single center experience

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Background: Older donors are a readily available source of livers that can significantly augment the donor pool. The aim of this study was to explore the clinical efficacy of liver transplantation using aged liver grafts(≥60 years) from donation after citizen´s death.
Method: Clinical data of 27 patients who underwent LT using aged liver grafts from organ donation after citizens death in Liver Transplantation Center, the Third Affiliated Hospital of Sun Yat-sen University from January 2015 to December 2017 were analyzed retrospectively.
Results: The mean age of the 27 elderly donors was ((62.89±3.50) years old. The elderly donors included 10 cases of donation after brain death (DBD, China category Ⅰ), 12 cases of donation after cardiac death (DCD, China category Ⅱ), and 5 cases of donation after brain and cardiac death (DBCD, China category Ⅲ).The age of 27 recipients was 45.56±11.4 years. All the 27 patients underwent LT successfully. The surgical procedure were modified piggyback LT with additional vena cava plasty (n=25) and classic OLT (n=2). Two patients died of infection and multiple organ failure during the perioperative period. The other 25 patients recovered smoothly. The average intensive care unit stay was 6 d, and the average postoperative hospital stay was 28 d. The patients were followed up for 6 ~ 42 months. Two cases died of tumor recurrence and metastasis respectively 17 months and 32 months after operation. One case suffered from portal vein thrombosis and four cases suffered from biliary tract complications, including 1 case of ischemic cholangitis and 3 cases of biliary anastomotic stenosis. Liver function of the left patients recovered well after operation with good prognosis.
Conclusion: Age should not be an independent taboo for LT. Using liver grafts from donor age over 60 years after strict selection can achieve good therapeutic effects in LT.

P-173

The role of liver graft cold ischemia in the development of post-transplant complications

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Background: Acute-kidney-injury (AKI) and early-allograft-dysfunction (EAD) are two of the most frequent and life-frightening post-liver transplant (LT) complications. However, the etiology and the variables involved are still unknown. The aim of our study is to identify graft-derived and cold ischemia time variables involved in AKI ad EAD development.
Methods: A prospective observational study was designed. During cold-ischemia (at the end of back-table) preservation fluids (PFs) were collected and analyzed. Recipients were divided in groups according to the development of post-LT AKI or EAD. Donor and recipient characteristics were collected. Results are expressed as median±standard deviation.
Results: 30 recipients were included in the study: 10 transplanted with graft from standard donors, 16 extened-criteria (ECD) and 4 cardiac-death. Fourteen (47%) patients suffered AKI. The incidence of donor cardiocirculatory arrests and the level of donor GGT were increased in AKI patients. Conversely, in PFs (Tab.I) the levels of TNF-alfa, IL-6, hemoglobin, glucose and the total number of cells number were increased in patients that didn't suffered post-LT AKI. EAD was found in 9 (30%) patients. Graft weight was increased in EAD patients, as well as the length of intensive-care-unit stay. PFs concentration (Tab.I) of GOT, GPT, bilirubin, GGT, LDH, and hemoglobin were increased. No differences in AKI and EAD development were found according to the type of donors. Only recipient transplanted with ECD-graft demonstrated a trend towards significance in the incidence of AKI.

	EAD	n-EAD	p
GOT U/L	3446 (484-8245)	1603 (61-4404)	0,048
GPT U/L	3143 (215-7371)	1292 (46-2598)	0,024
Bil mg/dL	0,4 (0,02-0,63)	0,2 (<0,03-0,32)	0,014
GGT U/L	6,11 (2-22)	2,85 (<1,5-4)	0,078
LDH U/L	6921 (784-18030)	2931 (125-6846)	0,056
Hb pre-lisi mg/dL	123,27 (16,44-217,13)	72,7 (19,2-132,4)	0,056

	AKI	n-AKI	p
TNFα	4,55 (1,1-18,93)	10,62 (1,8-16,2)	0,008
IL-6	66 (25,1-237,9)	2205 (13-12443,86)	0,066
Hb post-lisi mg/dl	590,97 (219,8-2478,66)	1349,07 (301,56-2296,8)	0,001
Cell tot/ml *10^6	102,7 (57-290)	272,6 (61-1530)	0,029
Glu mg/dl	225 (68-428)	287 (98-458)	0,053
GR/mmq	16200 (10000-20000)	236000 (100000-300000)	0,058

[Tab.I Statistically significant variables according to EAD and AKI onset]

Conclusions: PFs analyses enabled the identification of graft-derived factors and cold ischemia variables involved in AKI and EAD development. These variables could predict post-LT complications and allow the adoption of strategies to minimize their effect on the recipient.

P-174

Dropping off the transplant waiting list - how we can do better

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Background: The liver transplant allocation system in Singapore is based upon the Model for End-Stage Liver Disease (MELD) score, allocating organs to patients with the highest scores. Patients with hepatocellular carcinoma (HCC) are given exception points capped at 15. While this allows the sickest patients to receive organs in a timely manner, patients with HCC with good liver function run the risk of disease progression beyond transplantation criteria. We investigated the rate of waitlist drop-out and analyzed the underlying reasons.
Methods: 157 patients were placed on the waitlist for liver transplantation in the National University Hospital Singapore between 2011 and 2018. Excluding pediatric and acute liver failure patients, 127 patients were included for analysis. Data regarding patient characteristics and outcome were collected.
Results: Out of 127 patients, 83 (65.4%) patients eventually received transplantation while 44 (34.6%) patients dropped off the waiting list. There were no statistically significant differences when we compared the mean number of days spent on the waitlist (349±459 vs 303±387, p=0.572), mean age (54.1±11.3 vs 56.8±12.0, p=0.229), mean MELD score including exception points (17.4±6.8 vs 21.0±10.6, p=0.050) and mean Child-Pugh score (8.28±2.22 vs 8.25±2.77, p=0.955) between these two groups respectively. Of those who dropped off the waitlist, 23 (52.3%) had HCC with nearly half (n=11) dropping off due to HCC disease progression beyond transplantation criteria (UCSF).
Conclusion: More than one-third of patients listed on the waitlist eventually drop off with the majority of them attributed to progression of disease of HCC. Despite more than two-third of LT in our center being living donor liver transplantation, the gap in organ shortage is not met. More should be done to explore avenues to increase the organ allocation to HCC patients perhaps through progressive increase in MELD score, without compromising the chances of non-HCC patients.

P-175

Intravisceral fat as predictive factor for survival after liver transplantation

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Background: MELD-score alone is often not sufficient to reflect the nutritional and functional status of the patient, which is likely to be an important factor to predict survival after liver transplantation. An accurate survival prediction is essential for an optimal patient selection for liver transplantation.
Patients and methods: Between January 2008 and December 2015, 693 deceased donor liver transplantations were performed at our center. All patients who underwent preoperative computed tomography (CT) of the abdomen were selected. All demographic data, pre-, intra-, and postoperative data were reported. Additionally, subcutaneous and intravisceral fat and the psoas muscle were measured on the CT scan. The Body Mass Index (BMI) und the Psoasindex was calculated. The effect of these factors on postoperative complications and survival were analyzed by univariate and multivariate cox- regression analyses.
Results: There 370 patients included to the study. Die etiology is shown in **Table 1**. Major postoperative complications were seen in 116 patients (31,4%). Perioperative death within the first 90 days was seen in 89 patients (24.1%). The median survival was 104 months. The 1-year survival rate was 66 %. The factors listed on **Table 2** were analyzed by multivariable cox regression analyses as independent factors for major postoperative complications and survival. The psoasmuscle (p=0,02) and psoasmuscel index (p=0,012) were identified as independent positive predictive factors for major postoperative complications and survival. Intravisceral fat (p=0,035) was shown to be an independent negative predictive factor for survival after liver transplantation. The BMI could not be identified as predictive factor for major complications or survival.
Conclusion: We confirm that psoasmuscle and psoasmuscle index is also for liver transplantation an important positive predictive factor. Additionally our study shows that intravisceral fat is a negative predictive factor for survival and should be considered for accurate patient selection instead of BMI.

P-176

A novel surgical method in donor pancreas preparations without vascular reconstructions

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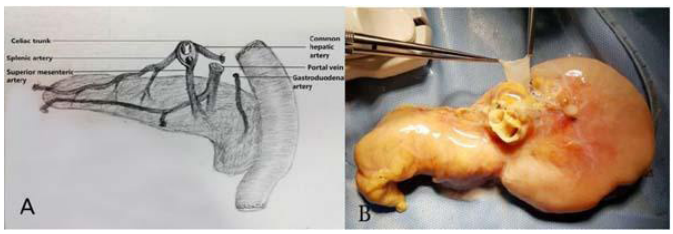
Objective: Donor pancreases always require vascular reconstructions due to complicated vascular structures in pancreas. We simplified the vascular preparation of pancreas grafts in this study called "no vascular reconstruction". This novel procedure significantly shortened the operative time of pancreas grafts and did not cause any vascular complications.
Methods: A total of 12 donor pancreas preparations without vascular reconstruction were studied. The abdominal aorta patch, the celiac trunk and the superior mesenteric artery were preserved as arterial inflow channels for the donor pancreas. The gastroduodenal artery was transected from common hepatic artery at a site 0.5 cm away from the bifurcation. The common hepatic artery was reserved for liver graft. Heparin saline was injected into the superior mesenteric artery, if water flowed from the stump of gastroduodenal artery that indicated artery arch of pancreatic head being intact. Then, the stumps of the gastroduodenal artery in pancreas graft could be ligated. As venous outflow pancreas graft, the portal vein was transected in the middle of the hepatoduodenal ligament.[Fig 1]
Results: The operative time of pancreas preparation without vascular reconstruction was between 2.5 and 3 hours, which was significantly shorter than that of control group with vascular reconstruction. During pancreas transplantation, the donor pancreatic artery patch was anastomosed to the recipient external iliac artery; the donor portal vein was anastomosed to the recipient external iliac vein. The lengths of the blood vessels were appropriate, and no significant tension was noted. The graft pancreas blood supplied well when vascular reflowed. After transplantation, the pancreas grafts functioned well, and no vascular complications were reported.
Conclusion: Times of the procedure for donor pancreas preparation without vascular reconstruction were significantly shortened than that of control group, while the incidences of vascular complications of pancreas did not increase.



[Fig 1]

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The role of trends and changes in donor and recipient characteristics on the outcome after liver transplantation

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Background: Aim of our study was to compare changes in donor characteristics and trends in outcomes of recipients after liver transplantation using three period cohorts of liver transplant recipients from 2007 to 2017.
Methods: One thousand three hundred eighty-two liver transplantation (LT) recipients from 2007 to 2017 were followed up until November 2018. Three periods (P1, P2, P3) based on transplantation dates were considered to account for developments in transplantation in a single center. Descriptive univariable and multivariable analyses were used to describe donor/recipient characteristics and transplant outcomes.
Results: There was no difference in the age of the recipients between the three periods. The rate of LT/ReLT decreased from P1 to P3 but without statistical significance. The number of living donor transplantation and pediatric transplantation increased from P1 to P3 (5.8% and 10.5% vs. 8.9% and 22.9%).
We demonstrate a decreased 30-day hospital mortality (P1 19.7% vs P3 8.9%, ($p< 0.0001$) and a significantly improved overall patient survival in the latter periods ($p< 0.0001$).
Conclusion: The impact of changes in donor quality and recipient characteristics in a MELD based organ allocation system needs to be reassessed. In this study, we analyzed a set of donor/recipient factors improving the overall patient survival and outcomes after liver transplantation.

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Fibroscan in the assessment of living liver donor candidates

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Background: As living liver donor transplantation continues to grow, non-invasive methods to determine intrinsic liver disease will become paramount during donor evaluation. We hypothesize that Fibroscan provides a safe and cost-effective approach to donor assessment.
Methods: Potential donors evaluated in the last year were included. Suitable candidates entered the clinical assessment phase in which laboratory, and Fibroscan data were collected. Fibroscan involves transient elastography (TE), acoustic radiation force impulse (ARFI), and controlled attenuation parameter (CAP) score assessments.
Results: 55 potential donors entered into preliminary screening from which 18 proceeded to laboratory and detailed demographic assessment, followed by 11 undergoing Fibroscan. Mean age was 34.9 (range: 19-47), 7 female, six assessed for adult to adult donation (54%), 4 for adult to pediatric (36%), with one nondirected/unrelated (9%). Fibroscan results were 4.9±0.8 kPa, 1.28±0.12 m/s, and 233.5±67.9 for TE, ARFI and CAP score, respectively. 6 patients had abnormal results, 5 of them had grade S1 (n=1) or S3 (n=4) steatosis and 1 had evidence of fibrosis. LFT were within normal limits in all but one of them.
Conclusion: Transient Elastography, a novel technology, provides clinically meaningful information that may prevent unnecessary testing of those who are not variable living donor candidates. TE enhances the efficiency of living donor evaluations, as LFTs might be normal during early stages of liver disease. Our project includes the use of this technology in the follow up of the donors and grafts transplanted.

P-179

ABO incompatible (ABOi) liver transplantation is a good option for salvage transplantation - single center experience

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Introduction: Liver transplantation(LT) is one of the most effective treatments for end stage liver disease, fulminant hepatic failure(FHF) and HCC. The mortality on the waiting list due to shortage of available organs made us find ways to expand the pool of liver grafts. These attempts include using „marginal" grafts, LDLT and ABOi grafts.
There is increasing evidence that ABOi LT is feasible and safe using titer-based protocols.
We are presenting the Rabin Medical Center experience in ABOi LT and an unusual case of salvage ABOi LT.
Method: Retrospective analysis of all ABOi liver transplants done in Rabin Medical Center using the transplant electronic database and the patient´s electronic files.
Results: Between the years 2007 to 2018, eight patients where transplant using ABOi grafts, 3 LDLT, 2 FHF and 3 salvage second LT after primary graft dysfunction(PGD) or HAT. All patient where treated with Rituximab and plasmapheresis aiming to reduce the antibody titer to ≤ 1:16. Since 12.2016 we are using an ABO absorbing column in the plasmapheresis to help in reducing the titer of the antibodies. Two (25%) of the transplant patients died within 30 days from severe infection, two patients (25%) had biliary complications treated with PTC and one patient (12.5%) had recurrent episodes of ACR and chronic rejection.
One of these patients had DDLT for PBC related liver cirrhosis. In the first day postOP he had signs of PGD with clinical deterioration secondary to severe toxic and inflammatory reaction. After multidisciplinary discussion he underwent urgent hepatectomy with continuous plasmapheresis and was kept anhepatic for 8 hours until second ABOi LT was available with prolong post-operative course complicated by humoral rejection and infection but end with good results.
Conclusion: ABOi LT may be a good option for fulminant hepatic failure salvage LT and in some cases for LDLT.

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Portal vein thrombosis: use of left renal vein as an option for portal inflow to the liver allografts. A single-center case series.

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Background: Portal vein (PV) thrombosis is a common finding in patients with end-stage liver disease awaiting for a liver transplantation (LT), with incidence as high as 26%. Once considered a formal contra-indication for a LT, nowadays a range os techniques of PV revascularization have been described, including the use of the left renal vein.
Objective: Describe a single-center serie of 3 cases with complete PV thrombosis and cavernomatous transformation that used the left renal vein as an option for portal inflow to the liver allograft.
Discussion: The major challenge of the complete PV thrombosis is to provide an adequate portal inflow at the time of reperfusion, and thereafter. Three patients with grade IV PV thrombosis, spontaneous splenorenal shunt, recurrent ascites and variceal haemorrhage

were managed with an end-to-end reno-portal anastomosis, using an iliac jump graft, with good outcome in all cases. This case series demonstrates the feasibility and safety of this technique when a preoperative vascular study is performed, and a satisfatory flow through splenorenal shunt towards renal vein is documented.
Conclusion: Reno-portal shunt with iliac graft is a safe alternative for a successful allograft inflow in grade III and IV PV thrombosis, once there is an adequate flow through the shunt and a correct match between donor and recipient.

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Allocation status for deceased donor liver transplantation after application of MELD score-based system: single center experience in Korea

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For more objective allocation of deceased donor liver, the allocation system was changed from CTP system to MELD system in 2016. The purpose of this study is to analyze the allocation status of deceased donor liver transplantation(DDLT). We identified 174 patients aged 12 years or older who received DDLT from June 2016 to May 2018, and analyzed their allocation status of DDLT. Among the 174 patients who received DDLT, 129 were male and 45 were female. The mean age was 52 years. By blood type, there were 65 in A+, 51 in B+, 28 in O+ and 30 in AB+. There were 11 patients who registered as status 1 and the MELD score at the time of transplantation ranged from 28 to 40. The MELD score of the 163 patients was 15~40(mean 36). By the blood type, A^+ was allocated from 15 to 40(mean 36) mainly in the status 2(38~40) and 3(31~37). B^+ was allocated from 29 to 40(mean 37) mainly in the status 2 and 3. O^+ was allocated from 33 to 40(mean 39) mainly in the status 2. AB^+ was allocated from 21 to 40(mean 33) mainly in the status 3. The mean waiting period to transplantation was 60.4 days in A^+, 25.7 days in B^+, 26.0 days in O^+ and 68.4 days in AB^+. Patients who received transplant while in hospital were 90.2% in A^+, 94.1% in B^+, 92.9% in O^+, and 90.0% in AB^+. Since there are differences in MELD scores in selecting recipients of DDLT depending on the blood type, a transplant coordinator can improve the selection opportunity by thoroughly updating the MELD score of waiting list. It is important to provide the status of allocation by blood type so that the transplant candidates and medical personnel can prepare liver transplantation at the appropriate time.

P-183

Efficacy of whole-body FDG-PET/CT in pretransplantation evaluation of asymptomatic parotid neoplasm

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Background: Positron Emission Tomography using F-Fluordeoxyglucose (FDG-PET) can detect metabolic changes in malignant and inflammatory cells and is a currently used tool for pretransplantation evluation for malignancy. However, the efficiency and accuracy for asymptomatic parotid neoplasm evaluation before transplantation and the relationship between partotid gland and PET were rarely reported.
Methods: We retrospective review our 400 LDLT recipient candidates who had receive PET-CT scan for preoperative survey. Parotidectomy was performed if image suggest mix tumor or PET scan showed high SUV level, otherwise, echo guide core biopsy was done for diagnosis. Correlation of FDG PET/CT with histology and follow-up outcome was performed.
Results: Parotid tumor was found accidentally in 12 patients. All the patients are male, with average 59-year-old and 9 patients (75%) temp to receive LDLT due to hepatocellular carcinoma. 6 cases underwent core biopsy and 6 patients were operated after PET/CT study. Warthin's tumor was present in 8 patients (66.7%) and 2 patients biopsy present negative result for malignancy in final pathology. Only 1 patient(8.34%) revealed adenoid cystic carcinoma after total parotidectomy and LDLT was abandoned for further malignancy treatment. The SUVs for parotid tumor varied from 2.6 to 41.2 in these patients with an average of 9.18, and the SUVs were higher for Warthin´s than for the cancer (3.5). None of the patient had facial palsy or other complication associated with parotidectomy.
Conclusion: Whole-body FDG-PET/CT is helpful for detecting the asymptomatic parotid masses for pretransplantation LDLT recipient survey. However, SUV level only is inadequate to predict malignancy. Additional workup of all patients including core needle biopsy or surgery to confirm the diagnosis is necessary.

PATIENT	Age	Sex	Site	Size(cm)	SUV	Core biopsy or Parotidectomy	Pathology	Indication for LDLT	LDLT
Patient 1	66	M	Left	1.6	Lt 4.7	Biopsy	Warthin's tumor	HCC	Performed
Patient 2	50	M	Right	2.2	Rt 5.6	Parotidectomy	Warthin's tumor	HCC	Performed
Patient 3	57	M	Bilateral	1.8	Rt 10.1 Lt 8.3	Biopsy	Warthin's tumor	Cirrhosis	Performed
Patient 4	57	M	Right	1.2	Rt 7.0	Biopsy	Warthin's tumor	Cirrhosis	Performed
Patient 5	65	M	Left	2.1	Lt 5.0	Parotidectomy	Warthin's tumor	HCC	Performed
Patient 6	54	M	Right		Rt 2.6	Not performed	Not performed	HCC	Not performed du to HCC progression
Patient 7	63	M	Right	1.2	Rt 5.7	Biopsy	Negative for malignancy	Cirrhosis	Not performed du to donor not suitable
Patient 8	55	M	Right	0.9	Rt 2.7	Biopsy	Negative for malignancy	HCC	Performed
Patient 9	70	M	Right	2.1	Rt 41.2, 9.3	Parotidectomy	Warthin's tumor	HCC	Performed
Patient 10	66	M	Right	0.5	Rt 3.5	Parotidectomy	Adenoid cystic carcinoma	HCC	Not performed du to adenoid cystic carcinoma
Patient 11	52	M	Bilateral	4.4	Rt 23.2 Lt 6.1	Biopsy then Parotidectomy	Warthin's tumor for both	HCC	Performed
Patient 12	53	M	Left	1.4	Lt 2.8	Parotidectomy	Warthin's tumor	HCC	Performed

[Patients details with Parotid Neoplasm and PET Scan]

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Liver retransplantation, is it still justified in the current era?

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Liver retransplantation (LRT) is the only therapeutic option for graft failure. Its indication is controversial due to its worse global results compared to primary LT. Our aim was to evaluate the rate of LRT at our institution, and to study its indications and short and long-term results.
Patients and methods: Retrospective study of a prospectively collected database including 1645 LT from 1984 to 2018.
Results: We performed 150 LRT in 140 patients. LRT rate was 9 %, and the main indications were: ischemic cholangitis (27%), primary non-function (15%), arterial thrombosis (12%) and HCV recurrence (13%). 45 LRT were early (30%), and the other 70% were late LRT. Mean operative time was 375 min. 88% of patients required blood tranfusion. 20% of the LRT required non-standard arterial anastomosis, and 70% required an hepaticojejunostomy. 70% had some kind of postoperative infection, 26 patiens (18%) were reoperated on, and postoperative mortality was 13%. One and 5 year actuarial survival was 71% and 58% respectively, being significantly better during the last decade (80 % and 64% respectively). During the last year, HCV recurrence has decreased as an indication of LRT. Indeed, 5 year actuarial survival for ischemic cholangitis, is better than other indications such as HCV recurrence (78% vs 49% respectively).
Conclusions: Liver retransplantation is complex and is associated with high morbidity and mortality. However, indications and long-term results have improved during the last years. Thus, LRT seems to still be justified in the current era.

P-185

Living liver donor evaluation, acceptance and rejection at a newly established liver transplant centre

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Background: Living donor liver transplantation (LDLT) increases the pool of available organs for patients with chronic liver disease especially in countries where deceased donor liver transplants (DDLT) are meagre. Our aim was to identify reasons for donor rejection and study outcomes of recipients whose potential living donors were rejected during assessment for transplantation.
Materials and methods: Potential living donors were assessed for liver donation from May 2017 to November 2018 at a newly established large tertiary care transplant centre in Mumbai, India. Donor evaluation was divided into 4 phases: liver quality assessment, liver anatomy and volume evaluation, cardiopulmonary assessment and independent transplant committee clearance.
Results: One hundred potential donors (52 females, 48 males; 19 spouses, 23 children, 12 siblings, 26 parents, 18 second degree relatives, 1 grandparent and 1 friend) were prospectively evaluated for 78 recipients. The mean age of donors was 35.33±10.61 years (19-58 years). Amongst the 100 donors, 45 successfully donated a part of their liver [right lobe(n=27), left lobe(n=1) and left lateral segment(n=17)] whereas 55 could not donate. Out of those 55, 38 (69%) were rejected during donor evaluation, 8 donors withdrew consent, 5 recipients passed away, 2 recipients underwent DDLT whereas 2 recipients were delisted. Reasons for donor rejection were liver steatosis(n=31), non-alcoholic steatohepatitis(n=3), newly diagnosed diabetes(n=2), unfavourable anatomy(n=3), low graft recipient weight ratio(n=2) and low remnant volume(n=2). Outcomes of recipients amongst the 38 rejected donors (for 31 recipients) were varied. 11 recipients died, 7 underwent LDLT with another donor, 4 underwent DDLT and 9 are awaiting DDLT.

Conclusion: Forty-five percent of potential evaluated donors could successfully donate their liver whereas 55% could not donate. Out of the 31 recipients whose donors were rejected, 35% died during the waiting period. LDLT thus offers an alternate and important source of organs in countries where DDLT is limited.

P-186

Profile of potential organ donors and factors related to non-donation at a university hospital

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The rate of organ donors in Brazil has been growing in the last decade. However, the discrepancy between the number of donors and recipients is still great, because the former is less than expected, Family refusal has been the main reason not to donate.
Goal: To characterize the profile of potential and effective organ donors and identify the factors related to lack of donation.
Methods: This is a cross-sectional study, with retrospective data collection, carried out at the Organ Procurement Organization of the Hospital das Clinicas of the State of Campinas (OPO-HC-Unicamp), called "information on the multiple organ donor", for the period January 2013 to April 2018.
Results: There were potential donors in 1,772 at the OPO-HC Unicamp. The main cause of brain death (BD) was stroke (56.2%), followed by traumatic (28.3%), tumors (3.5%) and others (1.5%). Of this total 682 (38.4%) were available for donation. The male gender predominated with 57.4%; the average age was 42.5±18.19 years and BMI average was 26.1±4.6. The relationship between chronic diseases (diabetes and hypertension) and life habits (alcoholism, smoking) was the cause of brain death (traumatic or non-traumatic). It was noted that diabetes, hypertension and smoking are more common in non-traumatic causes. Alcoholism, however, was more common in traumatic causes. The statistical analysis also demonstrated the relationship between non-organ donation and the presence of diabetes mellitus (DM), hypertension (SAH), smoking and alcoholism.
Conclusion: The profile of organ donors had the same characteristics as in the literature. There is a shortage of reports in the media about organ donation awareness. The development of disease prevention programs increases the opportunity to increase the number of donors, since it can reduce the occurrence of PCR and medical contraindication.

P-187

Nursing care of a patient receiving liver transplantation from a situs inversus donor

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Situs inversus (SI) is a rare congenital anomaly with complete reversal of all visceral organs. The incidence of SI is approximately 1/15,000-20,000 newborns, and the cause is still unclear.
Although few reports have demonstrated the feasibility of liver transplantation from SI donors, this disease entity remains rare and relevant experience remains limited. SI donor dramatically increases the difficulty of liver transplantation and postoperative nursing care. Herein, we report our experience of nursing care from a successful liver transplantation with SI donor. The donor liver was rotated 90 degrees clockwise and then implanted into a normal receipt. Delayed off-bed activity (postoperative 1 week) was applied. During in-bed period, right lateral position with less than 30 degrees was particularly carried out to decrease the risk of postoperative anastomotic bleeding or leakage. Early rehabilitation of lower extremity including ankle pump exercise (50-60 per time, 4-5 times per day), muscle kneading (15 minutes per time, 3 times per day) and air-pressure pump (20 minutes per time, 2 times per day) was performed to decrease the risk of venous thrombus. Instruction of deep breath and phlegm expelling together with machine-assistant phlegm expelling were prescribed to decrease the possibility of pulmonary infection. This patient was successfully recovered and discharged home. Our experience could help to accelerate the postoperative recovery of patients receiving SI liver transplantation, and could provide useful information for international colleagues.

P-188

Selection of liver graft from deceased donors using shore durometer

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Background: Various methods are available for measuring liver function and degree of liver fibrosis. Liver hardness is considered as using liver graft in deceased donors. However, currently there are no methods predicting liver hardness of liver graft in deceased donors.
Methods: A shore durometer was used to measure liver density in 14 deceased donors for donating patients with end-stage liver disease between August 2017 and December 2017. We compared with liver density between patients with graft failure (GF group) and patients without graft failure (Non-GF group).
Results: All patients were Child-Pugh class C and median MELD score was 38 (31-40). Five patients developed graft failure because of primary non-function. There were no statistically significant differences in preoperative and perioperative factors between GF group and Non-GF group. Median surface shore units (SU) in the GF group was higher than in the Non-GF group (20.8 vs. 16.6; P=0.205), but the difference did not reach significant level.
Conclusion: Hepatic hardness measured by the shore durometer may be used for predicting graft failure after deceased donor liver transplantation.

Poster Round I, Session 1, 2, 3: Living Donor

P-189

The impact of extra-anatomical hepatic artery reconstruction during living donor liver transplantation on biliary complications and graft and patient survival

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Background: This study was designed to analyze the feasibility of extra-anatomical hepatic artery reconstruction in living donor liver transplantation.
Methods: Patients who underwent their first living donor liver transplantation at our center between January 2008 and December 2017 were reviewed. Hepatic artery reconstruction was classified as anatomical or extra-anatomical reconstruction. We compared the background characteristics and post-transplantation outcomes, including complications, biliary complications, graft survival, and overall survival. The potential risk factors for bile leakage was analyzed using multivariable logistic regression while risk factor for biliary stricture-free, graft, and overall survival were analyzed using multivariable Cox regression.
Results: Among 800 patients, 35 (4.4%) underwent extra-anatomical reconstruction while seven patients (7/35, 20.0%) experienced hepatic artery complications after the initial anatomical reconstruction and required extra-anatomical reconstruction during reoperation. Patients who underwent extra-anatomical reconstruction (n=2/35, 5.7%) had a similar rate of hepatic artery complications compared to those who underwent anatomical reconstruction (n=46/772, 5.9%, P=0.699). Extra-anatomical reconstruction was a significant risk factor of bile leakage (OR=4.167, CI 1.928-9.006, P< 0.001) along with multiple bile ducts (OR=1.606, CI=1.022-2.526, P=0.040), and hepaticojejunostomy. (OR=4.108, CI=2.190-7.707, P< 0.001) However, extra-anatomical reconstruction had no statistical relationship to biliary stricture-free survival (HR=1.602, CI=0.982-2.613, P=0.059), graft survival (HR=1.745, CI=0.741-4.109, P=0.203), or overall survival (HR=1.405, CI=0.786-2.513, P=0.251). Hepatic artery complications were associated with poor biliary stricture-free survival (HR=2.060, CI=1.329-3.193, P=0.001), graft survival (HR=5.549, CI=2.883-10.681, P< 0.001), and overall survival (HR=1.958, CI=1.195-3.206, P=0.008).
Conclusion: Extra-anatomical hepatic artery reconstruction during living donor liver transplantation was not a risk factor of biliary stricture, graft failure, or overall survival.

P-190

Right lobe vs. left lobe for living donor liver transplantation: a systematic review and meta-analysis of donor and recipient outcomes

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Background: Living donor liver transplantation (LDLT) is an excellent means to expand the donor pool. Despite more than 20 years of experience with these procedures, it is still unclear it is better to transplant the right lobe (RL) or the left lobe (LL) in adults. We undertook a systematic review and meta-analysis to study this question, recognizing this type of analysis provides the highest level of evidence to choose between these options.
Methods: MEDLINE, EMBASE, PubMed, and Cochrane were searched from inception to June 2018 using the terms “liver transplantation”, “living donor”, and “lobes”. Studies comparing short-term outcomes after RL-and LL-LDLT for donors and/or recipients were included. Studies including patients 18-year-old or younger, comparing results after left lateral or right posterior lobes or case series with≤10 patients were excluded. We assessed overall complications, major complications (Clavien-Dindo≥IIIa), and specific complications including bile leak, biliary strictures, and small for size syndrome(SFSS) among recipients. Relative Risks(RRs) were pooled across trials using random-effect meta-analysis. Risk of bias was assessed using the Newcastle-Ottawa Scale.
Results: Fifty-nine studies were included; 46 comparing outcomes among 21,750 donors and 32 among 10,122 recipients. RL donors were more likely to experience any complication (RR=1.36,95%CI=1.17-1.60,I^2=42%) and major complications (RR=1.79,95CI=1.35-2.37,I^2=29%) compared to LL donors. The incidence of bile leaks (RR=1.71,95%CI=0.99-2.96,I^2=55) and biliary strictures (RR=1.47,95%CI=0.25-1.95,I^2=29) was not different between groups. Among recipients, the incidence of any complication was similar between RL-LDLT and LL-LDLT (RR=0.90,95%CI=0.77-1.06,I^2=0%). The rate of bile leaks (RR=0.99,95%CI=0.51-1.94,I^2=53%), biliary strictures (RR=1.68,95%CI=0.63-4.51,I^2=74%), and SFSS(RR=0.55,95%CI=0.21-1.46,I^2=77%) were also similar between recipient groups.
Conclusion: In conclusion, this systematic review and meta-analysis suggests that left lobe donation is the best option for live donation between adults. When compared with right lobe grafts, left lobe donor has lower risks and provides the same outcomes as a right lobe graft.

Left Lobe and Right Lobe Living Donor Outcomes

Outcome	No.of Studies	Left Lobe Events	Left Lobe Participants	Right Lobe Events	Right Lobe Participants	R
Any Complication	23	545	3,661	1,591	8,618	1.
Major Complications	18	126	3,413	494	8,359	1.
Bile Leak	17	52	1,887	169	3,583	1.
Biliary Stricture	8	7	803	22	2,161	0.

Left Lobe and Right Lobe Living Donor Liver Transplant Recipient Outcomes

[Summary forest plot of donor and recipient outcomes of RL vs LL LDLT]

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Even extensive Portal Vein Thrombosis (PVT) should not limit access to live donor liver transplantation

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Background: PVT is a common (incidence up to 26%) manifestation of chronic liver disease particularly when decompensation necessitates liver transplantation (LT). The impact of PVT on LT survival is debatable, but registry-based studies have noted inferior 30-day and 1-year outcomes. Consequently, extensive PVT remains a relative contraindication at some institutions especially in the setting of live donor LT (LDLT) on account of its additional anatomic challenges. The objective of our analysis, is to further clarify the influence of extensive PVT on LT outcomes.
Methods: 564 adult LTs were performed at our center between January 1, 2011 and June 30, 2018. Pre-LT contrasted imaging (CT/MRI) was combined with operative findings to generate PVT classifications via the Yerdel grading system. Operative management, including the utilization of venous grafts were reviewed, and outcome analyses focused on portal inflow patency and patient survival.
Results: PVT was noted in 10.1% (n=57) of the LT recipients, 68% (n=39) of whom underwent LDLT. PVT severity grades were as follows: I 33.3% (n=19), II 43.9% (n=25), III 17.5% (n=10), and IV 5.3% (n=3). Thrombectomy established adequate PV inflow in 93% (n=53) of the cases; five patients, all LDLT cases, required venous interposition grafts to complete end-to-end portal anastomoses. Meso-portal (n=2) and varico-portal (n=2; both Yerdel IV) venous jump grafts were utilized sparingly. Three patients (5.3%) developed recurrent PVT and the 1-year actual patient survival was 86%. None of the thirteen patients with extensive clot burden (Yerdel III & IV) re-thrombosed and they had a comparable 85% 1-year survival rate. Receiving a live donor graft did not compromise these outcomes.
Conclusion: Our experience suggests that PVT is a manageable challenge and should not contraindicate LDLT. This holds true for even extensive PVT provided that the requisite surgical expertise and preparation is in place to establish durable portal inflow.

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Intraoperative near-miss events during left liver lobe donation surgery: a potential quality-control tool to assess donor safety in living donor liver transplantation

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Introduction: Living donor liver transplantation (LDLT) is a well-established alternative to alleviate post-mortem organ shortage in pediatric liver transplantation. Such program, however, should be performed under strict ethical guidelines, and optimal living donor (LD) safety. We hypothesized that serious unexpected perioperative medical and/or surgical events during LD procedure indeed occur in a high volume LDLT center, being a major threat to donor safety.
Methods: From July 1993 to October 2018, 433 pediatric LDLT were performed at our institution. All LD medical records were retrospectively reviewed searching for the occurrence of near-miss events (NME). NME was defined as any potentially perioperative harmful event that was identified and controlled before definitive patient harm has happened.
Results: LD postoperative morbidity consisted mainly in cut-surface collections, transient pleural effusions, and incisional hernias, in less than 3% each. However, eight (1,8%) serious intraoperative NMEs occurred: accidental vena cava clamp releasing, left hepatic artery (HA) clip sliding both resulting in massive bleeding, donor right HA ligature and section, accidental section of left HA at liver graft hilum, tension pneumothorax following right subclavian vein catheterization, LD intravenous full-heparinization, donor common hepatic duct section, an injury of segment II bile duct. NME management consisted in: vascular control of intraoperative bleeding and microsurgical repair of the arterial lesions, pneumothorax drainage, intravenous protamine administration,

Roux-en-Y hepaticojejunostomy reconstruction, repair of segment II bile duct at back-table. None of these NMEs resulted in donor or recipient postoperative morbidity.
Conclusions: Despite our minimal morbidity and no mortality rates, 8 serious and potential harmful NMEs were identified in these 433 LDs. All NME were timely recognized and controlled without subsequent donor or recipient harm. NMEs systematic debriefing led to safety refinements in our LD protocol. Systematic record of LD/NME may be used as quality control tool to assess donor safety in LDLT programs.

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Clinical course of hepatic artery thrombosis after living donor liver transplantation using the right lobe

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Background: Hepatic artery thrombosis (HAT) can result in biliary tree necrosis and graft loss necessitating re-transplantation. The most effective treatment approach is still controversial. This study was performed to review the outcomes of HAT after living donor liver transplantation (LDLT), and to clarify the feasibility of different strategies.
Methods: From May 1996 to August 2017, LDLT using the right lobe was performed in 827 adult patients in our center. Our technique of hepatic artery (HA) reconstruction is end-to-end anastomosis under a microscope (× 10). Diagnosis of HAT was performed using Doppler sonography and computed tomography (CT) angiography. HAT was initially treated with surgical or endovascular procedure and re-transplantation was considered according to the graft condition.
Results: Among the 827 cases of LDLT using the right lobe, HAT occurred in 16 (1.9%) cases within 1 month after transplantation. Seven of these HAT cases (43.8%) occurred within the first week (early HAT), while the remaining nine cases (56.2%) occurred between the first week and 1 month (late HAT). The incidence of graft failure was high in early HAT (42.9%), and the frequency of biliary complications was high in late HAT (77.8%). The success rate of HA recanalization was 62.5% (10/16): 100% (5/5) after reoperation and 45.5% (5/11) after endovascular procedure. Of the patients in whom treatment failed in late HAT (n = 5), four underwent neovascularization during observation. Five patients underwent graft failure, and three of these patients underwent repeat LT. Mortality occurred in three patients, including one in the surgical group and two in the endovascular group.
Conclusions: Early diagnosis and aggressive treatment of HAT are necessary to avoid graft failure, and the choice of treatment depends on various factors. Although further studies are required, early HAT requires preparation for graft failure, while late HAT requires treatment for biliary complications.

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Benefits of graft preservation with IGL-1 solution over UW solution in a large volume LDLT center - a propensity score matched analysis

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Introduction: Even though outcomes with different preservation solutions in deceased donor liver transplantation (DDLT) are similar for cold ischemia times up to 6-8hours, there are very few studies(if any) reporting outcomes of Institut Georges lopes(IGL-1) solution in living donor liver transplantation(LDLT) and especially in a matched comparative analysis with UW solution (current standard).
Aim and methods: To analyse outcome of preservation with IGL-1 vs UW solution in LDLT recipients in respect to incidence of primary non function, early allograft dysfunction (EAD) (Olthoff criteria), post operative peak alanine transaminase (first week), morbidity, 90 day mortality and graft survival. 48 consecutive adult LDLT recipients with IGL-1 preservation were compared in propensity score matched (±0.03) analysis with 96 LDLT recipients with UW preservation from May 2017 to august 2018.
Results: Among pre-operative and operative factors, mean recipient age (48.1±5.8vs46.9±4,6yrs)(p>0.234), Sex ratio(79% male vs78%male) (p-0.45), proportion of patients with HCC(18%vs16%)(p-0.56), and HCV(14%vs15%)(p-0.33), mean MELD scores(18.8±2.3vs19.4±3.5) (p-0.21), incidence of pre-operative treated sepsis(12.3%vs13.5%) (p-0.44), mean donor age(34.3vs33.8yrs)(p-0.47), mean donor liver attenuation index(5.1vs5.6)(p-0.37), mean donor BMI(24.5vs25.3) (p-0.28), mean GRWR(1.01vs0.99)(p-0.58), mean intra operative blood transfusions(4.67vs4.59)(p-0.33), mean cold ischemia time(122±23vs118±19min)(p-0.43), mean warm ischemia time(45±5vs44±3)(p-0.38), mean operative time(603 vs584 min)(p-0.65) was not significantly different between IGL-1 vs UW groups. Among post-transplant outcome measures, the incidence of EAD (4.4% vs 12.5%)
(p< 0.032), mean first week postop peak ALT (172 IU/ml vs 245IU/ml)(p< 0.043), and 90 day mortality (4.2%vs9.37%)(p< 0.001) were significantly lower in IGL-1 group vs UW group respectively, whereas primary non function(2.1%vs2.1%)(p-0.5), 90 day graft survival(96%vs91%)(p-0.08), hepatic artery thrombosis(1.9%vs 2,1%) (P>0.0.05), biliary complications(4.47%vs5.3%)(p-0.23), acute rejection

(11%vs9%)(p-0.21) were similar in two groups.
Conclusions: Recipients of LDLT grafts preserved with IGL-1 solution had lower peak ALT levels, lower incidence of EAD and 90 day mortality, but similar 90 day graft survival when compared with UW group. IGL-1 is a safe and effective preservation solution for LDLT.

P-195

A role for the psoas muscle index in guiding operating room extubation after living donor liver transplantation: a retrospective observational cohort study

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Background: Early extubation after liver transplantation is safe and accelerates patient recovery. Patients with end-stage liver disease undergo sarcopenic changes, and sarcopenia is associated with postoperative morbidity and mortality. We investigated the impact of core muscle mass on the feasibility of immediate extubation in the operating room (OR) after living donor liver transplantation (LDLT).
Patients and methods: A total of 422 adult LDLT patients were retrospectively reviewed between January 2011 and December 2017. In total, 59 patients were excluded due to emergency and severe encephalopathy. Because of sex difference in muscle size or strength, only male LDLT patients (n = 255) were analyzed in the present study. According to the OR extubation criteria, the study population was classified into immediate and conventional extubation groups (39.6 vs. 60.4%). Psoas muscle area was estimated using abdominal computed tomography and normalized by height squared (psoas muscle index [PMI]).
Results: There were no significant differences in OR extubation rate among the five attending transplant anesthesiologists. The preoperative PMI was correlated with patient frailty and respiratory performance. The preoperative PMI was higher in the immediate extubation group than in the conventional extubation group. Potentially significant perioperative factors in the univariate analysis were entered into a multivariate analysis, in which preoperative PMI and intraoperative factors (i.e., continuous renal replacement therapy, significant post-reperfusion syndrome and fresh frozen plasma transfusion) were associated with OR extubation. The duration of ventilator support and length of intensive care unit stay were shorter in the immediate extubation group than in the conventional extubation group, and the incidence of pneumonia and early allograft dysfunction was also lower in the immediate extubation group.
Conclusion: Our study could improve the accuracy of prediction of immediate post-transplant extubation in the OR by introducing preoperative PMI into predictive models of patients who underwent elective LDLT.

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Comparison of postoperative outcome after pure laparoscopic and open donor right hepatectomy for adult living donor liver transplantation using propensity score analyses

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Laparoscopic surgery is now a standard procedure in donor left lateral sectionectomy as evidences demonstrate superior outcomes in laparoscopic surgery. However, there are concerns on donor safety as laparoscopic surgery expanded to the right hepatectomy. The aim of this retrospective study is to compare postoperative complication between pure laparoscopic and open donor right hepatectomy by propensity score matching analysis.A total of 320patients who underwent elective donor right hepatectomy were initially screened. After propensity score matching, the patients were divided into two groups; the open hepatectomy group (OH, n=104) and the laparoscopic hepatectomy group(LH, n=104). The frequency and type of postoperative complication was compared between the two groups. We also compared intraoperative and postoperative parameters. Overall complications were 60 of 10 (57.7%) in the OH group and 41 of 10(42.3%) in the LH group (difference in proportion, 18.2 %; 95% confidence interval [CI], 4.0 to 31.5%; p = 0.008). However, major complication was not significantly different between the two groups(OH group, 6 of 104[5.8 %] vs LH group, 11 of 104 [10.6 %]; difference in proportion, 4.5%; 95% CI, -2.9% to 12.8%; p =0.206). Pulmonary complication was significantly higher in the OH group than in the LH group (44.2% vs 23.1%,p = 0.001). Biliary (1.9% vs 7.7%, p = 0.101) and vascular (0% vs 1.9%, p = 0.498) complications tend to be higher in the LH group than in the OH group although not statistically significant. The postoperative outcomes such as hospital stay and time to first meal, and postoperative opioid consumption were superior in the LH group than in the OH group (p=0.003,p< 0.001,p =0.023, respectively). The pure laparoscopic donor right hepatectomy for living donor liver transplantation provided lower postoperative complication and improved recovery after surgery than in the open surgery.There was significantly fewer pulmonary complication in the laparoscopic surgery.

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Long-term outcome of ABO-incompatible adult living donor liver transplantation using a single protocol over 10 years

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Background: ABO blood-type incompatibility has long been a major obstacle to expand a exiguous donor pool in adult liver transplantation, especially in countries where cadaveric grafts are hardly available. Herein we present long-term results of adult ABO-incompatible (ABO-I) living donor liver transplantation (LDLT) using a single protocol for over 10 years.
Methods: Among 648 adult LDLTs, 77 cases (11.8%) were ABO-I LDLTs. The first 3 cases were managed by portal infusion therapy as previously reported. Since 2007, consecutive 74 cases were managed by an original single protocol including preoperative administration of a single dose of Rituximab (375mg/m2) at 3 weeks before LDLT, followed by several sessions of plasma exchange (PE) without portal infusion therapy. The target preformed isoagglutinin antibody titers was less than x126. Triple immunosuppression consisted of tacrolimus, mycofenolate mofetil (MMF) and steroids was exactly the same as that of ABO-compatible (ABO-C) LDLT except for MMF started 7 days before LDLT. A target trough level of tacrolimus in ABO-I LDLT was also the same as that of ABO-C LDLT. Splenectomy was performed in 89.8% of ABO-I and 61.8% of ABO-C cases (p< 0.0001).
Results: The incidence of antibody-mediated rejection in ABO-I LDLT was only 0.6%, which was comparable to that of ABO-C LDLT (0.5%). All of the other complication rates including acute or chronic rejection, hepatic artery thrombosis, sepsis, CMV infection and bile duct complication were also comparable. The 5- and 10-year graft survival rates in patients with ABO-I (n=74) and ABO-C (n=357) grafts during the same time period were 87.9% vs. 86.8% and 87.9% vs. 84.5%, respectively (p=NS).
Conclusion: ABO-I LDLT is no longer a contraindication but rather a recommended modality in adults.

P-198

Comparative study of CT LAI , MRI and liver biopsy for quantification of liver fat in 195 consecutive living donors

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Background: Assessment of graft steatosis is of paramount importance in living donor liver transplant as it affects outcome in both the donor and recipient. In our center, we routinely estimate the CT Liver Attenuation Index (CTLAI) as well as MRI fat fraction (MRFF) followed by Intra operative core biopsy.
The objective of this study is to compare all three modalities and identify the best method for liver fat quantification in donors.
Methods: Between September 2015 to November 2018, 195 donors hepatectomies were performed at our institute. The presence of steatosis was assessed radiographically using CTLAI and MRFF using standard quantitative radiologic criteria. This data was retrospectively analysed and compared with intraoperative core needle biopsy.
Linear regression analysis was used to correlate degree of macrovesicular steatosis with both LAI and BMI.
Results: A total of 108 males and 87 females with a mean age of 32.25 years (range 18-56 years) were studied. The mean BMI was 24.35 (range 15.79-32.2). A stronger correlation of liver fat was seen with MRI as compared to NCCT; correlation coefficients r = 0.671 P = 0.00 vs r = 0.213, P = 0.0003. This relationship was also maintained in 8 donors with fat more than 10% (p=.36 and p=.57 respectively). When the two imaging modalities were compared, a weaker correlation was seen between CTLAI and MRFF (r=.3352, p=.003).
Conclusion: MRFF alone is a better marker for quantification of liver fat and can prevent the need of preoperative CT and liver biopsy to quantify steatosis.

P-199

Expansion of the use of left lobe grafts in adult liver transplantation in a US center: different strategy between deceased and living donor grafts

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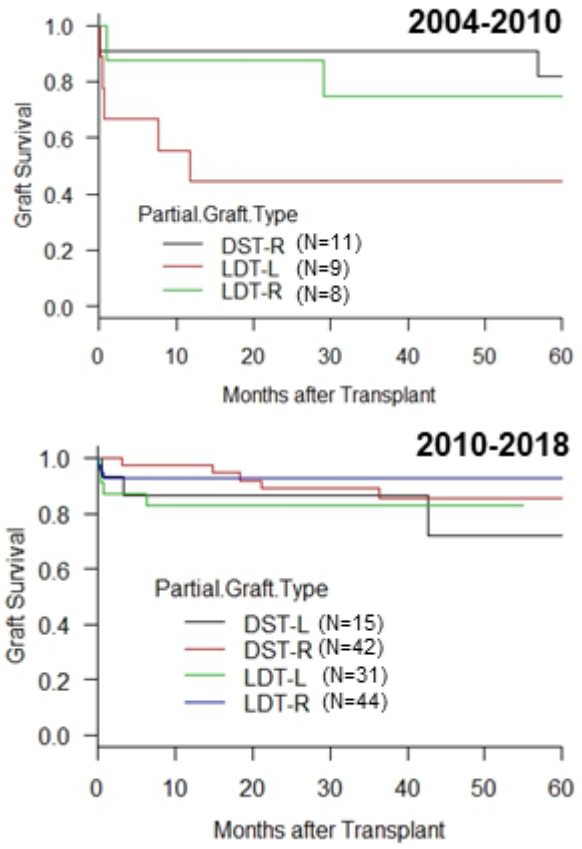
Methods: This is a retrospective review of 1465 primary adult-liver transplantations from 2004-2018 at a single US center, including 68 DSTs and 92 LDTs. Donor-recipient characteristics, left-lobe utilization and outcome of each graft type were analyzed before and after 2010. In 2010, our program introduced a novel triple-hepatic vein outflow technique for left-lobe graft along with splenectomy as the primary inflow modulation. Multivariate Cox-model was used to assess the risk of graft loss amongst other risk factors.
Results: Partial liver utilization among all transplants increased from 4% to 15% in the latter era. Left-lobe was used in about 45% of LDTs in both eras. In the recent era, left-lobe DST was introduced with judicious donor-recipient pairing with an adequate graft-to-recipient weight ratio (GRWR). Compared to DST, LDT using left-lobe was done with a significantly lower median GRWR (0.78 vs. 1.24) and higher portal flow (150 vs. 106 mL/100gLW), and more frequent inflow modulation (65% vs. 7%). In the early era, left-lobe was associated with increased risk of graft loss (HR 9.7, p< 0.01) as well as MELD score and donor age. In the latter period, left-lobe graft survival became equivalent to those of right lobe-grafts with diminished occurrence of small-for-size syndrome.



[Graft survival of partial liver graft]

Conclusions: Successful outcome of left-lobe grafts can be achieved with optimization of inflow and outflow modulation in LDT and judicious donor-recipient pairing in DST. Left-lobe grafts can be utilized further in North America.

P-200

Outcomes of liver donors with a future liver remnant less than or equal to 30%: a matched-cohort study

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Background: Living donor liver transplantation (LDLT) is an accepted strategy to reduce waiting list mortality. The main concern with LDLT is the risk to the donor. Given the potential risk of liver insufficiency, most centres will only accept candidates with a FLR above 30%. Outcomes of donors with a FLR below 30% are unknown. The goal of this study was to compare outcomes between live liver donors undergoing right hepatectomy with future liver remnants (FLR) ≤30% and >30%.
Methods: A prospective database of live donors who underwent right hepatectomy between April 2000 and June 2018 was retrospectively analyzed. Remnant liver volumes were estimated using computed tomography volumetry. Donors with a FLR ≤30% were matched 1:2 based on age, sex, body mass index, and era of transplant to donors with a FLR > 30%. Post-operative complications and post-hepatectomy liver dysfunction were compared between the groups.
Results: Six-hundred and four live donors were identified, 28 (4.6%) of which had a FLR ≤30%. Twenty-eight cases were successfully matched with 56 controls; matched cohorts were mostly similar in terms of donor and graft characteristics. Median FLR was 29.8 (range 28.0-30.0) and 35.2 (range 30.1-60.0) in each respective group. Median follow-up was 36.5 months (IQR 11.8-66.1). Post-operative outcomes were similar between groups. No difference was observed in overall complication rates (FLR ≤30%: 32.1% vs. FLR >30%: 28.6%; odds ratio (OR) 1.22, 95% CI 0.46-3.27) or major complication rates (FLR ≤30%: 14.3% vs FLR >30%: 14.3%; OR 1.17, 95% CI 0.33-4.10). Post-hepatectomy liver insufficiency, defined by the International Study Group of Liver Surgery post-hepatectomy liver failure criteria, was rare and no difference was observed (FLR ≤30%: 3.6% vs FLR >30%: 3.6% OR 1.09, 95%CI 0.11-11.1).
Conclusion: Right hepatectomy for live donation may be performed in selected patients with an FLR between 28-30% without increasing the donor morbidity.

P-202

Portal hyperperfusion syndrome after prophylactic ligation of spontaneous portosystemic shunts during living donor liver transplantation: analysis of risk factors

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Background: Routine ligation of spontaneous portosystemic shunts (SPSS) has been recommended by most high volume LDLT centers. However, shunt ligation is speculated to increase the incidence of portal hyperperfusion syndromes (PHS) such as delayed graft function and small for size syndrome despite having normal intraoperative flow/pressure parameters.
Methodology: We reviewed medical records of 82 adult patients with significant SPSS who underwent LDLT from June 2013 to May 2018 at Kaohsiung Chang Gung Memorial Hospital. Eighteen cases of PHS were identified and peri-operative recipient variables were analyzed using univariate analysis followed by multiple logistic regression in a stepwise method to identify independent risk factors for developing PHS.
Results: Intraoperative SPSS ligation (P=0.024), Recipient standard liver volume (P=0.030), graft weight (P=0.028), pre-operative portal vein thrombosis (P=0.019), portal vein flow before abdominal closure (PVF_0) (P=0.015), total bilirubin and INR on postoperative day 1 (P=0.033; 0.023) were found to be significant on univariate analysis. Multivariate analysis on the other hand, showed that left lobe donation (OR 15; P< 0.001), POD 1 total bilirubin of more than 8mg/dL (OR 5.3; P=0.017) and a PVF_0 of more than 150 mL/min/100g (OR 6.9; P=0.011), were independent risk factors to develop PHS.
Conclusion: In this study, the incidence of post-transplant PHS was significantly associated with prophylactic SPSS ligation during LDLT and a PVF_0 of more than 150 mL/min/100g was found to be an independent risk factor. And so, the authors recommend that additional prophylactic portal inflow modulation procedures such as splenic artery ligation or splenic devascularization may be combined with prophylactic SPSS ligation especially in high risk grafts (left lobe or GRWR < 0.8) to optimize early graft function and potentially, long-term outcomes after LDLT.

P-203

Minimizing donor complications. Lessons learned from 1213 consecutive living donor hepatectomies

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Background: Living donor liver transplantation (LDLT) has been performed widely to increase organ availability for the treatment of end-stage liver diseases. Despite the growing acceptance of LDLT, donor safety remains a critical concern.
Methods: A total of 1213 living donor hepatectomies were performed in our center from January 2004 to January 2017. We reviewed the donor complications and analyzed its relation to graft types and remnant liver volumes.
Results: There was no donor mortality at our center. No complications were observed in 1077 donors (88.8%). 136 donors experienced complications (11.2%), of which 88 were right graft donors (12.3%) and 48 were left graft donors (9.7%). Donors with remnant liver volume < 35% had significantly higher risk of developing complications (P=0.013). According to the Clavien-Dindo Classification, grades I, II, IIIa, IIIb, and IVa complications were experienced in 58 (4.8%), 45 (3.7%), 19 (1.6%), 13 (1.1%), 1 (0.1%) donors respectively. Biliary complications were the most common types of complications (3.2%), with the majority being bile leaks. Left lobe donors had significantly higher risk of bile duct injuries (P=0.005).
Conclusion: Most of our complications were minor and were managed conservatively. Although there was no donor mortality, there was one near-miss event resulting in a grade 4a complication. The vascular clamp on the right hepatic vein slipped causing intra-operative bleeding, which required suturing into the IVC. Post-operatively, the donor developed IVC thrombus, which was managed successfully with Coumadin. With experience and refined techniques, low complication rates can be achieved after living donor hepatectomy. Donor complications can be minimized by performing detailed pre-operative imaging study, meticulous surgical technique, minimizing blood loss, and ensuring proper venous outflow. With careful selection, right lobe donors and left lobe donors can achieve comparable outcomes.

P-204

Comparison of pure laparoscopic and open living donor right hepatectomy after a learning curve

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Objective: To compare the early outcomes of pure laparoscopic living donor right hepatectomy (PLDRH) to those of open living donor right hepatectomy (ODRH).
Comparison of the early outcomes of these two procedures is important as the extension of laparoscopic techniques to PLDRH is just emerging. However, PLDRH is a technically challenging procedure and, therefore, it is essential that its outcome be considered in light of known outcomes of ODRH.
Methods: Our analysis was based on 78 consecutive cases of living liver donor, who underwent right hepatectomy, of which 43 underwent ODRH and 35 PLDRH. The learning curve for each group was analyzed and compared to the surgeon's level of experience.
Results: Donor characteristics and liver anatomy were comparable between the two groups, with the exception of the size of the right portal vein (PLDRH 13.4±6.3 mm versus ODRH 10.8±3.2 mm; P=0.03). Two donors, with a large graft size, in the PLDRH required conversion to an open procedure due to bleeding. The following outcomes were comparable between the two groups: operative time (P =0.64); estimated blood loss (EBL; P=0.86); intra-operative transfusion (P =0.57); hospital stay (P=0.41), and postoperative complications (P =0.51). After the learning curve, the EBL was lower for PLDRH than ODRH (P=0.04).
Conclusion: PLDRH can be performed as safely as ODRH and with a lower volume of intra-operative blood loss once the surgeon has attained an appropriate level of learning.

P-205

Living donor liver transplantation for Budd-Chiari syndrome: a surgical challenge

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Background: Budd-Chiari syndrome (BCS) is characterized by hepatic venous outflow obstruction due to occlusion of the major hepatic vein and/or the inferior vena cava (IVC). Traditionally, caval resection is advocated for these patients; however, living donor liver transplantation (LDLT) for these patients represents a technical challenge. Consequently, the aim of the study was to report the optimal surgical techniques of LDLT in these patients at our center.
Methods: Etiological and surgical techniques characteristics of 23 patients with BCS who underwent right lobe LDLT at our center (12/2011-09/2018) were retrospectively reviewed. A durable LDLT technique with/without piggy-back hepatectomy was designed for reconstructing the hepatic outflow tract.
Results: Etiology for BCS was identified in 16 patients (70%). The most common causes were protein C/S deficiency, myelodysplatic syndrome, and hepatic echinococcosis. Eighteen (78.2%) patients had preservation of native IVC and 5 had resection of retrohepatic IVC with venous continuity established by a large-caliber synthetic interposition vascular graft. In 5 patients, the anastomosis was established directly between the graft hepatic vein (HV) and the right atrium. All patients were started on anticoagulation (fractionated/unfractionated heparin) perioperatively and switched to oral anticoagulant at discharge. None of the 23 patients developed recurrent BCS with a mean follow up of 4.8 yrs. One patient died 11-months post LDLT due to intracranial hemorrhage related to deranged coagulation profile.
Conclusion: Excellent outcomes are achievable with LDLT in patients with BCS, which carries important implications for countries with inadequate deceased donor pool.

P-206

Good outcomes of living donor liver transplantation (LDLT) for autoimmune liver diseases (AILD): a large single centre experience

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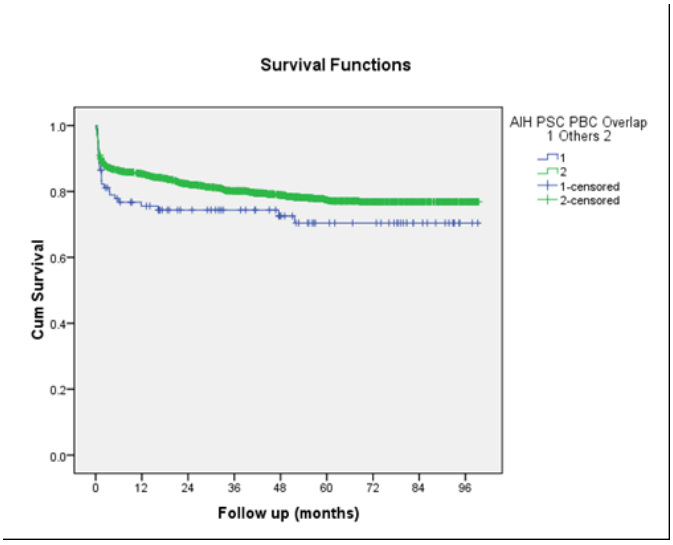
Background: Liver transplantation (LT) is an effective treatment for patients with end-stage AILD. There remains risk of disease recurrence after transplantation. Aim was to study the outcome of LDLT for AILD.
Methods: Retrospective analysis of database from Jun 2010 to Jul 2018 including 1750 patients who underwent LT was done. Analysis of clinically significant events like rejection, recurrence of disease and death was done.

Results: Of 1750 transplants, 96 (5.48%) underwent LT for AILD; 3 cadaveric and 93 Living Donor (LDLT). Mean age at transplantation was 51.5 ± 3.53 years (54M:42F). Most common disease type was AIH in 67 (69.8%), followed by PSC in 17 (17.7%), overlap syndromes in 7 (7.3%) and PBC in 5 (5.2%). Acute cellular rejection occurred in 17 (17.7%) and chronic rejection occurred in 2 patients. Disease recurrence was seen in 6 (6.2%) patients; recurrent AIH in 5, and recurrent AIH with PSC overlap in one. Most of the recurrences were seen 1 year after LT at median 38 (IQR 19.7-44.7) months. All the recurrences were successfully treated by increasing steroids and modification of immunosuppression. There was no allograft loss till a median follow up of 9.5 (IQR 7.7-29.5) months after disease recurrence. At average follow up of 50.2 months (IQR 5.3-63.2), there were 26 (27%) deaths. Sepsis was the most common cause of death in 21 patients (Acute Coronary Syndrome, Renal failure, Outflow tract obstruction, Intracranial bleed, HCC recurrence in each of the remaining). Overall survival was not different in patients with AILD as compared to other etiologies (72.9% Vs 79.6%, p=0.086).
Conclusion: LT in patients with AILD has good outcomes and survival as compared to other etiologies. Patients with disease recurrence can be managed with modification of immunosuppression without allograft loss.



[Kaplan Meier Surival Analysis. AILD Vs Others]

P-207

Analysis of 124 consecutive laparoscopic and robotic living donor left lateral sectionectomies for pediatric liver transplantation at the King Faisal Specialist Hospital

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Objectives: The adoption of fully laparoscopic living donor hepatectomy approach (LAP) in our institution in May 2013 as the standard approach for pediatric liver transplantation. Recently, the robotic approach (ROB) has been implemented. we describe our results.
Methods: From May 2013 until November 2018, a total of 124 left lateral sectionectomies (LLS) have been done. Five out of 124 donor hepatectomies were carried out with the robotic approach. The parenchyma transection was done using the surgical ultrasonic aspirator (LAP) and the harmonic scalpel (ROB). The trans-umbilical approach was routinely applied. After cutting the hilar plate and the bile ducts, the transection plan followed the line until the confluence of the left hepatic vein into the IVC. The S2-3 artery stump was secured with two Hem-O-lock clips, the left portal vein and the LHV secured and transected by the 45 mm vascular stapler after preparing a short Pfannestiel incision for graft extraction.
Results: M/F ratio was of 60/64. The mean BMI was of 24.5±3.8. Graft weight was of 224±47 g. The operative time was of 264±28 min. and 375±31with an estimated blood loss of 111± 93 ml vs 37±14 (p=0.0001 and 0.07 respectively for LAP and ROB). The hilar dissection time was of 65±12 min. in the Lap vs 50±5 min in the ROB cases (p=ns). Overall donor complications were 4 (3.2%)(LAP). The conversion rate was 2.4% (n=3 cases, LAP). The overall 3-y actuarial recipient survival was of 92.7%.
Conclusions: Laparoscopic LLS for donor hepatectomy is a safe and efficient procedure with a very low conversion rate. The ROB approach could be the ultimate evolution potentially shortening the hilar dissection time and providing its intrinsic and valuable advantages for the surgeon as better ergonomy, stable view, detailed anatomy and less manipulation of the graft. Further data are needed to validate this.

P-208

Higher incidence of VTE and PE in the live liver donation

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Living donor kidney and liver transplant are widely accepted as an effective approach to address organ shortage. The massive hepatectomy is a Known risk factor for temporary hypercoagulable state during the immediate postoperative period. The aim of this study is to compare venous thromboembolism (VTE) and pulmonary embolism (PE) incidence in living liver donors compared to living kidney donors.
We have retrospectively reviewed the medical record of all patients who underwent living donor procedure between January 2008 through November 2018. During this period 178 living donor procedures were performed. 42 Patients underwent living donor hepatectomy, 136 patients underwent living donor nephrectomy. All patients prior to donation underwent extensive medical and surgical evaluation according to our protocol including hypercoagulable workup. Patients with positive hypercoagulable markers were excluded from donation. SPSS version 25 Was used to analyze data. Chi-square was used for parametric and t-test for continuous variables, to perform the test of significance.
There was no significant difference between the liver and kidney donors with respect to sex, race, height, and weight (p³0.05). Donor age was significantly lower in the liver donors (40±17) compared to kidney donors (49±20) (p=0.013). Regarding coagulation factors pre-donation, no significant difference was found in factor V Leiden, Cardiolipin G, Cardiolipin M, Protein S, Protein C activity, Lupus anticoagulant between the two groups (p³0.05), and all patients were considered to have normal coagulation profile. The incidence of donor VTE was significantly higher among liver donors (12%) versus no VTE in kidney donors (p=0.001). Higher incidence of PE was noted in living donor liver (4.8%) compared to living donor kidney patients (0%), with P-value approaching significance (p= 0.055).
This study demonstrates, live liver donors compared to kidney donors are at significantly higher risk of developing VTE and PE during the postoperative period, requiring a more robust VTE prophylaxis.

P-209

Pure laparoscopic versus conventional open living donor right hepatectomy using a propensity score matched analysis: challenge to 0% of complication

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Because donor hepatectomy is not a surgical procedure under pathological conditions, it is important to consider the quality of life such as postoperative pain or cosmetic effect. Therefore, laparoscopic donor hepatectomies has been attracting attention recently and is being performed gradually in various centers. The aim of this study was to compare the result of pure laparoscopic living donor right hepatectomy (LLDRH) and conventional open living donor right hepatectomy (OLDRH) to evaluate the safety and efficacy of LLDRH. From November 2014 to October 2017, total of 38 cases of LLDRH and 907 cases of OLDRH were performed. To minimize selection bias, 1:1propensity score (PS) matching was performed between the LLDRH and OLDRH cohorts. After PS matching, finally 36 patients were included in each group. The operative time was significantly longer in LLDRH (372.47 ± 53.06vs. 313.39 ± 47.79 min, p=0.000); however, the estimated blood loss was significantly much less in LLDRH (175.56 ± 47.24 mL vs. 283.89 ± 53.47 mL, p=0.000), and the postoperative hospital stay was also shorter in the LLDRH (8.58 ± 1.95 vs. 10.17 ± 1.40 days, p=0.000). Our study showed that LLDRH can be safely performed by a well-experienced surgeon in donors selected using strict indications.

P-210

Role of serum levels of intraoperative brain natriuretic peptide for predicting acute kidney injury in living donor liver transplantation

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Background: Patients with end-stage liver disease frequently experience acute kidney injury (AKI) after living donor liver transplantation (LDLT). Serum levels of brain natriuretic peptide (BNP) have increasingly been accepted as a predictor of AKI. This study investigated the predictive role of intraoperative BNP levels in the early development of AKI after LDLT.
Patients and methods: Adult patients (≥19 years old) who had undergone elective LDLT from January 2011 to December 2017 were classified into the non-AKI and AKI groups according to the Kidney Disease: Improving Global Outcomes criteria. Serum levels of BNP were measured three times in the preanhepatic, anhepatic, and neohepatic phases. Perioperative data in recipients and donors were analyzed retrospectively.
Results: Sixty-one patients (22.4%) suffered from AKI immediately after LDLT. Severity according to AKI stage was as follows: 28 patients in stage 1 (10.3%), 18 patients in stage 2 (6.6%), and 15 patients in stage 3 (5.5%). In the neohepatic phase, both BNP levels and proportions of patients with high BNP levels (≥100 pg/mL) were higher in the AKI group than in the non-AKI group. Only BNP levels in the non-AKI and AKI stage 1 groups significantly decreased from the preanhepatic phase to the neohepatic phase; those in AKI stages 2 and 3 groups did not. In particular, BNP levels of all AKI stage 3 patients increased to more than 100 pg/mL, and the proportion of patients with high levels also increased significantly through the surgical phases in the AKI stage 3 group. In multivariate analyses, BNP levels in the neohepatic phase were significantly associated with early development of AKI after LDLT, as well as the total amount of packed red blood cells in transfusions and total duration of graft ischemia.
Conclusions: Monitoring serum levels of BNP is useful for predicting the early development of AKI after LDLT.

P-211

Laparoscopic-hand assisted living donor right hepatectomy: 19 cases at a single center in USA

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Background: One of the major limitations of living-donor liver donation is the associated morbidity of the procedure. Right-laparoscopic liver resection has been successfully done by very few centers. Here we described our first 19 cases of total hand-assisted laparoscopic right hepatectomy for adult liver transplantation.
Methods: We retrospectively reviewed the medical records of all laparoscopic right lobe living donor liver resections performed at UMass Memorial Medical Center between 10/25/2016 and 11/30/2018. A total of 19 living donors underwent hand-assisted right hepatectomy for adult LDLT. A hand gelport was placed on the right subcostal incision and four laparoscopic ports were introduced. The operations were done laparoscopically with hand assistance until removal of graft. Parenchymal division was performed after delineation of the ischemic line with indocyanine green (ICG) under Spy scope system visualization. Division was performed using CUSA, bipolar coagulation, clips, and endovascular stapler device. A real-time near infra-red ICG fluorescent cholangiography and an intra-op traditional cholangiography were performed to identify the bifurcation and to cut the right hepatic duct. The right liver graft was removed through the 10-cm right subcostal incision (fig. 2).
Results: The median age of donors was 46 years, median graft vs recipient weight ratio was 1.0. The median estimated blood loss was 500ml (mean 512ml). No blood products were given except in two cases. The postoperative course was uneventful in all cases except two because of bile leak. The donors were discharged at median postoperative day 8. The donor liver function tests returned close to baseline within a week post donation. There was no graft loss and no delayed graft function.
Conclusions: Hand-assisted laparoscopic living donor right hepatectomy can be safely performed. This technique may allow early discharge and recovery and has the potential to increase living donation.

P-212

Guidance for optimal port system in pure 3D laparoscopic donor right hepatectomy

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Introduction: The position of the port is important in laparoscopic hepatectomy. The method of choosing the proper port location for will be the first step needed for those who initiate laparoscopic hepatectomy. However, the direction of the surgical plane is diverse and the positions per person are slightly different, It is necessary to standardize of port location and to make the appropriate guidelines. Standardization is not easy. Pure 3d Laparoscopic donor Rt. hemihepatectomy is more standardized procedure than other laparoscopic liver resection.
Method: From December 2015 to December 2017. 158 donors were underwent pure 3d laparoscopic Rt. hemihepatectomy. We described advantage and disadvantage depending on the role and location of each port through the experience of surgery in the past year.

Results: Our institute is the only center in the world that has performed pure laparoscopic donor surgery over 100 cases. Making good guidelines provides the experience of an experienced surgeon to initiate laparoscopic surgery and is very important for proper training. It is not appropriate to describe fixed anatomical landmark like a mid-clavicular line or below a few centimeters from the rib. It is necessary to determine the position of the port step by step after confirming that role of each port and 1st assistant in the surgical procedure and role of the hand of the surgeon are taken into consideration.
Conclusion: Making an optimal port system for pure 3D laparoscopic donor Rt. hemihepatectomy is the first step. By sharing our experience, we believe that it will be useful for the center to enforce future pure laparoscopic donor Rt. hemihepatectomy.

P-213

Factors predicting cholestasis in post right lobe donor hepatectomy in the era of standardized donor selection protocols - analysis of 340 donors over 19 months

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Introduction: Despite over 10000 LDLTs completed worldwide the Right lobe donation continues to carry high risk donation status. Of all the reported donor mortalities post-operative liver failure secondary to small remnant is still the highest. Hence we analyzed the factors which leads to post donor hepatectomy cholestasis.
Materials and methods: Retrospective analysis of 340 donors during the time period of 06-02-2017 to 12-09-2018 was done. Our donor selection and operative protocols have been highly standardized with zero donor mortality in 2800 donor hepatectomies over a period of 11 years. Data analysis was done based on two cut off values of Total bilirubin (TB) one based on the median of Peak bilirubin(PB) of the study cohort and another based on 5 mg % which is universally accepted as the cut off for defining post-operative liver failure and small for size syndrome.
Results: On analysis 2.3mg % was found to be the median PB. With 2.3 mg% cut off Day -1 TB, Day-5 TB, POD to normal TB, Peak INR, % of liver remnant were statistically significant @ P< 0.05. On analysis with 5.0 mg % cut off Male gender, BMI, Blood Group-O, Area of middle hepatic vein congestion, Day -3 INR, peak INR, Day -1 TB, Day-5 TB, POD to Normal TB and Hospital Stay were statistically significant @ P < 0.05.
Conclusion: High risk factors for post donor hepatectomy choestasis includes Males, High BMI, Blood Group "O" and high middle hepatic vein congestion area. Peak INR and POD -3 INR were significantly higher in this group. They tend to have significantly higher serum bilirubin on POD-1, POD-3 and Peak Bilirubin along with prolonged hospital stay. On multivariate analysis male donors alone tend to be at high risk.

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Series of totally robotic living donor hepatectomy

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Introduction: Robotic surgery is emerging as a surgical technique to enable resection of the liver using minimally invasive techniques; however, very few living donor liver transplantation centers have reported their experience with totally robotic donor hepatectomy.
Methods: This is a retrospective review of our initial series of robotic donor hepatectomy focusing on operative feasibility and early post-operative outcomes.
Results: From June to September 2018, our living donor liver transplantation program performed our first 4 totally robotic donor hepatectomy operations. There were 3 female and 1 male donor (average age 33). We performed 2 robotic right hepatectomy (RH) and 2 robotic left lateral segmentectomy (LLS) for live donation. The recipients were all relatives; 2 adults (primary biliary cirrhosis and primary sclerosing cholangitis), and 2 children (alpha-1-antitrypsin deficiency and biliary atresia). Average estimated graft weight was 903g (RH) and 220g (LLS). Average GBWR was 1.01 (adult recipients) and 2.04 (pediatric recipients). Average procedure time was 558mins (RH) and 424mins (LLS) while transection time was 228mins (RH) and 150mins (LLS) . All grafts were extracted via Pfannenstiel incisions. It took an average of 11.75 minutes from cross-clamp to flush. Estimated blood loss was 175mls (RH) and 150mls (LLS). Conversion rate was zero. Average highest postoperative bilirubin was 2.4mg/dL (RH) and 1.3mg/dL (LLS). INR did not rise above 1.6 for any donor. One LLS donor had a bile leak which resolved after 4 days; there were no other 90-day post-operative complications. Average length of hospital stay was 5.5 days. There was zero incidence of small for size syndrome, early vascular or biliary complications in the recipients. All donors reported excellent patient satisfaction with the surgery and post-operative course.
Conclusions: Totally robotic donor hepatectomy appears feasible for selected patients in centers with large experience in living donor liver transplantation and complex robotic hepatobiliary surgery.

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Learning curve of laparoscopic living donor right hepatectomy: review of a single surgeon's 96 laparoscopic cases

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Purpose: This study is designed to evaluate the feasibility of laparoscopic living donor right hepatectomy and analyze the factors related to overcoming the learning curve.
Methods: Data of living donors who underwent right hepatectomy during the period of 2014 to 2018 by a single surgeon at Samsung Medical Center were reviewed. Comparisons regarding the anatomical characteristics, operation, postoperative recovery were performed between open and laparoscopy group. Surgical videos of laparoscopic living donor right hepatectomy were reviewed and times spent during each procedure were calculated. Linear regression model was used for analyzing whether each procedure showed linear decrease in time along with increase in cases.
Results: During the period, 96 donors and 96 donors underwent open and laparoscopic living donor right hepatectomy. There was no difference in anatomical variations except for bile duct type. (54.2% vs 68.8% of type I bile duct in open and laparoscopy, P=0.038) Mean operation time was shorter in the laparoscopy group. (301.3±63.3 vs. 254.9±43.0 minutes, P< 0.001) Median estimated blood loss was smaller (300 vs. 200 mL, P< 0.001) and median hospital stay was shorter in the laparoscopy group. (10 vs. 8 days, P< 0.001). There was no difference in complication rate (24.0% in open vs. 15.6% in laparoscopy, P=0.147) and severity of complications. (P=0.342) Total operation time of laparoscopy showed linear decrease along with increase in laparoscopic cases. (R^2=0.374, β=0.945, P=0.001) and it significantly decreased between the second and third quartile of laparoscopic cases (276.5±41.7 to 234.5±32.3, P=0.001). Inflow control and ischemic line marking (R^2=0.146,β=-3.9,P< 0.001), transection above hilum (R^2=0.207,β=-16.5,P< 0.001), total parenchymal transection time (R^2=0.242,β=-23.5,P< 0.001) and Pfannenstiel incision (R^2=0.148,β=-3.0,P=0.001) showed the most significant decrease in time.
Conclusion: Laparoscopic living donor right hepatectomy was feasible with comparable safety to open surgery and nearly 50 cases are required for decreasing operation time.

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Anatomy based biliary reconstruction technique during right lobe LDLT with multiple bile ducts

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Background: Biliary complications are reported in 11-40% of adult right lobe living donor liver transplants(ARLLDLT), incidence being higher with multiple graft ducts.
Method: We reviewed the technique and outcomesof biliary reconstruction in ARLLDLT's with ≥2 graft ducts. ABO incompatible, retransplants, and primary sclerosing cholangitis recipients were excluded. For 2 ducts on the same axis< 5 mm apart, we preferred single anastomosis to recipient common bile duct(r-CBD), whereas for ≥2 ducts wide apart or on separate axis, 2 separate anastomoses were done to a combination of r-CBD, r-RHD, r-LHD, r-cystic duct(CD) or Roux -en -Y hepaticojejunostomy(RYHJ).
Results: Multiple ducts were present in 810 (53%) amongst 1536 ARLLDLTs from 2011-17. **Single anastomosis**(2D-1A or3D-1A)was performed in 436(54%), of which 405 had 2 graft ducts, and 31 had ≥3. r-CBD was used in 413(95%) and RYHJ in 23(5%). **Multiple anastomoses**(≥2) were performed in 374 (46.2%); 285 had 2, 85 had 3, and 4 had 4 ducts. The type of anastomoses were: 2 graft ducts, 2 anastomoses(2D-2A); 285(76%); 3D-2A;70(19%), 3D-3A;15(4%), and 4D-2A;4(1%). For multiple anastomoses, r-RHD and r-LHD were used in 283, r-CBD and r-cystic duct in 64, rCBD+RYHJ in 10, and only RYHJ in 17. At a median follow up of 36 months, biliary complication rate was **16.9%**, higher than overall series(**13.5%**;p=0.03). Of 28 leaks(3.45%), 20 were re-explored, 9 converted to RYHJ. Of 109 strictures(13.45%), 87% were managed by ERCP, 13 with ERCP+PTBD. At last follow up, 93% were stent free, with remodelled strictures. Stricture rate was higher with 2D-1A compared to 2D-2A(16% vs.10%;p=0.01). Stricture rate was higher although statistically insignificant, when r-CD was used for one of the two(2D-2A) anastomoses(23% vs 15.9%;p=0.14). The 5-yr OS in this group with multiple ducts was similar to overall cohort(90.4% vs.89%,p=0.293).
Conclusion: Judicious selection of reconstruction method can help obtain good outcomes in RLLDLT with multiple graft hepatic ducts.

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Impact of frailty in cirrhotics awaiting liver transplantation in LDLT setting: preliminary experience

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Background: Frailty is a validated construct that objectively measures progressive decline in functional reserve and is an important determinant of clinical outcomes. In this pilot study, we aimed to determine the degree of frailty and its impact in patients with cirrhosis awaiting Liver Transplantation (LT).
Methods: Consecutive adult cirrhotics from March 2018 to July 2018 were included and followed for at least 3 months. Frailty assessment was done at enrollment using Fried Frailty Instrument and other Frailty indices (Table 1).
Results: Of 99 adults included in the study (88 males, 11 females; age 50.7±11.3 years); 13 belonged to Child-Turcotte-Pugh (CTP) class A, 51 to class B and 35 to class C. The median MELD Na score was 17 (IQR 12-23). A total of 77 (77.8%) patients were classified as frail and 22 as non-frail by using Fried Frailty Instrument. There was significant difference in various frailty measures across these two groups (Table 1). Frail patients had higher number of unplanned hospitalisations (1.4±0.13 Vs 0.73±1.13, p=0.03). Over a median follow up of 114 days, there were 192 admission events, with sepsis (28.6%) being the most common indication for admission followed by admission for paracentesis (15.6%). Thirty-six patients (30 frail; 6 non-frail) underwent LDLT [median time from enrollment to LT 16 (IQR 2-26) days]. Frail patients had longer hospitalisation during LT (21.4±14.4 Vs 14.1±2.3 days, p=0.014). Amongst the frailty indices, LFI was independent predictor of overall mortality (AUROC - 0.737) and grip strength, LFI & MELD Na were independent predictors of infection (AUROC - 0.695, 0.682 and 0.673 respectively).
Conclusion: Frailty adversely impacts course of cirrhotics awaiting LT. Frail patients require frequent hospitalisations and longer hospital stay in peri-transplant period as compared to non-frail patients.

Table 1

Characteristic	Total (n=99)	Frail (n=77)	Non-frail (n=22)	p value
Mean age - yr	50.7 ± 11.3	50.43 ± 10.9	51.64 ± 12.7	0.662
Male sex – no. (%)	88 (88.9)	68 (68.7)	20 (20.2)	0.732
BMI	25.03 ± 2.9	24.05 ± 6.4	25.3 ± 8	0.416
Etiology of Liver Disease – no. (%)				0.951
Alcohol	37 (37.4)	31	6	
NASH	25 (25.3)	19	6	
HCV	8 (8.1)	6	2	
HBV	13 (13.1)	10	3	
AIH	4 (4)	3	1	
PBC	3 (3)	2	1	
Cryptogenic	7 (7.1)	5	2	
Others	2 (2)	1	1	
Mean CTP	8.76 ± 1.9	8.87 ± 1.8	8.3 ± 2	0.271
Median MELD Na Score	17 (12-23)	18 (12-26)	14 (10-21.25)	0.109
LT waitlisted	50 (50.5)	41	9	0.307
Liver Transplantation	36 (36.4)	30	6	0.499
Death	9 (9.1)	8	1	0.679
Frailty Indices				
Mean SPPB	7.3 ± 2.4	6.9 ± 2.4	8.9 ± 1.5	<0.001
Mean IADL	6.9 ± 1.7	6.7 ± 1.9	7.7 ± 0.5	0.020
Mean KPS	75.9 ± 11.7	73.2 ± 11.7	85.4 ± 5	<0.001
Mean ECOG	1.6 ± 0.7	1.78 ± 0.68	1 ± 0.6	<0.001
Mean LFI	4.85 ± 0.67	4.98 ± 0.68	4.4 ± 0.37	<0.001

** Abbreviations: Short Physical Performance Battery (SPPB), Instrumental Activities of Daily Living Scale (IADL), Karnofsky's performance status (KPS), Eastern Cooperative Oncology Group (ECOG) performance status and Liver Frailty Index (LFI).*

[Clinical characteristics and frailty measures at baseline]

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Altruistic liver donation in the Netherlands

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Background: Living donor liver transplantation (LDLT) in the pediatric program was started in our centre in 2004 because of a growing shortage of suitable postmortal donor liver grafts. Altruistic liver donation is controversial and in some countries not allowed. In 2010 the first potential altruistic donor was screened. It took six months to agree on donation, mainly because of ethical concerns, but after extensive screening no contraindications for donation were found. The liver was accepted for a child who did not have a parent suitable for donation. This procedure was succesfully performed anonymously. Despite preoperative concerns we also saw an advantage for the parents who repeatedly expressed their gratitude not only for this generous gift by the donor, but also for the fact that they could both take care of their sick child after transplantation. This study aims to compare outcome between altruistic non-directed and related living liver donation.

Methods: Donor and recipient parameters were collected from our prospectively maintained living donor and recipient database.
Results: So far, 60 LDLT procedures were performed. Six procedures (10%) were performed in altruistic donors. Median follow-up was 267 days. Altruistic donors were significantly older than related donors (50 vs 34 yrs old). Previously 5 out of 6 altruistic donors already donated a kidney anonymously, but the liver donation did not have impact on their kidney function. Complication rate was statistically similar in both altruistic (0 gr 3 Clavien Dindo) and related donors (4%). Recipient outcome was also similar in both groups.
Conclusion: This study shows that the donor outcome after altruistic non-directed left lateral liver donation is good without increased risks in donor or recipient, despite the fact that the donor is older and has a more extensive medical history.

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Living donor liver transplant from an HIV-positive mother to her HIV-negative child - opening up new therapeutic options

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Objective: Transplant a liver from an HIV positive mother to her HIV negative child in order to save the child's life.
Design: A unique case of living donor liver transplantation from an HIV positive mother to her HIV negative child in South Africa (SA). Two aspects of this case are groundbreaking.
Firstly, it involves living donation by someone who is HIV positive and secondly it involves controlled transplant of an organ from an HIV positive donor into an HIV negative recipient, with the potential to prevent infection in the recipient.
Methods: Standard surgical procedure for living donor liver transplantation at our centre was followed. HIV-prophylaxis was administered pre-operatively. Extensive, ultrasensitive HIV testing, over and above standard diagnostic assays, was undertaken to investigate recipient serostatus and is ongoing.
Results: Both mother and child are well, over one year post-transplantation. HIV seroconversion in our recipient was detected with serological testing at day 43 posttransplant.
However, a decline in HIV antibody titres approaching undetectable levels is now being observed. No plasma, or cell-associated HIV-1 DNA has been detected at any time-point since transplant
Conclusions: This case potentially opens up a new living liver donor pool which might have clinical relevance in countries where there is a high burden of HIV and a limited number of deceased donor organs or limited access to transplantation. However, our recipient's HIV status is equivocal at present and additional investigation regarding seroconversion events in this unique profile is ongoing.

P-220

Single orifice venous outflow reconstruction in living donor liver transplantation using right lobe grafts: feasibility and outcomes compared to conventional dual outflow technique

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Background: In LDLT using right lobe grafts, the dual orifice outflow technique used commonly is time consuming and may lead onto compromise of the outflow as the graft regenerates.
Method: All patients undergoing LDLT using right lobe grafts between July 2016 and August 2018 were categorized as Group A (medial wall of RHV and half circumference of Neo-MHV were anastomosed to create a single outflow).The outcomes were compared with Group B (dual outflow, June 2011 to June 2016).
Results: Out of 310 patients, 203 patients were in Group A which were compared with 107 patients in Group B. Recipient and donor baseline characteristics were comparable. In Group A, IVC cross clamping was needed only in 3/203(1.4%) patients whereas 100/107(93.4%) patients were cross clamped in group B($p < 0.001$). Group A had lesser WIT (26.9 mns vs 45.7 mns, $P < 0.001$), surgery duration (680 mns vs 861 mns, $p = 0.01$), less transamnitis (peak AST; 239 vs 335, $p= 0.05$, peak ALT; 230 mn vs 385 mn , $p= 0.03$) and less serum creatinine levels(1.03 vs 1.16, $p = 0.05$). However; blood loss, INR, ascites amount,graft dysfunction (29.5% vs 34.5 %, $p= 0.34$), neo-MHV patency at 3 months (96.1% vs 94.4 %, $p= 0.06$), hospital stay (23.9 vs 27.4 days, $p = 0.11$) and grade III/IV complications (35.6% vs 37.8%, $p= 0.3$) were comparable.The in-hospital survival rates 94.1% vs 92.4% ($p= 0.53$) and overall survival rate was not significant (87.8 % vs 79.9%, $p = 0.30$).
Conclusion: The single orifice outflow technique is simpler and feasible with > 99 % completion rate. It has significant advantages over the dual outflow technique in terms of much lesser need of IVC crossclamp, lesser WIT, postoperative transamnitis and serum creatinine levels. There is no difference between overall complications and survival rates

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Post-operative opioid requirements in living liver donors

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Introduction: Approximately 6% of opioid-naïve surgical patients develop opioid dependence post-operatively. The CDC found that patients prescribed >50 morphine equivalents (MEQ) per day have twice the risk of opioid overdose compared with patients prescribed < 20 MEQ/day. Living donors undergo surgery with no medical indication, and nearly all donors are discharged with opioid prescriptions, placing them at risk for dependence. This study examined opioid requirements in living liver donors at a single, high volume transplant center.
Methods: We conducted a retrospective review of living liver donors at our institution between 2012-2018. We perform left donor hepatectomies via a vertical midline incision and right donor hepatectomies via a bilateral subcostal incision. Left lobe donors typically receive epidural analgesia.
Results: 156 donors were included. Liver donors were 53.8% female, donated their right lobe (53%), and had a median age of 46 years. Median hospital stay was five days. On the day prior to discharge, patients required a median of 40 MEQ (IQR 20-61). Patients were discharged with a median of 375 MEQ (IQR 300-500) for 7 days, resulting in a median of 50 MEQ/day (IQR 45-90). 21% of patients required opioid refills between 60-90 days post-discharge.Compared with right lobe donors, left lobe donors required more MEQs on the day of discharge (44.4 IQR 25-83 vs. 27.5 IQR 15-50, p=0.002) and were discharged with more total MEQs (375 IQR 300-500 vs. 300 IQR 262-500), p=0.01). There was no difference in refills for right versus left lobe donors.
Conclusion: Liver donors receive a large number of opioids after donation. In addition, one in five donors requires opioid refills as far out as 90 days after discharge. We are implementing new strategies to protect this population from opioid dependence, including aggressive multimodal pain control, locoregional blocks, and prescriber education.

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Considerations for use of domino cross-auxiliary liver transplantation in metabolic liver diseases: a review of case studies

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Background: Domino cross-auxiliary liver transplantation represents an innovative procedure for the treatment of selective non-cirrhotic metabolic liver diseases.
Methods: The treatment strategies and experiences in domino cross-auxiliary liver transplantations, including the world's first case in 2013, are reviewed.
Results: The 6 patients with non-cirrhotic metabolic liver diseases receiving domino cross-auxiliary liver transplantation included: FAP (Case 1), OTCD (Cases 3,5,6) and Wilson's disease (Cases 2,4). Five patients achieved a favorable postoperative survival outcome and quality of life, while Case 2 died of multiple organ failure at 3 months post liver transplant (LT). Case 1 experienced an imbalance in portal vein blood perfusion between the two domino livers at 6 months after LT, but improved after interventional radiology treatment. Cases 3 and 4 showed domino grafts associated with hypercholesterolemia after LT, but total cholesterol levels decreased to normal ranges after dietary adjustment. Case 5 showed an effortless recovery after surgery with no complications during the follow-up period. Case 6 experienced an occult domino liver graft rejection, which resulted in graft dysfunction and eventual recurrence of the primary metabolic liver disease (OTCD). A liver re-transplantation may be required for this patient.
Conclusions: Domino Cross-auxiliary liver transplantation is an innovative and effective treatment for metabolic liver diseases in the patients who are strictly selected as based upon pathophysiological and genetic criteria. Special attention to rejection monitoring and imbalance regeneration are required with this procedure.

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Clinical outcomes of living versus deceased donor liver transplantation for primary sclerosing cholangitis: a multicenter 15 year experience

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Background: MELD-based allocation is known to reduce access to deceased donor liver transplantation (DDLT) for patients with primary sclerosing cholangitis (PSC). Living donor liver transplantation(LDLT) provides improved access and shorter waiting time for such patients. There is limited data on long term outcomes of PSC patients who underwent LDLT compared to DDLT.
Methods: 441 patients from 3 academic centers underwent LT for PSC between 1/1/2002 and 12/31/2016. Children (< 18 yr), cholangiocarcinoma or hepatocellular carcinoma, and those with prior LT were excluded (153 patients). Kaplan-Meier survival analysis and log-rank comparisons based on the type of organ donation were performed.
Results: Of the 288 patients, 21.9% (63/288) underwent LDLT. Overall, LDLT patients were younger (41.6±14.4 vs. 50.9±13.3 yr; p=0.001 [95% CI 5.6-13.1]), and had lower MELD at transplant (15.9±5.2 vs. 21.7±7.0; p=0.001 [95% CI 3.9-7.7]). The donor age was lower in LDLT (39.0±11.0 vs. 48.3±21.3 yr; p=0.001 [95% CI 3.8-14.8]. Recipient sex and BMI were not different (60.3% vs. 65.8% male, and 24.9±4.7 vs. 26.2±5.6, respectively).
Overall survival at 3, 5 and 10 years were 90.5%, 90.5% and 86% after LDLT, and 91.6%, 89.5% and 80% after DDLT. Graft survival at 3, 5 and 10 years were 88.8%, 88.8% and 79.9% after LDLT, and 88.5%, 85.8% and 71.6% after DDLT. Kaplan-Meier patient survival distributions were not statistically different among those who received LDLT compared to those who received DDLT (log-rank p=0.804). Similarly, graft survival distributions were not statistically different (log-rank p=0.373) (Figure).
Conclusions: Patient and graft survival rates are high among PSC patients undergoing LDLT and are comparable to those of DDLT. This study demonstrates excellent long term outcomes after 10 years among LDLT recipients for PSC.

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Temporal improvements in graft survival following living donor liver transplant for patients with NASH in the United States

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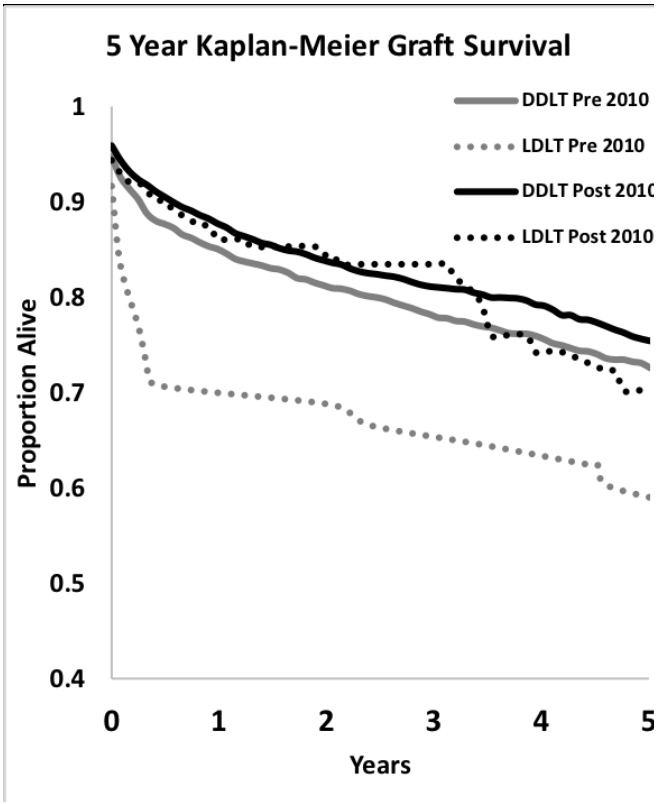
Background: The number of NASH patients listed for deceased donor liver transplantation (DDLT) continues to grow in the United States. As such living donor liver transplant (LDLT) remains an attractive option for such patients and has been demonstrated in small case series to be a safe therapeutic option. However, it is unclear whether improvements in technique/management of LDLT over the past 20 years have resulted in improvements in outcomes for these patients.
Methods: A retrospective analysis of the OPTN/UNOS database was performed to include recipients of a LDLT and DDLT with NASH as their primary liver diagnosis. Exclusion criteria included age of recipient less than 18 years. Recipients were stratified by time of transplant into two Eras (Pre and Post 2010). Graft and patient survival were analyzed utilizing Cox proportional hazards modeling
Results: In the Pre-2010 Era, 48 LDLT were performed and 1,466 DDLT were performed for NASH; LDLT patient had statistically similar five year patient survival (69% [LDLT] vs. 75% [DDLT], P=0.56), but inferior graft survival (59% [LDLT] vs. 73% [DDLT], P=0.009) compared with DDLT. In the Post-2010 Era, 241 LDLT were performed and 12,719 DDLT were performed; LDLT patient had similar five year patient (75% [LDLT] VS. 77% [DDLT], P=0.61) and graft survival (70% [LDLT] VS. 75% [DDLT], P=0.92) compared with DDLT.
Conclusions: Graft survival following LDLT for NASH has significantly improved in the United States over the past 20 years, and are now comparable to outcomes following DDLT. Further utilization of living donor grafts should be encouraged for patients with NASH.



[5 Year Kaplan-Meier Graft Survival]

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Spectrum and predictors of sepsis in patients undergoing living donor liver transplant.

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Background: Sepsis is a leading cause of morbidity and mortality in patients undergoing living donor liver transplant (LDLT).
Aim: To describe the spectrum and outcome of sepsis in patients undergoing elective LDLT.
Methods: Prospectively collected data for consecutive patients who underwent LDLT at our institute from July 2012 to August 2018. Sepsis was defined as new onset bacteremia or presence of SIRS with infection post transplant. Severe sepsis included the cohort of patients with organ dysfunction or need for vasopressor support to maintain MAP of 70 mm Hg. All patients were culture negative prior to transplant. The spectrum, outcome and predictors for mortality were calculated.
Results: A total of 342 adult patients underwent liver transplant for CLD/ACLF of which 301(93.4%) were males with a mean age of 46.8 years (18-71), a median MELD of 25 and a median GRWR of 0.96. The most common etiologies indicating transplant were ethanol (n=136, 39%), cryptogenic (n=58, 16.9%) and NASH (n=37, 10.8%). A total of 128 patients (37.4%) developed sepsis during their hospital admission, with 69 of 128 (53.9%) developing severe sepsis requiring vasopressor support. The median day of developing sepsis was 9. The incidence of bacteremia was 75/342 (21.9%). 15/128(11.7%) patients developed fungal sepsis with culture positivity in blood or respiratory secretions. 19 of 128 (14.8%) of patients with sepsis also had an episode of clinically significant acute cellular rejection requiring methylprednisolone pulsing during the peri-operative period.
An absolute graft weight of less than 600 gm (p=0.014), re-exploration(p< 0.001) and post operative dialysis (p< 0.001) were independent predictors of sepsis (p=0.014). The overall 90 day survival was 88.4%; 93.8% in the non septic group, 80.5% in the septic group and 65.8% in those with severe sepsis.
Conclusion: Sepsis is the leading cause for mortality in patients undergoing living donor liver transplant.

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Totally laparoscopic and conventional open living donor right hepatectomy in adult-to-adult living donor liver transplantation: a comparative study of outcomes

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Although laparoscopic liver resection has progressively developed with increased surgical experience and the improvement of laparoscopes and specialized instruments, Only a limited number of centers have performed laparoscopic living donor hepatectomy to date because of concerns about donor safety, graft outcome and the need for expertise in both laparoscopic liver surgery and living donor liver transplantation(LDLT). For these reason, a totally laparoscopic living donor right hepatectomy (LDRH) technique has not been investigated for efficacy and feasibility. We describe the experiences and outcomes associated with LDRH in adult-to-adult LDLT to assess the safety of the totally laparoscopic technique in donors.
Between December 2014 and October 2018, we performed 97 cases of living donor right hepatectomy. Among them, 50 donors underwent totally laparoscopic living donor right hepatectomy and 47 donors

underwent conventional open living donor right hepatectomy. We retrospectively reviewed the medical records to ascertain donor safety and the reproducibility of LDRH; intra-operative and post-operative results including complications were demonstrated after performing LDRH.
The total operation time was longer (367.0±74.3 vs 323.5±62.5; P=.002) and the warm ischemic time was also longer(9.2±4.6 vs 1.8±1.6;P< .002) in LDRH group. However, the length of postoperative hospital stay was similar in both groups and no donors in LDRH group required blood transfusion, conversion to open surgery, or reoperation. The postoperative mortality was nil and postoperative complications were identified in two donors. One had fluid collection in the supra-pubic incision site for graft retrieval and the second had a minor bile leakage from the cutting edge of the right hepatic duct stump. All the liver function tests returned to normal ranges within one month.
In conclusion, our study reveals LDRH seems to be a safe and feasible procedure with acceptable outcomes. However, LDRH can be initially attempted after attaining sufficient experience in laparoscopic hepatectomy and LDLT techniques.

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Biliary complications after donor hepatectomy in living donor liver transplantation: analysis of 855 living liver donors at a single center

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Background: Biliary complication is one of the major donor complications after donor hepatectomy in living donor liver transplantation (LDLT). We evaluated risk factors and investigated the long-term outcomes of biliary complications in LDLT donors.
Methods: From December 2011 to September 2018, 855 consecutive donors who underwent donor hepatectomy at our center were reviewed. Biliary complications were recorded and stratified as per Clavien-Dindo classification.
Results: The majority of the graft types were right hemiliver without the middle hepatic vein (91.9%). Biliary complications occurred in 37 donors (3.2%): bile leakage in 33, intraoperative bile duct injury in 2, and biliary stricture in 2. The most common reasons for biliary complications were left lateral sectionectomy, multiple right lobe duct orifices, and missed caudate ducts. Twenty-one (56.7%) patients recovered with routine conservative treatment. Additional computed tomography and/or ultrasound-guided percutaneous drainage was required in 8 patients and surgical re-exploration was done in 2 patients. Six (0.7%) donors had a grade III biliary complication (4 leakage and 2 strictures) requiring endoscopic retrograde cholangiography with/without papillotomy and stenting. All inserted stents were successfully retrieved after a median 204 days (range, 142 to 302) and there were no recurrences of stricture or leakages during a median follow-up of 4.8 years.
Conclusion: Left hepatectomy and multiple right lobe ducts are the most common reasons for biliary complications after donor hepatectomy. More than 50% of donor biliary complications, especially biliary leakage recovered with routine medical management. None of the donor had a long term sequelae. With careful donor selection and a standardized surgical technique, biliary complications can be minimized.

P-228

Randomized trial between Histidine-Tryptophan-Ketoglutarate [HTK] and Institute of George Lopez (IGL-1] perfusion solutions in Living Donor Liver Transplantation [LDLT]

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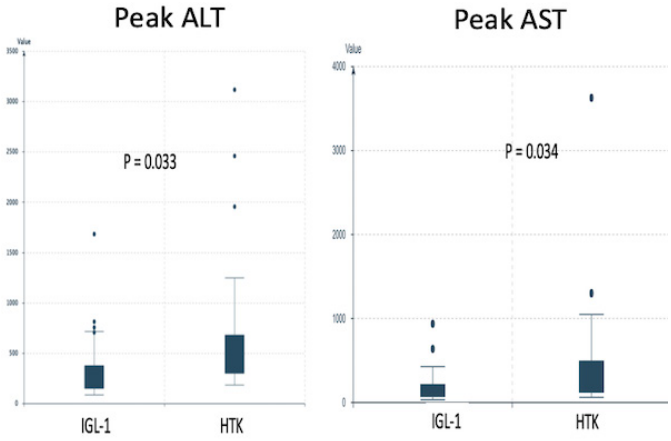
Aim: To compare early graft dysfunction, outcome and graft survival in recipients of Living donor liver grafts perfused with either HTK or IGL-1 solution on the bench.
Materials and methods: Over 9 months, 40 (32M:8 F) adult patients undergoing living donor liver transplantation (after excluding ABO incompatible transplants(n=3), pediatric liver transplants(n=5) and multivisceral transplants(n=1)), in Amrita Institute, were randomized into two groups by computerized block randomisation. Early graft dysfunction [EAD defined by Olthoff criteria -bilirubin > or =10mg/dL on day 7, INR >or=1.6 on day 7, and alanine or aspartate aminotransferases >2000 IU/L within the first 7 days], peak bilirubin, INR, and transaminases. Incidences of biliary complications, hepatic artery thrombosis [HAT], biopsy proven acute cellular rejections [ACR], 90-day mortality and graft survival within the first 6 months were compared between the two groups. Pre-transection and post reperfusion liver biopsies were taken.
Results: Both groups were matched in terms of base line characters and intraoperative parameters. There was no statistically significant difference in incidence of EAD between the two groups [IGL-1 - 3(15%) vs HTK - 5(25%),]. The peak transaminase level in the first week, was significantly lower in the IGL group. [peak alanine transaminase (ALT): IGL-1 (median-222; range 73 - 1502) vs HTK (median - 465; range 108 - 3154) p = 0.033, peak aspartate transaminase (AST): IGL-1(median - 105, range 35-986) vs HTK (median - 190, range - 63-3672); p = 0.034].

There was no significant difference between incidences of ACR, HAT, biliary complications, 90-day mortality and graft survival between the two groups.
Conclusions: Recipients of grafts perfused with IGL-1 had lower peak transaminase levels compared to HTK however there was no difference in EAD, biliary complications, rejections, 90-day mortality or graft survival between the two groups.



[transaminases]

P-229

Validating Controlled Attenuation Parameter (CAP) in assessment of hepatic steatosis in living liver donors

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Background: Hepatic steatosis assessment is essential for donor workup in living donor liver transplantation (LDLT). Liver biopsy is the gold standard and despite its invasiveness, there is no consensus on alternative modalities. The Controlled Attenuation Parameter (CAP) quantifies hepatic steatosis and cumulative data are promising though little is known on its utility in LDLT donor workup.
Objective: To assess CAP in quantifying steatosis in donors undergoing workup for LDLT.
Methods: A prospective study conducted in King Faisal Specialist hospital (January 2018 - September 2018). All consecutive potential living donors had Fibroscan/CAP measurements and liver biopsy. The CAP cut-off values range is 180-350 dB/m and graded as S0 (≤218), S1 (218-250), S2 (250-305) and S3 (> 305 dB/m). Steatosis score by liver biopsy was S0< 5%, S1 (5%-33%), S2 (33%-66%) and S3 >66%.
Results: A 100 liver donors were included and their scores were S0 (39 donors), S1 (20), S2 (26) and S3 (15). The liver biopsy score was S0 (72 donors), S1 (16), S2 (6) and S3 (6). CAP exhibited a significant ability to differentiate moderate to severe steatosis (AUC=0.817, 95%CI: 0.727 to 0.887, p< .001). A score of ≥ 2 is selected as the best cut-off value using Youden index. The sensitivity and specificity were 91.7% (95% CI: 61.7% to 99.8) and 65.9% (95% CI: 55.0% to 75.7%). While a score of ≤ 1 strongly excludes the presence of moderate-severe steatosis (NPV=98.3%, 95%CI: 89.8% to 99.7%), a score of ≥2 was poor in confirming the presence of moderate-severe steatosis (PPV= 65.9%; 95%CI: 55.0 to 75.7%).
Conclusion: CAP reliably identifies donors with no or mild steatosis. It is however not a good predictive test for moderate to severe steatosis. LDLT donors with a score > S1 should be considered for liver biopsy.

P-230

What matters and what does not, in an adult receiving a right lobe graft: living donor liver transplant. Outcome from >1500 cases

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Introduction: Living Donor Liver Transplant (LDLT) is a complex surgical procedure with many lacunae in understanding. There are many factors (pre, intra, postoperative) determining the outcome of a patient undergoing LDLT. We want to study the factors affecting the outcome of our biggest cohort of patients, adults receiving a right lobe graft.
Method and material: All patient who underwent primary LDLT between 2008- 2018 (n=1532), with a right lobe graft and aged >18 yrs were included in the study. Among them patient who had hospital stay less than 30 days with no intervention were categorised as smooth recovery patient (SR= 1003), whereas those who required longer than 1 month hospital stay or required intervention (ERCP, PCD) for complication or rexploration were categorised as Delayed recovery patient (DR=273) and those who died post-transplant were categorised as death (Death= 256). Various preoperative and intraoperative parameters were compared between the study groups.
Result: Amongst the preoperative parameters history of jaundice, Hepatorenal Syndrome (HRS) and Spontaneous Bacterial Peritonitis (SBP), MELD score, CTP score, INR, serum bilirubin and creatinine levels were found to have a significant impact on the outcome after LDLT (p< 0.05). History of ascites, Hepatic Encephalopathy

(HE), GI bleed, Age, BMI, albumin were found to have no effect on the outcome (p>0.05). Amongst the intraoperative parameters graft weight and GRWR were found to impact the outcome, whereas Cold Ischemia Time (CIT) and Warm Ischemia Time (WIT) were not.
Conclusions: There are many pre, intra and post operative factors that contribute to the outcome after LDLT in an adult receiving right lobe liver transplant. Optimization of these parameters wherever possible might help us to improve with outcomes after LDLT.

P-231

Impact of body mass index ≥30 on pure laparoscopic donor right hepatectomy

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Background: Recently, pure laparoscopic technique has been increasingly adopted for donor hepatectomy, even for right hepatectomy. Obesity is generally thought to be a risk factor for potential complications and technical difficulties. The application of pure laparoscopic right hepatectomy for obese donors remains controversial. The aim of this study is to investigate the impact of donor obesity, defined as body mass index (BMI) ≥30 and clinical outcomes after pure laparoscopic donor right hepatectomy (PLDRH).
Methods: The records of all living donors who underwent pure laparoscopic donor right hepatectomy (PLDRH) at Seoul National University Hospital between November 2015 and May 2018 were retrospectively reviewed. To evaluate the effect of donor BMI on the outcomes of PLDRH, the donors were divided into two groups; BMI < 30 and BMI ≥30.
Results: There were 7 donors with BMI ≥30. All of these 7 donors were male and they were compared with 65 male donors with BMI < 30 who underwent PLDRH. There were no significant difference in age, estimated remnant volume, estimated graft-to-recipient ratio (GRWR), and preoperative blood tests between the two groups. Graft weight was significantly heavier in BMI ≥30 group than in BMI < 30 (935.7 vs. 775.2 ml; *P*=0.010). However, real GRWR and operative time were similar between the two groups. The lowest hemoglobin (Hb) level was higher (13.4 vs. 12.4 g/dl;P=0.012) and the ΔHb%, calculated as ΔHb% = [(preoperative Hb-postoperative Hb)/preoperative Hb] ×100, was significantly lower in BMI ≥30 group compared with BMI < 30 group. Postoperative complication rate, hospital stay, and readmission rate was similar between the two group.
Conclusion: This study revealed that PLDRH is feasible in donors with BMI ≥30.

P-232

Serum tumor necrosis factor-α is inversely associated with the psoas muscle index in both male and female patients scheduled for living donor liver transplantation

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Introduction: Patients on a waiting list for liver transplantation frequently show core muscle wasting, referred to as sarcopenia, which results in poor prognosis. To date, there has been a lack of research on the association between inflammation mediators, including cytokines, and loss of core muscle mass in cirrhotic patients scheduled for living donor liver transplantation (LDLT).
Patients and methods: Cytokines in serum, such as interleukin (IL)-2, IL-6, IL-10, IL-12, IL-17, interferon-γ, and tumor necrosis factor (TNF)-α, were retrospectively investigated in 234 LDLT patients 1 day before surgery. The psoas muscle area (PMA) was measured using abdominal computed tomography (CT) within 1 month before surgery and used to calculate the psoas muscle index (PMI = PMA/height^2). The study population was classified into two groups according to the interquartile range of PMI: a non-sarcopenia group (>25th quartile) and a sarcopenia group (≤25th quartile) in each sex.
Results: In both sexes, IL-10 and TNF-α levels were significantly higher in the sarcopenia group than the non-sarcopenia group. In a univariate analysis, male patients showed that serum IL-10 and TNF-α were potentially associated with sarcopenia. After a multivariate analysis, serum TNF-α was independently associated with sarcopenia. In female patients, TNF-α was significantly associated with sarcopenia in both univariate and multivariate analyses. Male patients with a PMI ≤ 25th quartile had significantly higher TNF-α levels than those in other quartile ranges, and female patients with a PMI ≤ 25th quartile had a significantly higher TNF-α level than those with a PMI > 75th quartile.
Conclusion: Serum levels of TNF-α are inversely associated with skeletal muscle wasting in both male and female patients scheduled for LDLT.

P-233

Recovery of the Psoas Muscle Index in living donors after a right lobe hepatectomy for liver transplantation: a single-center experience

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Background: The development of sarcopenia leads to adverse postoperative outcomes. However, no study has investigated perioperative loss in core muscle and the correlation between core muscle and residual liver volume in living donors for liver transplantation (LT).
Patients and methods: A total of 457 adult healthy living donors who underwent a right lobe hepatectomy without the middle hepatic vein for elective LT were retrospectively analyzed. Abdominal computed tomography (CT) was regularly performed within 1 month before surgery, and the first week and 3 months after the surgery. The average psoas muscle area (PMA) between lumbar vertebrae 3 and 4 was measured and normalized by height squared (psoas muscle index [PMI] = PMA/height^2). The initial whole liver volume and remnant left lobe volume were measured on CT images.
Results: The study cohort included 279 males (61.1%) and 178 females (38.9%). The preoperative PMIs were 420.9 (360.6-487.0) mm^2/m^2 in males and 280.9 (243.5-318.7) mm^2/m^2 in females. The PMIs in males and females significantly decreased during the first week after surgery, and gradually recovered to preoperative levels during the first 3 months after surgery. Based on the ratio between the remnant left lobe and initial whole liver volume (at least $\geq$ 30%), the increase in remnant left lobe volume was not correlated with the decrease in PMI on postoperative day 7. A postoperative U-shaped recovery in the core muscles was present in both male and female living donors, independent of the remnant liver ratio.
Conclusions: Despite the requirements of partial liver regeneration and surgical wound repair, healthy living donors did not suffer from sustained core muscle loss after surgery.

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Outcomes of portal vein reconstruction with technical modifications in pediatric living donor liver transplantation for biliary atresia

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Background: The native portal vein (PV) in biliary atresia (BA) often becomes sclerotic and technical modifications of PV reconstruction should be applied in some instances. The aim of this study is to evaluate the outcomes of PV complications (PVCs) and analyze risk factors of PVCs in pediatric living donor liver transplantation (LDLT) for BA.
Patients and methods: By the end of 2017, 200 pediatric patients with BA underwent LDLT at our center. Median age at LDLT was 7.0 months, ranging from 4 months to 16.7 years. The types of PV reconstruction were selected, based on the size discrepancy between graft and native PVs, and the extent and severity of sclerosis of native PV. If the native PV became severely sclerotic, vein graft interposition technique was selected (VG-group, n=40). Otherwise, direct anastomosis by using native PV was selected (non-VG group, n=160). Patient demographics, clinical and laboratory data, surgical details, and outcomes were reviewed.
Results: PVCs occurred in 12 cases (6.0%), including 5 cases in VG group and 7 cases in non-VG group. Although majority of the cases were successfully treated by percutaneous transhepatic balloon dilatation, two cases received stent insertion for a short-term recurrence. Four cases were surgically treated after failed radiological treatments. Patient survival rates in the VG group and the non-VG group were 95.0% and 97.5% at 5 years, respectively. Significant risk factors were sclerotic PV, retrograde PV flow, and intraoperative PV thrombosis formation in univariate analysis. Multivariate analysis revealed that sclerotic PV (odds ratio [OR], 4.07; 95% confidence interval [CI], 1.18-14.02; p = 0.026) was an only independent risk factor.
Conclusions: To select appropriate PV reconstruction is crucial to avoid PVCs in pediatric LDLT, especially when native PV reveals sclerosis. Vein graft interposition technique is a feasible option with an acceptable rate of PVCs.

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Optimal timing for introduction of total laparoscopic living donor right hepatectomy: based on the experience of laproscopic hepatectomy

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Background: As total laparoscopic living donor right hepatectomy (TLDRH) should ensure the donor safety, accumulation of experience for the laparoscopic liver resection (LLR) is essential before starting TLDRH. This study was aimed to determine the most appropriate time to start TLDRH based on the experience of the LLR.
Methods: We retrospectively reviewed data from 567 consecutive patients underwent LLR and 78 consecutive patients underwent donor hepatectomy between from 2003 to 2017. The operative outcomes of Laparoscopic major hepatectomy(LMH) were compared between two periods which was based on introduction of TLDRH. (Phase I 2003-2009 vs Phase II 2010-2017). The learning curve of LLR was evaluated using the cumulative sum (CUSUM) method to re-evaluate when was the optimal time to introduce the TLDRH program.
Results: 132 LMH (Phase I: 38 cases, Phase II: 94 cases), and 38 TLDRH were performed. In cases of LMH, the hospital stay (12.63±6.75:9.61±8.20 days, P=0.009) was significantly shortened, and the EBL (1122.89±1460.20: 931.88±1855.85 ml, P=0.024) were significantly decreased in the Phase II. Although TLDRH was introduced after experience of 38 LMH, the learning curve of LMH was achieved after 73 cases in CUSUM analysis. When 73 cases of LMH performed, it was the time when 15 TLDRH were already performed. When comparing the operative outcomes before and after 15 cases of TLDRH. Operation time (min, 578.1±110.65 vs. 422.3±230.6, P=0.024) and hospital stay (days, 10.46±3.45 vs. 9.09±4.63, P=0.23) and EBL (ml, 769.23±523.02 vs 423.23±323.38, P=0.026) were different significantly.
Conclusion: Accumulation of experience of at least 73 cases of LMH is needed to start TLDRH program for the donor's safety in the LT minor centers.

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Assessment of the global practice of living donor liver transplantation: Comparison of U.S. and international programs

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Background: As programs have become more experienced with living donor liver transplantation (LDLT), technical hurdles have been overcome and superior graft and patient survival has been reported. While surgical aspects of LDLT are well established, other parameters regarding acceptable donor and recipient selection criteria are not well defined.
Study Design: The WHO Transplant Observatory was analyzed to determine global prevalence of LDLT. A 34 question survey was designed to address common aspects of donor and recipient selection in LDLT and distributed globally to individuals associated with LDLT programs in 2018.
Results: There were 125 survey respondents representing 41 countries. The U.S. Program (USP) response rate was 97.7%. At least one respondent was obtained from 94.9% of countries with >10 LDLT cases in 2016 (International Programs, "IP"). USP were more likely to have defined donor age criteria (93.1% vs. 82.4% for IP, p=0.03) and recipient MELD ranges (76.7% vs. 43.9% for IP, p< 0.01). IP were more likely to consider LD of any blood group (66.7% vs. 36.9% for USP, p=0.02) or consider LDLT for fulminant recipients (61.0% vs. 27.9% for USP, p< 0.01). Overall, 68% of programs have defined donor BMI ranges (median 18-32), and the mean acceptable macrosteatosis cutoff was higher for IP (19.0% vs. 14.9%, p=0.02). USP were more likely to consider anonymous donors (65.1% vs. 36.6%, p=0.003). There were no differences in willingness to consider complex anatomical variations. Overall, 79.5% of programs perform LD surgery via an open approach (p=NS).
Conclusions: This study represents the first comprehensive global analysis of living donor selection and utilization for LDLT. While there are considerable global variations in LDLT practice patterns largely due to availability of deceased donor organs, this study has identified key aspects of donor selection criteria and utilization that can establish the standard of care for this procedure.

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Comparison of safety and efficacy of early drain removal vs conventional drain removal in living donor liver transplant (LDLT)

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Background: Prophylactic drainage after LDLT remains a universal practice. The timing of removal, conventionally, is once the drain output is below a certain level. However, there is little or no evidence to support this.
Methods: From February 2017 to July 2018, 273 patients were included in the study. From February 2017 to October 2017 (Group 1), the drains were removed once the output was below a certain level. From November 2017 to July 2018 (Group 2), the drains were removed on POD 3 and POD 4 if the output wasn't bilious, chylous or hemorrhagic irrespective of the amount. Post drain removal, a colostomy bag was applied at the drain site for continued paracentesis. The post operative outcomes like time to drain removal, post transplant stay, average ascitic output at day 7 and the appearance of symptomatic abdominal fluid collection requiring intervention were compared using student t-test for continuous variables and chi-square test for nominal variables.
Result: First group had 157 patients and second group had 116 patients. The time to drain removal (8.11±5.67days vs 3.68±0.64days) and average post-transplant stay (25.15±15.58days vs 19.54±9.22 days) was significantly shorter (p-value < 0.05) in the second group. Average ascitic output at day 7 (1330.83ml vs 814.91ml) was significantly lower (p-value < 0.05) in the second group. The appearance of symptomatic abdominal fluid collection requiring intervention (12.1% vs 12.9%) did not differ (p-value 0.96) in the two groups.
Conclusion: Prolonged prophylactic drainage after LDLT beyond day 5 is not beneficial. Early drain removal results in significantly lower ascites and shorter post transplant stay.

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Clinical outcome of residual liver volume and hepatic steatosis after right lobe living donor hepatectomy.

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Background: To determine the residual liver volume (RLV) and hepatic steatosis (HS) of living liver donors and to discuss the regeneration process and clinical outcomes.
Methods: We retrospectively enrolled 58 donors who underwent right-lobe hepatectomy during the period March 2014 to March 2015 at a single medical institution. The patients were classified based on RLV (30~< 35%, 35~< 40%, 40~< 50%) subgroups and HS (< 10%, 10~< 30%, 30~< 50%) subgroups. Clinical parameters such as clinical outcomes, liver volumetric recovery (LVR, %) rate and remnant left liver (RLL, %) growth rate were collected for analysis.
Results: The clinical features of the patients were not significant in the three RLV subgroups. Body mass index (p= .017), preoperative ALT (p < .001), and pleural effusion (p= .038) were significant in the three HS subgroups. The LVR rate and RLL growth rate equations showed significant regeneration degrees in three RLV subgroups based on repeated measures ANOVA. The LVR rate and RLL growth rate equations did not show significant regeneration degrees in three HS subgroups.
Conclusions: Small RLV or HS donors are at risk of major morbidity after right hepatectomy. The safety of living donors were a major concern while we compiled the extended living donor criteria presented in this paper.

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Laparoscopy-assisted hybrid versus open living donor right hepatectomy: a comparison of surgical outcomes

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Background: Applications of minimally invasive surgery in living donor hepatectomy (LDH) is increasingly accepted in worldwide. However so far, pure laparoscopic living donor hepatectomy has only been performed at experienced large-volume transplant centres due to the concerns over donor safety. Laparoscopy-assisted

(hybrid) approach has been designed to not only provide reduced small wound and emotional stability to donors but also minimize the risk of technical complexity. The aim of this study is to evaluate the safety and efficacy of our laparoscopy-assisted (hybrid) living donor right hepatectomy and compare with conventional open surgery in terms of perioperative outcomes.
Methods: Between January 2013 and November 2018, total 311 Living donor right hepatectomy (LDRH) were performed at our institution. Among them, 41 robotic LDRH were excluded. Finally, total 270 LDRH case were enrolled in this study. We divided the patients into two groups [hybrid group (n=126)] and open group (n=144)]. Donor characteristics, perioperative surgical outcomes, postoperative complications were retrospectively reviewed between the two groups.
Results: Total 270 LDRH were performed with zero mortality. All of the hybrid techniques were completed without any extra additional subcostal incision. Hybrid procedure was associated with a reduction in operative blood loss (258 vs 307, p=0.032); shorter hospital stay (8.5 vs 10.8, p=0.01) There was no significant difference between two groups in donor characteristics, the incidence of postoperative complications greater than or equal to Clavien-Dindo class III. operation time, transfusion rate, and postoperative liver function tests, recipient outcomes.
Conclusions: Donor safety is major cornerstone in living donor liver transplantation. Our experience suggests that hybrid approach in living donor right hepatectomy appears to be a safe and feasible procedure. It could be considered an alternative minimally invasive approach.

P-240

The outcomes of liver transplantation using the graft of protein S-deficient living donor

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Introduction: The choice of donor in liver transplantation should be done very carefully. However, the feasibility of liver transplantation is still controversial in the case of donors that meet all other conditions but only have coagulation disorder. Among them, we analyzed the influence of Protein S on living donor liver transplantation.
Method: In this study, we analyzed 837 cases of liver transplantation proceeded between Dec, 2006 and Mar, 2016. Among them, protein S deficiency was found in 78 donors. We compared the effects of protein S deficiency on the coagulopathy - related complications of donor and recipient in perioperative period. The normal value of Protein S was defined as above 70.
Result: The mean values of protein S and protein C of protein S deficient donors were 62.9 and 100.8, respectively. It was significantly low compared to normal range group(98.6 and 106.8, p value < 0.05). 4 of the donors and 7 recipients underwent postoperative bleeding in low protein S group. But there no statistically significance compared to normal range group. We experienced 39 cases of arterial re-anastomosis either intraoperatively or postoperatively because of hepatic artery thrombosis, 9 cases for protein S deficient group(11.5%) and 30 for normal range group(4%) showing significant difference. In multivariate analysis, the degree of low protein S level was found to be a significant risk factor for hepatic artery thrombosis. But none of the donors experienced any thrombogenic event despite low protein S level.
Conclusion: In the liver transplantation with a donor who has protein S deficiency, we should keep in mind the possibility of hepatic arterial thrombosis. And it seems to be unnecessary to use anticoagulants to prevent thrombosis in the donor with low protein S level.

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Synergistic effect of prophylactic shunt and splenic artery ligation during living donor liver transplantation: hitting one bird with two stones

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Background: Routine ligation of spontaneous portosystemic shunts (SPSS) during LDLT is necessary to prevent portal flow steal (PFS) but also increases the risk for portal hyperperfusion syndrome (PHS) even with normal-sized grafts. Splenic artery ligation is proven to be safe and effective in augmenting hepatic artery flow and modulating portal inflow. Our aim is to determine whether combining prophylactic ligation of both SPSS and splenic artery can improve early graft function and to describe its influence on graft hemodynamics.
Methodology: Medical records from 88 adult patients with significant SPSS who underwent LDLT from June 2013 to May 2018 at Kaohsiung Chang Gung Memorial Hospital were retrospectively reviewed. Patients were divided into Non-ligated [NL (n=42)], Ligated [L (n=40)] and combined SPSS and splenic artery ligation [L+SAL (n=6)] groups. Preoperative and intraoperative data were analyzed using Kruskal-Wallis test followed by pairwise comparison. Liver function and graft hemodynamics within two weeks post-transplant

(POD1,3,5,7 and 14) were analyzed using generalized estimating equations.
Results: Preoperative data were comparable in all three groups. The L+SAL group had significantly lower post-transplant total bilirubin levels from POD1-14 (P = 0.014, 0.045, 0.023, 0.012, 0.037). Other liver function tests did not show any significant difference between groups. Post-transplant portal vein flow (PVF) was significantly higher in L vs NL (P=0.006) while L vs L+SAL had similar PVF. Hepatic artery velocity was highest in the L+SAL group but the difference did not prove to be significant. Combined incidence of PHS was 20% for L and NL vs 0% for L+SAL.
Conclusion: Combined prophylactic SPSS ligation and SAL during LDLT appears to work synergistically to prevent post-transplant PFS and PHS leading to improved early graft function and potentially, long-term outcomes.

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The impact of donor BMI on outcomes following adult to adult live donor liver transplantation

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Background: Live liver donors with BMI >30 are usually not considered for donation due to concerns of fatty changes and post-surgical complications. We aimed to evaluate the post-transplant outcomes for both donors and recipients with different BMIs and characteristics.
Methods: Records of donors and their recipients who underwent adult to adult live donor liver transplantation (LDLT) between 2013 and 2018 at Johns Hopkins were reviewed. Liver steatosis >20% was excluded in all donors by imaging or liver biopsy. Survival curves were generated using Kaplan-Meier plots. Significant variables had P-values < 0.05.
Results: 43 donors and 43 recipients were identified. 54.7% of donors were male, had a mean BMI of 26, average age of 34.6 years and length of stay of 7.23 days. 90-day outcomes were measured and complications were reported in 11 donors. Two donors visited the ED for pain. Four needed admission with duration of 1 to 4 days. No mortality was reported in the donors. 17 donors had BMI< 25, 9 BMI 25 to < 28, 9 BMI 28 to < 30 and 7 BMI ≥ 30. Recipients had an average age of 51.9 years, BMI 26.3, MELD of 13.8 and 64.2% were male. The most common indications for LDLT were NASH cirrhosis (23.8%), alcohol (21.43%) and PSC (16.6%). The right lobe was used in 85.7% of patients. Recipients were followed for a median of 884 (9-1984) days. Two recipients needed retransplantation within one year and overall 3 expired. Donor BMI was not associated to complication rates, ED visits or readmission among donors. Furthermore no difference was observed in recipient mortality (p=0.2) or need for retransplantation (p=0.3).
Conclusion: We conclude that LDLT from donors with BMI≥ 30 in the absence of graft steatosis has similar outcomes than donors with BMI < 30 and can be considered for LDLT.

P-243

An innovative public-private-philanthropic model to fund liver transplantation (LT) in a developing country

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Introduction: In developing countries LT needs to be funded by the patient, with little governmental or insurance support. This additional burden has significant impact on affordability and decision making for patients and significantly impacts the ability to deliver this life saving treatment. This abstract investigates funding stream for LTs at newly started program in corporate hospital located in major Indian metropolis.
Methods: 50 LTs were performed at Apollo Hospital Mumbai from May 2017 to Nov 2018. Retrospective analysis of financial costs was performed. The cost of living donor LT in children was 20000 USD, 27000 USD in adults, and cost of deceased donor LT was 30000 USD.
Results: Total of 50 LTs (34 adults; mean age-49.0 yrs, and 16 children; mean age-5.3 yrs,) were performed with 36 grafts from living and 14 from deceased donors. Of these, 26 recipients were from metro cities and 22 were from tier 2 cities or rural areas and 2 were international. 32 recipients received financial support, 11 received complete financial help, 21 had partial contribution, and on an average 36% payment was raised through charitable sources with 81% of children (n=13) and 55 % of adults (n=19) receiving help. This included 7 receiving help through insurance, employers' support and hospital concessions. The remaining 25 received support through: Crowdfunding n=5, NGOs n=5, Government schemes n=4, Government+NGO n=9, Government+NGO+crowdfunding n=2. The mean income of recipients who received financial support was 9576 USD vs. without was 22303 USD.

Conclusion: The costs of LT can be contained to make this treatment more accessible to poorer sections of society. Innovative funding streams using combination crowd funding, charitable donations and institutional lowering of costs can make LT more affordable, and is easier to achieve for children. This model may be applicable for countries without state funded health care delivery systems.

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Insertion of internal stent in duct-to-duct biliary reconstruction to reduce bile duct complication in living donor liver transplantation

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Background: Biliary complication is still considered to be a technical "Achilles´ heel" of LDLT due to the high incidence, requiring long-term interventional treatment, and potential risk for graft failure. The purpose of this study was to evaluate the effectiveness of internal stent for duct-to-duct anastomosis in LDLT.
Methods: From December 2016 to October 2018, LDLT was performed in 91 patients in our center. Duct-to-duct anastomosis was performed in all LDLT patients. The internal stent was a silicone tube of various diameters considering the duct size. Ninety-one patients were divided into non-stent group and stent group according to presence or absence of internal stent. Biliary complications were diagnosed as anastomosis leakage by bile color of drainage fluid and anastomosis stricture when interventional treatment was required.
Results: Biliary complications occurred in 22 (24.2%) patients and anastomosis site leakage occurred in 8 (8.8%) patients. Among 8 patients, four (4.4%) patients required interventional treatment. Their mean age was 56.6 ± 8.2 years and 61 (67.0%) were male. Of the 91 patients, non-stent group was 48 (52.7%) patients and stent group was 43 (47.3%) patients. Anastomosis site leakage was higher in the non-stent group (n=5, 10.4%) than in the stent group (n=3, 7.0%), although there was no statistical difference (p=0.56). Biliary complications were also higher in the non-stent group (n=15, 31.3%) than in the stent group (n=7, 16.3%), although there was no statistical difference (p=0.09). In univariate analysis, the ischemic time was longer in the leakage group (p = 0.05), the operation time was longer in the biliary complications group (p = 0.01).
Conclusions: Although there was no statistically significant difference due to small case number, when internal stent was inserted, biliary complications including anastomosis leakage were reduced compared to no insertion. Further large-scale analyses of clinical data are required to support this study.

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Are Glucose 6 phosphate dehydrogenase deficient donors acceptable for living donor liver transplantation?

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Background: Living donor liver transplant is common in Asian countries. Asymptomatic Glucose 6 phosphate dehydrogenase deficient (G6PD-deficient) population is common in many parts of Asian countries. Routine screening of liver donors and careful perioperative care can prevent risk to living donor postoperative recovery.
Method: All potential asymptomatic donors were screened for G6PD deficiency along with any evidence of haemolysis. On evaluation, six potential donors were found to be G6PD-deficient. G6PD-deficient donors without evidence of haemolysis were only evaluated for donation, if there was no other suitable donor. Therefore four out of six underwent donor hepatectomy. Intraoperative & postoperative course of donors were closely monitored for hemolysis and medications. The medications which can induce haemolysis, were avoided. Perioperative analgesia was individualized and close monitoring of liver function and hematological profile was done. Postoperative course of these donors was also compared with a cohort of 12 consecutive non-G6PD-deficient donors. We present the outcomes of our first 4 G6PD-deficient liver donors.
Results: There were 192 living donor Hepatectomies in the period from September, 2015 to November, 2018. There were four G6PD-deficient male liver donors. All 4 underwent right lobe donation. One G6PD-deficient donor had biochemical evidence of postoperative haemolysis, requiring one unit of packed red blood cell transfusion. Postoperative liver function tests, intensive care unit stay, hospital stay, and morbidity (greater than Clavien II) were similar in the G6PD-deficient and non-G6PD-deficient donor cohorts.
Conclusions: Hepatectomy in G6PD-deficient donors is safe. Considering the fact that G6PD-deficiency has high prevalence in Asia, G6PD-deficient donors may enlarge the donor pool for LDLT.

P-246

Outcomes of patients undergoing living donor liver transplantation with lower graft-to-recipient weight ratio

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Introduction: Small for size grafts (SFSG) carries a high morbidity and mortality but in Asian countries where there is lower deceased donation rate, living donor liver transplantation is the only option to save life of these patients. Minimum GRWR (Graft to Recipient Weight Ratio) of ³ 0.8% has been recommended but lower limit of graft size is undefined.
Aim: To analyze the impact of small for size grafts on post-transplant outcome.
Material and methods: Patients who underwent adult LDLT between January 2011 to September 2018 were divided into 2 groups: one with GRWR ³ 0.8% and the other with GRWR < 0.8%.
Results: 240 patients were analyzed after exclusion. 197 (82.1%) had GRWR ³ 0.8%. and 43 patients (17.9%) had GRWR < 0.8% .Of these 43, 25 were right lobe grafts and 18 were left lobe grafts. Among SFSGs, most were procured from left lobe (41.9% Vs 5%, p< 0.0001).SFSS was found to be more with patients with GRWR< 0.8% (20.9% Vs 5.1%). The cold and warm ischaemia times were comparable in both the groups, but the an-hepatic phase was significantly lower in low GRWR group (182 Vs 219 mins). Both the groups were comparable in terms of postoperative ICU stay (6.6 Vs 6.4 days), hospital stay (18 Vs 16.4 days), graft rejection (23.2% Vs 12.7%) and graft survival at 90 days (9.3% Vs 7.1%). There was no significant difference in mortality between the two groups at 90 days of transplantation; rates being 11.6% Vs 8.1% (p=0.46).
Conclusion: In our experience, though we noted higher incidence of SFSS with liver grafts of GRWR < 0.8%, there was no difference in length of postoperative hospital stay, ICU stay, graft survival and mortality at 90 days. Hence we recommend that SFSG may be used to increase the donor pool in selected cases.

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Living donor liver transplantation (LDLT) in the elderly patients: Analysis of safety and long term outcomes

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Background: Population ageing is a global phenomenon; 65 years and above is one of the fastest growing age groups. Consequently more patients from this age group are expected to require liver transplantation in future.
Methods: We performed a retrospective review of 2330 LDLT recipients done between June 2006 and June 2018. 37 patients older than 65years of age (Group 1; 65years to 74years, n=37) were compared to the computer based randomly selected patients of the younger cohort in 4:1 ratio (Group 2; 18years to 65years, n = 148). 10 recipients were above 70yrs age. Patient characteristics, intra-operative variables, postoperative morbidity and mortality and long term survival were analysed. Univariate and multivariate analyses were performed to assess the impact of age on outcomes. Median follow up was 5.7yrs (6months -12yrs).
Results: Patient characteristics were comparable except for lower mean MELD scores in group 1(16.9±6.74 vs 19.0±7.0, p=0.024). Graft characteristics and intra-operative variables were similar. Cardiovascular (p=0.03), respiratory(p=0.02) and infectious complications(p=0.001) were higher in the immediate postoperative period in group1, however the hospital stay and in hospital mortality were not significantly (p=0.25) different. 1yr, 3yr and 5yr survival rates were 85.4% vs 90.2%, 71% vs 80%, and 61% vs 77% respectively for Group 1 and Group 2. 1 out of 10 recipients aged above 70 died in immediate post op period. Cox proportional hazards regression analysis showed p-value of 0.032 and Hazards ratio(HR) of 1.029 with respect to age, p-value of 0.169 with HR of 1.028 with respect to MELD, and p= 0.44 and HR=0.56 for Child's B & C status. Cox proportional hazards regression model for multiple variables showed significance only for preoperative renal dysfunction(p=0.001 and HR=6.91).
Conclusion: LDLT in the elderly may have slightly higher post-operative complications, but it´s safe and long term outcomes are acceptable in carefully selected patients.

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Hepatic blood flow after right lobe living donor liver transplantation

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Aim: The aim of this study was to systematically evaluate the role MHV on hepatic hemodynamic changes.
Materials and methods: 75 patients undergoing right lobe LDLT between January 2003 and December 2016. We compared hemodynamic changes after right lobe LDLT with MHV (group 1; n = 37) or without MHV (group 2; n = 38). The patients age ranged from 15 to 50 years old and the male-to-female ratio was 41:34. The two groups were compared in portal venous flow volume (Qpv), peak systolic velocity (PSV) and resistance index (RI) on postoperative days (PODs) 1, 3, 5, 7, 30 using colored doppler ultrasonography.
Results: Group I had higher values of Qpv - 687±220 ml/min ;1251±491 ml/min; 1324±372 ml/min; 1231±284 ml/min; 1042±211ml/min; 1131±301 ml/min compared with group II - 647 ± 230 ml/min; 1128±385 ml/min; 1132±372 ml/min; 1019±263 ml/min; 967±254ml/min; 935±293 ml/min on PODs 0, 1, 3, 5, 7, 30 respectively. Qpv increased after graft implantation, it was higher in group I - by 564 ml/min on POD 1 (compared to preoperative measure on POD 0); however, in group II this parameter increased by 481 ml/min. PSV and RI on POD1 increased much more in group II (from 0,53m/s to 0,66m/s and from 0,63 to 0,72 respectively) compared with group II (from 0,57m/s to 0,58m/s and from 0,62 to 0,66 respectively).
Conclusion: After right lobe LDLT with MHV, there is an increase of Qpv and total hepatic blood flow with a decrease of PSV, as a result of optimization of the venous outflow from the graft compared with blood flow of the right lobe graft without MHV.

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The correlations between preoperative hepatic venous pressure gradient and graft hemodynamics after reperfusion in living donor liver transplantation

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Background: Hepatic venous pressure gradient (HVPG) is known to correlate with severity of portal hypertension in patients with liver cirrhosis. The aim of the present study was to investigate the correlations between preoperative HVPG and graft hemodynamics after reperfusion in patients who underwent adult-to-adult LDLT.
Methods: Seventy-five patients who underwent adult-to-adult LDLT at our institution were divided into two groups (HVPG < 16 mmHg or ≥ 16 mmHg, as previously reported). The correlation between preoperative HVPG and patient characteristics, surgical outcomes, and graft hemodynamics including portal vein flow (PVF) and hepatic artery flow (HAF) after graft reperfusion were investigated retrospectively.
Results: Thirty-five patients (46.7%) had an HVPG ≥ 16 mmHg. The patients with HVPG ≥ 16 mmHg had significantly higher international normalized ratios (INR), creatinine levels, and MELD scores compared to the 40 patients with HVPG < 16 mmHg. They had higher rates of varices bleeding, encephalopathy and intractable ascites, and lower albumin levels and platelet counts compared to those with HVPG < 16 mmHg. There were no significant differences in surgical outcomes after LDLT between these two groups, except for postoperative ascites. Preoperative HVPG showed a positive correlation with PVF and a negative correlation with HAF after graft reperfusion (p = 0.038 and p = 0.027, respectively). In linear regression analyses, preoperative HVPG was independently associated with PVF after graft reperfusion.
Conclusion: Preoperative HVPG was associated with hepatic hemodynamics after graft implantation in LDLT. Preoperative HVPG measurement may be helpful for surgical planning of portal inflow modulation.

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A novel reconstruction method for adjacent multiple bile duct during living donor liver transplantation; dunking with mucosal eversion technique

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Biliary stricture (BS) is still major concern for living donor liver transplantation (LDLT) and multiple duct and multiple anastomoses have been considered as major risk factors for biliary complication. For multiple bile duct during LDLT, various surgical techniques have been introduced and especially, most surgeons have performed unification ductoplasty for adjacent bile ducts during LDLT. However, ductoplasty could cause hemobilia and is difficult to perform in cases with duct size discrepancy. The aim of this study is to introduce our novel biliary reconstruction technique and its effects

on biliary complication and graft function compared to ductoplasty. We compared clinical outcomes with two biliary reconstruction techniques through retrospective review of 50 recipients who underwent LDLT using right lobe grafts with two adjacent bile duct at our institution from January 2013 to July 2018; group I (n=20) received unification ductoplasty and group II (n=30) received dunking with mucosal eversion technique (Fig.1). Overall biliary complication rates were 20% in group I and 6.7% in group II, respectively. Moreover, the BS incidence in group II was lower than that in group I (15.0% vs 3.3%) although there is no significant difference (p=0.136). Moreover, BS incidence in group II was not higher than that in single duct group during same period (p>0.05). Peak total bilirubin value (within one month after LDLT) in group II was significantly lower than that in group I (4.2 mg/dL vs 6.7mg/dL, p=0.032). In conclusion, our novel technique could be a useful reconstruction method for two adjacent bile duct during LDLT and good alternative to ductoplasty. Moreover, it may be also considered as good option for adjacent 3 or more bile duct.

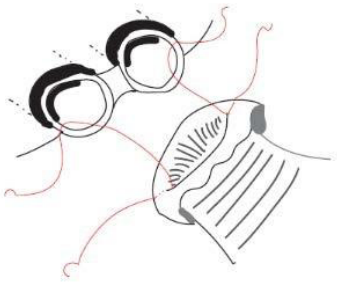

Figure 1. Dunking with mucosal eversion technique. The lateral corners of bile duct for graft were connected with inner mucosa of everted bile duct from the recipients using 6-0 PDS. The posterior wall of graft bile duct opening was continuously sutured including connective tissue between two ducts, avoiding the medial corners.

[Dunking with mucosal eversion technique]

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Living donor liver surgery: nine years experience

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Introduction: The use of living donor livers for transplantation is well standardized. Donor safety is the most important point of this procedure. Extreme attention is paid to reduce complications and avoid mortality during and after donor hepatectomy. We presented our living donor hepatectomy series.
Patients and method: We retrospectively evaluated the records of all living donors operated between June 2009 and June 2018. All demographic data, radiological and laboratory findings, characteristic of the harvested lobe, characteristics of the remnant liver, intraoperative and postoperative complications were noted. All complications were classified according the clavien-dindo classification system. Results were analysed statistically.
Results: A total of 122 living donor operations were done during this period. They were done by the same surgical team. Seventy-three were males (59%). Mean age was 33 years. Mean follow -up was 50,8 months. Twenty patients (16,3%) suffered from postoperative complications. There were 10 grade 3A and 10 grade 3B complications. Grade 3A complications were biliary complications (6 patients) and pleural effusions (4 patients) that were managed percutaneously in 9 and with ERCP in one. Grade 3B complications were managed operatively. These were bleedings in 7, small bowel obstruction in one, diaphragmatic hernia in one and incisional hernia in one. All bleedings occurred at the early postoperative period and managed without evolving to a more severe complication. There were no grade 4 complications or deaths.
Conclusion: Living donor hepatectomy is a safe procedure. It has to be done under strict safe surgery rules. Close follow-up at the ICU and the ward is necessary. Although biliary complications are classified as grade 3A they are mostly managed with percutaneous drainage and easily relieve after the drainage. Bleedings however can life-threatening and must be managed with high attention. Routine ultrasound examination is necessary for early recognition of complications.

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Experience of hepatic artery anastomosis in living donor liver transplantation using surgical loupe: in small volume center

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Background: The hepatic artery (HA) reconstruction in living donor liver transplantation (LDLT) is a crucial step because of the smaller diameter of the artery and the increased risk of HA related complications. Also, any occurrence of the HA flow abnormalities in the immediate postoperative period may lead to fetal complications. Therefore, many centers use a micro-surgical technique for HA reconstruction. The aim of our study was to investigate the outcomes that HA reconstruction was performed under surgical loupe.
Methods: This study included 44 LDLTs with various end stage liver diseases at Dong-A university hospital Busan, Korea from January, 2014 to August, 2018. The medical records were retrospectively analyzed for the outcomes and HA related complications in these patients.
Results: LDLT was performed in 44 recipients. HA reconstruction for the initial 13 LDLT surgeries was performed using a micro-surgical technique with interrupted suture on both side HA wall. From 14 LDLT case, HA reconstruction was performed in 31 recipients under surgical loupe with interrupted suture on posterior HA wall and running suture on anterior wall.
We performed HA reconstruction in 30 adults, 1 pediatric patient (one year old) under surgical loupe, which included one dual graft LDLT. The most notable factor in surgical loupe group compared with micro-surgical group (33±5 minutes) was the quick HA anastomosis procedure with a mean time of 12±3 minutes.
Fortunately, there were no HA related complications and death in both groups.
Conclusion: Although our case is not enough, with a zero HA related complication, we could consider that the HA reconstruction using surgical loupe even in smaller diameter hepatic arteries is a reliable technique and can easily be applied by an experienced surgeon

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Early postoperative high or low oxygen level had negative impact on outcomes after living-donor-liver transplantation: a retrospective study

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Objective: To investigate the impact of postoperative partial pressure of arterial oxygen (PaO2) on outcome after living-donor-liver transplantation (LDLT).
Background: Due to prolonged ischemia time and subsequent ischemia reperfusion injury, liver grafts immediately after transplantation are thought to be quite susceptible against change of blood oxygen concentration. However, the relationship between postoperative PaO2 and outcome after LDLT remains unclear.
Method: We retrospectively analyzed 258 cases of primary adult-to-adult LDLT in Kyoto university between April 2008 and March 2016. Recipients were divided into 3 groups according to the postoperative PaO2 level: PaO2 < 120mmHg (n=64); 120-160mmHg (n=93); >160mmHg (n=101). One year-graft survival and the association with various clinical factors were investigated.
Results: PaO2 120-160mmHg group showed significantly better one-year graft survival (P =0.015) and overall survival (P =0.017) compared to PaO2 < 120mmHg or >160mmHg group. PaO2 120-160mmHg group showed significantly lower 90-day mortality rate (P =0.003), re-operation (P =0.004) and early graft dysfunction (P =0.012) compared to PaO2 < 120mmHg or >160mmHg group. Multivariate analysis showed PaO2 < 120mmHg and >160mmHg (vs. PaO2 120-160mmHg, HR 2.448, 95%CI 1.095-5.709, P =0.029 and HR 2.770, 95%CI 1.341-6.161, P =0.006, respectively), along with donor age (P =0.003) and final portal vein pressure >15mmHg (P < 0.001), were the independent risk factors for worse one-year graft survival.
Conclusion: This retrospective study first showed postoperative PaO2 < 120mmHg or >160mmHg was an independent risk factor of graft loss within one year after LDLT.

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Is left lobe live donor liver transplant (LDLT) adequate, for patients with an unsuitable right lobe donor

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Background: Left lobe is not a routinely used graft in adult living donor liver transplants, due to the smaller size. This causes a certain shortage of the available grafts , and also rejection of the donor, in whom the right lobe graft, is not feasible. A left lobe graft is a possible alternative in such patients. The aim of this study is to evaluate the possibility of a left lobe graft in adult LDLTs.
Methods: We have analysed retrospectively of the all the LDLTs at our centre from January 2014 to January 2018, a comparison was made between the right and left lobe transplant patients. The left lobe transplants were offered to recipients, for whom the RL donation was not feasible. Outcomes of the donors were also analysed. The statistical analysis was done using unpaired t-test for continuous variables and Chi square test for nominal variables.
Result: The left lobe graft was most commonly used in the small right lobe donors. LL grafts had a shorter cold ischemia time (69.54±32.44mins vs 107.35±45.02mins, p=< 0.0001), shorter surgery times for the donor and the recipients , SFSS (10.2% vs 6.6% ,p=0.38) and the donor hospital stay was significantly less in LL (10.05±1.07days 10.42±2.0, p value < 0.04). 1 year survival and the other post operative parameters of the LL comparable to the RL.
Conclusion: The left lobe LDLT is a viable alternative in donors whose right lobe donation is not feasible. We found the morbidity and mortality of the LL are similar to that of the right lobe, and the chances of the SFSS, is statistically comparable. It is superior in donor safety and comparable with the RL in recipient outcomes.

P-255

Is routine reconstruction for all sizeable anterior sector drainage veins necessary in right lobe living donor liver transplantation?

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Introduction: In right lobe (RL) living donor liver transplantation (LDLT), a good hepatic venous outflow is one of the basic principles. However, the issue of whether anterior sector (AS) drainage veins should or should not be routinely drained has been controversial. This study investigates the early outcome of reconstructed Segment 5 (S5) and 8 (S8) veins using polyester (Dacron®) grafts.
Material and methods: Between January 2018 and October 2018, of 34 adult patients who underwent RL LDLT in our institution, 30 (88.2%) received a RL graft with AS venous reconstruction including S5 (n=13), S8 (n=2), or combined S5-8 (n=15) drainage. All patients underwent contrast enhanced CT/MRI within two weeks after the transplant and were routinely followed with Doppler Ultrasound thereafter.
Results: Median donor age was 33 and median graft-to-recipient-weight ratio (GRWR) was 1.0%. All reconstructed veins were ≥5 mm in size. Two-week graft patency rate was 60%. The rate of graft thrombosis was significantly higher in patients with a GRWR of >1.1% (70% vs. 25%, p=0.02). The patent S5 and S8 veins were significantly larger than the thrombosed veins (S5: 7.5±1.8 mm vs. 6.2±1.1 mm, p=0.04; S8: 6.4±0.7 mm vs. 5.1±0.3 mm, p< 0.001). The patency rate showed a significant positive correlation with the size of both S5 (Pearson coefficient=0.382, p=0.04) and S8 veins (Pearson coefficient=0.773, p< 0.001). There was only one peri-operative mortality (2.9%) and early graft thrombosis was not associated with either lower graft regeneration rate or increased risk of graft dysfunction.
Conclusion: After two of our recipients developed infection in the thrombosed polyester grafts, we questioned our policy of routine drainage for all sizeable (≥5 mm) AS veins. Considering the low early patency rate and the risk of graft infection, RL grafts with GRWR >1.1 and AS veins < 7 mm in diameter may not need drainage.

P-256

Effects of omega-3 fatty acids on outcome after living donor right hepatectomy: a pilot study

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Purpose: In this trial, we will assess the use of a fish oil-based lipid emulsion as a potential preconditioning strategy for the reduction of ischemic injury in living liver donation.
Methods: This trial was a prospective, open-label, single-arm trial to assess the effect of two preoperative doses of 10% purified fish oil-based lipid emulsion (Omegaven, Fresenius-Kabi) on outcome after living donor right hepatectomy. Live liver donors scheduled to undergo right hepatectomy were given preoperative infusions of Omegaven 100 mL, on the day prior to surgery and on the morning of surgery.
Results: Ten donors were enrolled in the trial from January to July of 2018. Nine donors completed the trial. One subject did not undergo liver donation due to moderate steatosis upon liver biopsy and was dropped from the trial. All patients underwent fully laparoscopic right hepatectomy and mean operative time was 273 minutes. Serum levels of omega-3 fatty acid significantly increased following two infusions of Omegaven (mean 145.0 ug/mL to 199.4 ug/mL, p=0.034), while omega-6 fatty acid decreased (mean 1090 ug/mL to 977.8 ug/mL, p=0.063). Estimated blood loss during surgery was 238.9 ml and none of the patients received intraoperative RBC transfusions. One patient required postoperative RBC transfusion. Peak postoperative aspartate aminotransferase and alanine aminotransferase levels were 205.3 U/L and 233.1 U/L, respectively. Values peaked on the day of surgery or postoperative day 1 and continued to decline during the first 5 days. The serum total bilirubin peaked on postoperative day 1 with a mean of 2.7 mg/dL. The peak mean prothrombin time international normalized ratio was 1.65. All donors were discharged without complications.
Conclusions: Preoperative intravenous infusion of Omegaven in living donors undergoing right hepatectomy was associated with significant increase in serum omega-3 fatty acid levels and was not associated with perioperative adverse events, including postoperative bleeding.

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Living liver donor surgical complication: single center experience with 512 cases

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Background: Korea is the one of the most common country to do living donor liver transplantation. But almost big liver transplantation center is in Seoul which is capital of Korea. Beside Seoul, There are no big living donor liver transplantation center except Dague catholic university medical center. We were reached to 500th living donor liver transplantation in 2017. We review our donor complication and find way to reduce the rate of morbidity.
Methods: Institutional LT database was searched from 2005.05.08. to 2017.12.31. Their medical records and imaging studies were reviewed.
Result: From 2005.05.08 we did first living donor hepatectomy, we did 513 living donor hepatectomy until 2017.12.31. Among them, 324 were male and 188 were female. Graft types were Right liver graft in 457 (89.3%), Left liver graft in 47 (9.2%), Left lateral section graft in 2 (0.4%) and Right posterior section graft in 6 (1.2%). Mean age of total donor was 30 years and Mean BMI was 22. Mean hospital days was 10days. All of the donors, surgical complication occurred in 32donors.(6.3%) Minor complication was 10 cases(1.9%). Major complication was 22case.(4.2%) Between major complication, the most common complication was biliary complication (n=17) and the Other complications were pleural effusion drainage(n=2), bleeding control(n=2), Portal vein stent insertion(n=1). There are no mortality. The most common complication was biliary complication which were 20cases(3.8%). Among them intra-op T-tube insertion were 9 case and 3 case were PTBD insertion and 3case did ERCP. There are re-operation case was just one case, which was immediate right hepatic artery bleeding.
Conclusion: Our center's complication was very low. But still biliary complication is the most common complication. When we meet abnormal biliary anatomy we must be careful and we try to reduce intra-op T-tube insertion.

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Living donor liver transplantation in septuagenarians: better late than never

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Background: The group of elderly population in the world is increasing .Moreover, improvements in quality of chronic liver disease care, which leads to expanding population of septuagenarians (≥ 70 years) in need of liver transplantation (LT). In the early 1990s, numerous publications reported non-inferior LT outcomes in sexagenarians, reflecting the combined advances in surgical techniques, anaesthesia/critical care, and infection control. Further liberalization of age limit has generated a published experience replete with encouraging outcomes in selected septuagenarians undergoing deceased donor LT (DDLT). Cultural obstacles in many Eastern countries including Saudi Arabia have restricted access to DDLT and there is a paucity of experience in the live donor liver transplant (LDLT) world pertaining to elderly LTx outcomes. The objective of this study is to examine the justification of the gift given by LDLT to those patients.
Methods: 295 adult patients underwent LDLT between January 1, 2011 and December 31, 2016 .Twelve (4%) of these patients were septuagenarians and this group was compared to younger cohort (n=283) via a retrospective analysis which included standard clinical parameters, operative variables, and post-transplant graft and patient survival.
Results: Comorbidity profiles between the two groups were similar and no statistically significant differences were noted in warm/cold ischemia times, operative duration, or blood product utilization. ICU and total hospital stays were comparable. Septuagenarian 1-and 5-year graft and patient survivals were identical at 91.7%. Their younger counterparts had 1-and 5-year patient survivals of 91.1% and 84.0 % accompanied by 1-and 5-year graft survivals of 89.8% and 82.7%, respectively.
Conclusion: Despite its relatively modest sample size, our study highlights recognition that LDLT can afford highly selected elderly patients (free of significant comorbidities, frailty, and sarcopenia) access to transplant with equivalent outcomes to younger recipients. Septuagenerian patients should not excluded from liver transplant based on their chronological age only.

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Initial experience of laparoscopic living donor hepatectomy for pediatric liver transplantation in a Southeast Asian transplant center

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Background: Donor laparoscopic left lateral sectionectomy (DLLLS) for pediatric liver transplantation is safe and feasible but technically demanding, and a significant learning curve has to be overcome first. The National University Hospital, Singapore, performed the first DLLLS in South East Asia in November 2017. We describe our learning curve and our institution´s experience with the first 4 cases of DLLLS.
Methods: Data regarding our centre's laparoscopic hepatectomy program and 4 cases of DLLLS was collected. The outcomes of LLLS group were compared with that of 4 consecutive most recent cases of open laparoscopic left lateral sectionectomy (OLLS).
Results: Prior to the first DLLLS, our centre had performed 379 liver transplants, of which 244 (64.4%) were adult recipients and 135 (35.6%) were pediatric recipients. We had a cumulative experience of 173 laparoscopic hepatectomies, of which 38 (22.0%) were major resections. The overall conversion rate was 12.3%. Comparing the LLLS and OLLS group, donor baseline characteristics were similar. Median operative durations were identical at 330 minutes (290 - 420 min vs 270 - 420 min). Intraoperative blood loss (p=0.486), length of stay (p=0.686), postoperative day 1 pain score (p=0.686) and number of days to ambulation (p=0.686) were similar in both groups. There were no wound related complications in the LLLS group but 1 patient had an intra-abdominal hematoma that resolved with conservative management. One patient had wound dehiscence in the OLLS group. The LLLS group had a faster return to their active lifestyle (30.0 days vs 42.5 days; p=0.029).
Conclusion: DLLLS is a technically demanding procedure with a significant learning curve. It is possible to scale the learning curve in a small - medium liver transplant center after achieving necessary experience from laparoscopic major hepatectomies.

P-260

Minimal invasive living donor right hepatectomy: an experience of consecutive 114 cases by a single surgeon

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Background: Because the donor is not performed operation under pathologic condition, it is important to consider the quality of life such as cosmetic effect. The aim of this study was to evaluate the safety and feasibility of minimal invasive living donor right hepatectomy.
Methods: All consecutive cases of minimal invasive living donor right hepatectomy between January 2014 and March 2018 in a tertiary referral hospital were enrolled in this retrospective cohort study. All surgical procedures were performed by one surgeon. All patients underwent subcostal incision and incision length was applied flexibly according to the weight of the graft (9-12cm). The group was analysed in terms of donor demographics, preoperative data, postoperative outcomes.
Results: The mean age of the donors was 27.4 ± 6.7 years, the gender ratio for men and women was 18:96. The mean operative time was 402.5 ± 78.8 minutes and mean postoperative hospital stay was 10.1 ± 1.7 days. The number of complications was 6 cases (5.3%) and among them, the Clavien-Dindo classification III or higher complication was 2 (1.8%). There were no mortality cases.
Conclusion: Minimal invasive living donor right hepatectomy was a safe and feasible procedure for donors. It showed an acceptable incidence of complications. The authors suggest that minimal invasive living donor right hepatectomy could be a reasonable operative option for donors in terms of cosmetic effect.

P-261

Waterjet: an effective and safe tissue-selective tool for parenchymal transection in live donor liver transplantation

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Background: Live donor liver transplantation has changed the perception of what was considered “acceptable” morbidity associated with major hepatectomy. None of the transection techniques described so far have shown significant differences in time taken, blood transfusion or outcomes. Waterjet as a transecting tool is appealing in live donor hepatectomy in view of minimal tissue damage and clear visualisation of vascular structures in the field. We analyzed our experience with this technique in 100 consecutive live donor hepatectomies.
Method: Retrospective observational study of our database of 100 living donor hepatectomies performed at a single institution between 2015 and 2018. All donor hepatectomies were performed with Hydrojet (ERBE). Prior to this period, all transections were performed using CUSA. The donor hepatectomy was performed by standard techniques previously described. The donor profile, operative time, requirement for blood transfusions, perioperative morbidity, hospital stay were recorded.
Results: There were 67% females and 33% males, age ranging from 19-57 years. The grafts were mostly Right lobe (78%) followed by left lateral (15%) and left lobe (7%). The average length of stay was 6.95 days ranging from 5-16 days. Blood transfusions were required in 5% of donors. The complications according to Clavin-Dindo classification were GrII in 24% and GrIII in 2%. Bile leaks were noted in 6% of donors but were managed without surgical intervention. Mortality was 0.
Conclusion: The Waterjet is an effective alternative for parenchymal transection in live donor liver transplantation, the main attraction being absence of thermal injury to the graft or remnant. A clear operative field and ease of handling of the probe are other advantages. Inadvertent spray of water outside the field is the main reported disadvantage overcome with experience and use of standard eye protection. However, the incidences of serious complications were lower with Waterjet (unpublished data).

P-262

Experience of living liver transplantation for anti-donor HLA antibody positive patients

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Presence of existing antibody in donor´s HLA (DSA) is regarded as a risk of antibody-mediated rejection (AMR) in organ transplantation and is regarded as a factor of poor prognosis. We report the strategies to DSA positive patients in our institute (Patients) 67 cases of liver transplantation from 2011 to 2017 were enrolled in this study.
Result: The DSA positivity was confirmed in 5 cases. 2 cases were PBC, 1 case was NASH, 1 case was alcoholic liver cirrhosis and 1 case was type C cirrhosis. All cases were female, blood transfusion history and pregnancy history were confirmed. Average age was 57 years old, average MELD score was 21.8. In DSA, only Class I showed positive results in 4 cases, both Class I and II showed one case. In the case of strong positive cases with MFI of 10,000 or more in the single bead method, Class I, II positivity was 3 cases and Class II only positive case was 2 cases. In all cases desensitization therapy using rituximab was administered. The transplanted liver was engrafted in all cases, but one case was lost due to infection. The transition of DSA after surgery was searched in 4 cases. Class I was negative conversion in 3 cases, 1 case was weak positive in Class II. Two cases showed cellular rejection, but AMR was not seen. A case of bile duct stricture was confirmed.
Discussions: Since liver transplantation may not develop AMR even if it is positive for DSA, its clinical significance is hard to realize. However, AMR is refractory and poor prognosis, prevention is important. Dementing with rituximab was considered to be useful for postoperative antibody negative conversion.
Conclusion: There are many unclear points about the clinical significance of DSA in liver transplantation, and further cases Stacking was deemed important.

P-263

Redo living donor liver transplant. Is it a futile procedure or reality? A case report

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Background: Success of liver re-transplantation in patients due to disease recurrence mainly depends on patient's condition and intra-operative difficulties. We here present the technical challenges we faced in 2 such cases.
Case-1 Patient developed liver dysfunction 1 ½ year post LDLT, due to noncompliance of medications and HCV recurrence which progressed to end stage liver disease 6 months later. MELD score was 40, CTP 14. He underwent LDLT with right lobe graft without MHV. Graft weight was 540g and GRWR 0.75. Patient had severe intraoperative hemorrhage due to dense adhesions and extensive portosystemic collaterals requiring very high inotropic support. Forty four PRCs, 36FFP, 11 cryoprecipitate and 2.5 SDPC were required intraoperatively. Total duration of surgery was 15 hour and 51 minutes.
Case-2 Patient developed re-cirrhosis in transplanted liver after 7 years due to reindulgence in alcohol. MELD score was, CTP-10. He underwent LDLT with right lobe graft without MHV. Graft weight was 650g and GRWR 1.38. Intraoperatively adhesions encountered were much less, patient required minimal inotropic support with 7 PRCs and 5 FFP intraoperatively. Total duration of surgery was 12 hours and 30 minutes. Standard reconstruction was done as recepeint portal vein and artery were patent in both cases. Both patients were discharged in stable conditions
Conclusion: In view of huge organ shortage in Asian countries, redo LDLT can be an equally realistic alternative as DDLT in recurrent disease leading to graft dysfunction.

P-264

Middle Hepatic Vein (MHV) anatomy and its effect on the outcomes in Modified Right Lobe (MRL) grafts in Living Donor Liver Transplant (LDLT)

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Background: Right lobe is the usual graft of choice in LDLT. The anatomy of the MHV(V5,V8) is an important determinant of the venous outflow of the anterior segment. Modified Right lobe grafts are commonly used grafts which usually require the reconstruction of the MHV. This Neo MHV is also prone to thrombosis which could be early or late in the post operative period. We reviewed the impact of MHV reconstruction and the effect of late MHV thrombosis on outcome after transplantation.
Material and method: All the 287 patients who underwent MRL -LDLT between February 2017 to November 2018 were enrolled in the study.MHV anatomy was classified according to number of Segment 5 (V5) and Segment 8 (V8) vein present in the graft into, MHV type 1 (V5-1,V8-1,n=133), type 2 (V5-2,V8-1, n=47), type 3 (V5-1,V8-2, n=51), type 4 (MH2= V5-2,V8-2, n=25), type 5A (V5≥3,V8-any number,n=10), type 5B (V5-any number, V8≥3,n= 12), type 6 (X5= V5-0, V8- any number,n=4), type 7 (X8=V5-any number,V8-0,n=4). Statistical analysis was done using chi-square test for nominal variables and wilcoxon test for continuous variables.
Results: There was no difference in any of the patient demographics or pre-op parameters. Cold ischemic time was significantly prolonged in MHV5A type (136.5 ±11.6) and least in Type 7 (75.7 ±18.4) F (7,278) = 4.2,p= 0.0002). **All other intraoperative and postoperative parameters were comparable among the groups. MHV thrombosis was seen in 33.1% of all patients and they had a higher morbidity(51.57%vs19.79%). Postoperatively, the incidence of MHV thrombosis was similar between the groups (p=0.56).**
Conclusion: None of the MHV types affected the outcome in our cohort. Thus, if proper outflow is given during benching all graft can function well irrespective number of veins. However, late MHV thrombosis has a significant effect on the morbidity and re admission rates.

P-265

The presence of preoperative portal vein thrombosis does not affect survival in living donor liver transplantation

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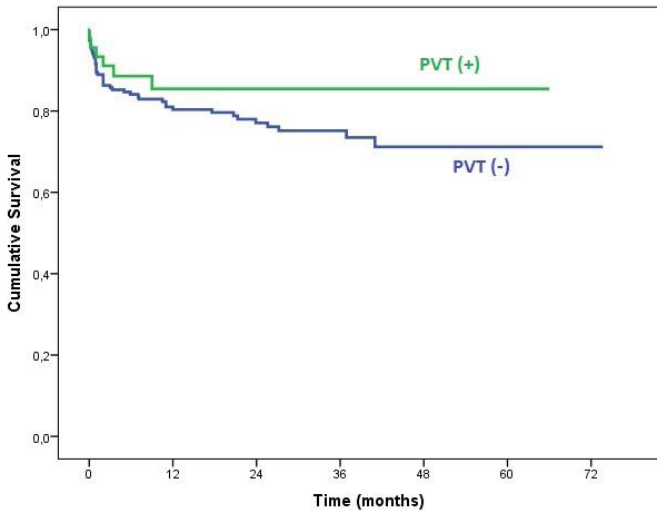
Introduction: In living donor liver transplantation (LDLT), the presence of portal venous thrombosis (PVT) increases the complexity of surgery. Our aim was to compare the survival rates of patients with and without preoperative PVT.
Materials-methods: Ankara University and Guven Hospital Liver Transplantation database were used for this analysis. Pediatric cases (age < 16) were excluded from the analysis. All adult liver transplantation (LT) cases between 2012-2018 were included in the analysis. During this period, 273 liver transplantations were performed [(38 cadaveric (14%);235 living related; 180 M/93F; median age: 55 (16-74)]. Of them, 53 had preoperative PVT (8 in cadaveric transplantation, 45 in LDLTs). PVT was graded 1-4 according to the Yerdel classification system. Patients with and without preoperative PVT were compared. Kaplan Meier test was used for survival analysis of groups.
Findings: In LDLT patients (n:235), baseline clinical and laboratory findings were similar in patients with and without PVT groups. Baseline MELD score were also similar (15 vs 17;p:0.11 respectively). Median follow up time was 20 (0-73) months. During posttransplantation period, 50 patients died and of them, 6 had preoperative PVT. Kaplan Meier analysis shows similar survival rate in patients with and without preoperative PVT in LDLT patients. (figure 1;p:0.26). Findings were similar in cadaveric transplants. Preoperatively, 22 patients had grade 1, 12 patients grade 2, 9 patients grade 3 and 2 patients grade 4 in LDLT patients. When we compare the patients with preoperative grade 2-4 PVT (n:23) vs without PVT (n:190), survival rate also did not differ (p:0.87).
Conclusion: This suggests that LDLT can be performed even in advanced PVT cases using appropriate treatment modalities if the surgical team has experience in circumventing PVT.



[Cumulative survival]

P-266

Surgical technique for native hepatectomy in liver transplantation with vena cava preservation: summary of 12 cases experience

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Background: Orthotopic liver transplantation (OLT) has become the procedure of choice for end stage liver disease with three commonly described methods of vena cava anastomosis. However, to date, no report has focused on techniques that isolate the liver or finish native hepatectomy. Here we show a new technique of native hepatectomy which is safe and simple.
Methods: From January 2018 to March 2018, patients who underwent OLT using a newly improved operation technique were recorded. Clinical data, venous anastomotic times, anhepatic phases, and the recovery of liver function were retrospectively collected for analysis. Graft function index and complication were collected post transplantation.
Results: 12 patients underwent OLT with new technique that divides the second porta and isolates caudate lobe from inferior vena cava (IVC). The anhepatic phase were 30.92 9.1 mins. The alanine transaminase levels were 138-2027 U/L, with a median 361.5 U/L. All ALT level reduced gradually down to normal in the following 7-10 days. Only two recipients showed high level of ALT more than 1000 U/L. One third of patients did not transfuse red blood cells (RBC) in operation process. 4 of 12 cases appeared to early allograft dysfunction, while others recovered smoothly.
Conclusion: The new technique of recipient hepatectomy with preservation of the IVC could be helpful for the achievement of liver transplantation. This new technique would shorten the anhepatic phase and decrease transfusion. It can be used for most patients and does not increase risk of complication or impair the prognosis.

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Vascular anastomosis of liver retransplantation for graft failure after pediatric living donor liver transplantation

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Background: Liver retransplantation is the only fundamental treatment for graft dysfunction after pediatric living donor liver transplantation (LDLT), but is technically complicated. Here, the vascular anastomosis of liver retransplantation was examined.
Patients and methods: We have performed 309 liver transplantation (LT) for 300 recipients through August 2018. Thirteen patients received a retransplantation, one of whom received the third graft. The total number of retransplantation was 14 times. Four patients of retransplantation underwent the initial LT at other hospital. The original liver diseases included biliary atresia in 9 cases, Alagille syndrome in 1, fulminant hepatitis in 1, primary sclerosing cholangitis in 1, and neonatal hemochromatosis in 1. Left lateral segment graft (domino graft in 1 case) was mostly used, and then, left lobe or monosegment graft was selected.
Results: Although hepatic vein anastomosis in the initial LT was relatively simple, inferior vena cava (IVC) transection, addition of anterior wall patch for IVC, and anterior wall incision of initial graft vein were performed in the retransplantation. In portal vein anastomosis, there were 2 cases of vascular graft interposition in the initial transplantation and retransplantation, respectively. As vascular graft, the ovarian vein of the donor in the initial LT and the inferior mesenteric vein and the splenic vein of the donor in retransplantation were used. Hepatic artery anastomosis by 9-0 nylon interrupted suture was done in end-to-end fashion under a microscope. In the recipient, the left or right hepatic artery was basically used, but proper hepatic artery, the first jejunal artery, or the branch patch between left hepatic artery and anterior-posterior area of the right hepatic artery was selected in the retransplantation.
Conclusion: Vascular anastomosis of liver retransplantation for graft failure after pediatric LDLT is often more complex. More careful and advanced surgical techniques are required.

P-268

Early allograft dysfunction does not predict graft or patient survival in recipients of living donor liver transplantation

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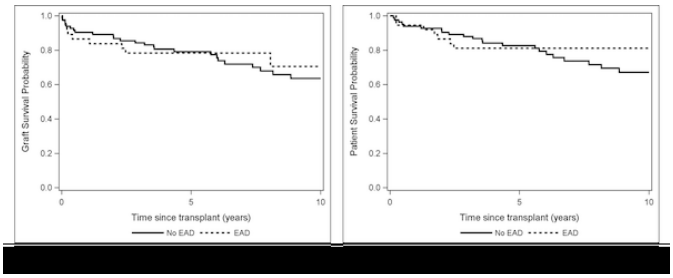
Introduction: Left lobe grafts are utilized in living donor liver transplantation (LDLT) to decrease donor risk, however smaller grafts have been associated with adverse short and long term outcomes in LDLT recipients. Early allograft dysfunction (EAD), defined as INR>1.6 on post-operative day (POD) 7, tbili>10 on POD7, or transaminases > 2000 within the first seven days after transplant, is associated with smaller grafts and inferior recipient outcomes after LDLT. The purpose of this study was: 1) to determine whether a difference in predicted and actual graft volumes predicted EAD, and 2) to evaluate whether EAD predicted graft and patient survival in LDLT recipients.
Methods: Demographic, clinical, and laboratory data were collected from LDLT donors and recipients at our institution from 2003-2016. Statistical analyses were performed using Wilcoxon rank sum, chi-squared tests, regression modeling, and Kaplan-Meier methods.
Results: 136 patients underwent LDLT; 123 are included with full data. Recipients were predominantly female (54.5%), related to their donor (71.0%), transplanted for HCV (34.1%), and received a left lobe (51.2%). Among all recipients, the median predicted graft volume was 755 cm^3, median actual graft volume was 600 cm^3, and median actual:predicted ratio was 0.78. Thirty seven (30.8%) patients developed EAD. Patients with EAD were more often recipients of a left lobe, but there were no other significant differences. In univariate and multivariable analyses, actual versus predicted graft volume did not predict development of EAD. There was no significant difference in graft or patient survival when outcomes were stratified by EAD (Figure 1).
Conclusion: EAD correlates with graft and patient survival in recipients of deceased donor liver transplantation. Our findings demonstrate that EAD occurs more frequently in recipients of left lobes, but that EAD does not impact graft or patient survival in LDLT recipients.



[Figure 1]

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Health status of living-donor liver transplantation in a new transplant center of Vietnam

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There were 34 out of 66 liver transplants from 2007 to 2017, were donors being alive in Vietnam. Living donor liver transplantation is a remarkably effective lifesaving procedure for patients with end-stage liver disease. Since 2017, 108 Military Central Hospital has performed three liver transplants from living donor. This study was conducted with the aim to describe the health status and the ability of liver growth of living donor after hepatectomy.
Method: Retrospective combines a cross-sectional in all 3 patients who were living-donor liver transplantation in 108 Military Hospital. Liver and kidney function as well as red cell, white cell, and platelet counts were measured before hepatectomy and post-transplant management.
Result: All patients were under right hepatectomy. The age range was 25-year-old to 35-year-old. The surgery took 61.8% of liver volume on average from donors. The mean number of days in the intensive care unit was 4.3 days (3-6 days). The mean of hospital stay after hepatectomy was 16 days (15-18 days). The kidney function of all patients which was measured by urea and creatine indicators was stable during the hospital stays. The liver function was fluctuated, however, after the 4th day these indicators were improved. A donor developed obstructive jaundice on the 3rd day after the operation. Two weeks after the operation, the liver function of the donors has been adapted to normal activities with decreased liver enzymes and improved bile secretion. The left livers accounted for about 38.2% of the total liver volume before donor, grew up to 61.9% after two weeks. All patients were discharged from the hospital with stable health.
Conclusion: It took about two weeks for the donor to recover from the surgery. The remainder of the donor´s liver grew back well. Good post-transplant management will be helpful to minimize the morbidities in living donor.

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Approach to dual S4 (segment 4) artery during living donor hepatectomy

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Background: Occasionally in right lobe living donor liver transplant, there is dual arterial supply to S4 with one artery arising from distal right hepatic artery (RHA). To prevent ischemic necrosis of S4, the options are, to recover graft with a shorter RHA or two arteries (compromise approach). Other approach is to ligate the vessel with potential to undermine donor safety (sacrifice approach). We report our approach to similar situation in 9 such cases.
Materials and methods: Out of 296 cases transplanted till date, 9 cases had dual S4 supply, which needed either approach. We used intra-operative Doppler to assess the dominant artery supplying S4. Bulldog clamp was placed on S4 artery arising from RHA. In 2 cases Doppler showed no or poor flow to segment 4 from contra-lateral artery, RHA was cut distal to the origin of S4 artery with resultant 2 artery in the Right lobe graft (compromise approach). Seven out of 9 cases had good flow to S4 from contra-lateral artery arising from LHA. In these cases the clamped artery was safely ligated (sacrifice approach). Propensity score matching was used to compare post-operative LFTs, bile leak, ascitis and hospital stay of these 7 cases with single S4 artery donor hepatectomy
Results: There was no difference in terms of post-operative LFTs, bile leak, ascitis and hospital stay between single S4 and dual S4 artery donor hepatectomy

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Robotically created jejunogastrostomy to regain endoscopic access to Roux-en-Y hepaticojejunostomy after right lobe live liver transplant

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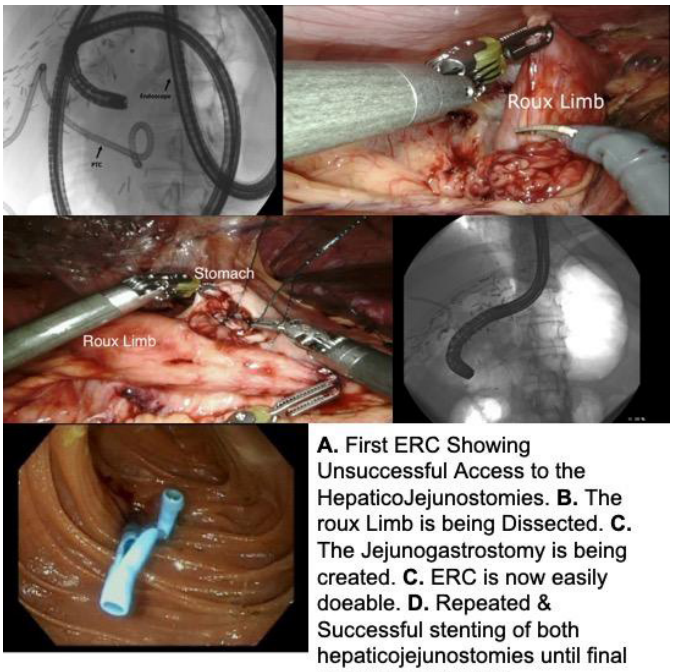
Introduction: Biliary strictures are common after live donor liver transplantation. When a roux limb is used, Endoscopic Retrograde Cholangiography (ERC) is commonly not possible. Percutanous Cholangiography Tubes (PTC) are the second choice, but they are morbid and often unsuccessful in resolving strictures.
Case report: Patient is a 22 year old female with combined Primary Sclerosing Cholangitis (PSC). She received a right lobe live liver transplant. Biliary reconstruction was done with two independent hepaticojejunostomies to a roux limb. Anastomotic strictures developed at both ducts about a year later. PTC was tried, only one duct was successfully cannulated. Attempted ERC failed due to anatomy. After multiple failed PTC´s and episodes of cholangitis we decided to devise a surgical approach. Options were revision of the biliary anastomoses, which was the highest risk option, Hutson loop, which will commit her to a stoma, or open jejunogastrostomy (JG). We elected to perform a side to side JG using robotic assisted surgery. This allowed access far from the original field of surgery. This was immediately accessible in the OR. Four weeks later we started ERC´s and both ducts were stented. Less than six months later patient is stent free with no episodes of cholangitis.
Conclusions: Robotic assisted surgery can be a valuable tool to perform complex new operations like one mentioned above. The magnification and reticulation offered by the technology allows the minimally invasive technique to applied safely.



A. First ERC Showing Unsuccessful Access to the HepaticoJejunostomies. **B.** The roux Limb is being Dissected. **C.** The Jejunogastrostomy is being created. **C.** ERC is now easily doeable. **D.** Repeated & Successful stenting of both hepaticojejunostomies until final result was achieved

[Steps Illustration]

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Single center experience of liver transplantation for primary hyperoxaluria type 1

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Background: Primary hyperoxaluria type-1 (PH1) is a rare autosomal recessive disorder caused by impaired activity of hepatic-specific enzyme alanine-glyoxylate aminotransferase (AGT) that leads to nephrocalcinosis and end-stage renal disease (ESRD). A definitive diagnosis is often delayed until ESRD appears. We present our management of young adult with PH1 with ESRD on hemodialysis (HD) who underwent liver and kidney transplantation (LKT) at our institution.
Methods: From 2012 to 2017, we retrospectively reviewed medical records of 2 patients undergoing LT for PH1.
Case1: 28-year-old woman had suffered from kidney stone recurrences from 17 years of age. Transurethral lithotripsy was performed at age 24 years, and she was initiated on HD due to renal failure at age 27 years. The serum level of oxalic acid was high, and the AGT level in the liver tissue was decreased. She was given a diagnosis of PH1. Living donor liver transplantation (LDLT) was performed at age 28 years, and received LDKT from the same donor 9 months after LDLT. HD was successfully withdrawn. She is doing well.
Case2: 39-year-old man had suffered from kidney stone recurrences from 9 years of age. From age 10 years, extracorporeal shock wave lithotrity (ESWL) was performed several times. He was given a diagnosis of PH1 at age 28 years, and he was initiated on peritoneal dialysis due to ESRD at age 29 years and HD had been introduced at age 37 years. Simultaneous deceased donor liver and kidney transplantation (DDLKT) was performed at age 39 years. HD was maintained for 3 months to decrease serum level oxalic acid. He is doing well.
Conclusions: LKT an acceptable treatment for PH1 patients with ESRD. An early diagnosis of PH1 is important, and preemptive LT alone can provide a good chance of cure for PH1 patients.

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Cystic duct patch closure of remnant bile duct in living donor hepatectomy when primary closure is difficult: an easy solution

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Background: In living donor hepatectomy, hepatic duct division is a crucial step and often a technical challenge, with the aim of obtaining a good hepatic duct for anastomosis in the recipient and an adequate stump in the donor for closure. Very rarely, after duct division, the remaining stump may not be adequate for primary closure. In such a difficult situation the options would be either to close stump transversely or RYHJ. We describe a novel surgical technique of "Cystic duct patch repair", utilizing the available local tissues for closure of bile duct wall.
Case description: This is a 28 years old donor with Type I Biliary anatomy (Choi et al classification) whose right duct had been cut flush with the common hepatic duct. Completion cholangiogram, after graft retrieval and bile duct stump closure, revealed narrowing of CHD at the site of closure. Sutures were dismantled and repaired with a cystic duct patch. Post operative period was uneventful and MRCP 2 years later didn't show any evidence of biliary stricture.
Surgical technique: The neck of the gallbladder and cystic duct used for transcystic cholangiogram was fashioned to the size of defect of the transection site on the CHD. After aligning proper orientation, a single layer tension free anastomosis was done between the wall of gall bladder neck and the defect in the CHD with interrupted 6.0 PDS sutures. Completion cholangiogram after the anastomosis with 20G peripheral intravenous catheter placed in the CBD didn't show any anastomotic leak or narrowing of the duct.
Conclusion: In living donor hepatectomy, "Cystic duct patch closure" may be used if the post closure cholangiogram is not satisfactory. Although the best method is prevention by ensuring a stump for closure, very rarely this error can occur and can be sorted by cystic duct patch repair.

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Living related donor liver transplantation for a large hepatocellulair carcinoma in an identical twin

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Background: Hepatocellular adenoma (HCA) is a benign estrogen sensitive liver tumor that rarely develop into a hepatocellular carcinoma (HCC). HCA's are asymptomatic and occasionally found. According to guidelines, HCA should be excised when they grow fast or are >5 cm. Sometimes HCA are ß-catenin positive and thereby more susceptible to HCC transform. These HCCs are often large and thereby beyond all curative treatment algorithms. In some cases, an alternative curative treatment could be offered as described in the case.
Method: A 32-year-old woman presented with pain and a swollen abdomen six month after pregnancy. Additional investigations including sonography, MRI and liverbiopsy confirmed the diagnosis HCC with remnants of a HCA. The tumor was 23cm in the right and 7cm in the left lobe, not eligible for liver transplantation according to all criteria.
During the operation for resection, the volume of the multifocal tumor appeared to be too large as it involved the whole right lobe but also segment 2/3/4 and liver veins. A living donor liver transplantation (LDLT) as an alternative option was questioned because her sister was an identical twin.
Results: After ethical approval, and preoperative screen a hemi hepatectomy took place. The postoperative recovery of both women was uncomplicated and nearly four years later the physical, psychological and liver biochemistry are normal without immunomodulatory medication.Histological and genetic investigations showed an inflammatory hepatocellular adenomaand HCC with an exon 8 (CTNNB1:p.N387K) ß-catenin mutation.
Conclusion: To date three LDLT in identical twins have been described with long term HCC recurrence free follow up. Especially this case would usually not considered for transplantation. The lack of postoperative immunosuppression may be crucial to improve oncological outcome of patients with HCC out of Milan after transplantation. Therefore, tolerance inducing concepts may be a future approach to increase survival in HCC limited to the liver.

P-275

Conjoined venoplasty using recipient umbilical portion of portal vein in type III portal vein anomaly

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Background: Anomalous portal vein (PV) branching of the donor liver is uncommon and usually makes two, or rarely, more separate PV branches at the right liver graft. Autologous PV Y-graft interposition has long been regarded as the standard procedure, but is currently replaced with the newly developed technique of conjoined unification venoplasty (CUV) due to its superior results. Herein, we presented a case of CUV application to two PV openings of a right liver graft using recipient umbilical portion of portal vein.
Methods and results: The recipient was a 55-year-old male patient with hepatitis B virus-associated liver cirrhosis. The living donor was his 31-year-old son who had a type III PV anomaly. We used umbilical portion of recipient PV. After putting right anterior and posterior PV together and sutured half, we add recipient umbilical PV to make one lumen. After portal reperfusion, the conjoined PV portion was bulged enough to deliver portal flow. The patient recovered uneventfully from the liver transplantation.
Conclusion: When type III portal vein anomaly was found, conjoined venoplasty using recipient umbilical portion of portal vein can be a useful technical option for reconstruction of anomalous PVs.

P-276

Asymptommatic late hepatic artery thrombosis after living donor liver transplantation: a case report

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Objective: Late hepatic artery thrombosis (HAT) is a rare complication after orthotopic liver transplantation and generally associated with a milder clinical course than acute HAT. We report an asymptomatic late hepatic artery thrombosis after living donor liver transplantation. The patient was well recovered without retransplant.

Description: The recipient was a 59 years old male with the right lobe graft. Postoperative day 58, after successfully treating of CMV infection, he had abnormal liver enzyms tests, without any clinical symptom. CT scaner showed no specific changes of the graft, we suspected acute rejection, therefore liver biopsy and steroid pulse therapy were applied; liver biopsy results found no rejection and the level of serum liver enzyms were still high. Angiogram showed hepatic artery thrombosis at the anastomose site, but there were some collaterals. Because there was no donor for retransplant, close observations and prophylatic treatments were conduced. 4 months after liver transplantation there was no biliary complication.
Discussion: HAT is usually associated with CMV infection. Angiography is better than CT in diagnose HAT and confirm if collaterals is available. Colaterals was the good prognosis factor even though it wasn't enough. Prophylatic treatments and close observations including blood test and CT scaner are very usefull. Retransplant should be considered but not always available.
Conclusions: Late HAT with good colaterals could be recovered without retransplant. Digital Subtraction Angiography is usefull to detech those colaterals.

P-278

Living donor right lobe liver graft re-transplantation in adult

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With the population of post-transplantation continues to expand, re-transplantation is the ultimate treatment when the transplanted liver is depleted again due to various reasons. The patients of re-transplantation will confront more complex challenges. It is of great practical significance to improve the relevant techniques of re-transplantation and to summarize the experience. Our transplant center implemented an adult living donor right lobe graft re-transplantation, patient who underwent a second LT successfully. Herein, we describe the patient who underwent living donor re-transplantation. When she was 21 years old, she LT in other hospital one year ago due to "explosive liver failure, drug-induced liver damage". The hepatic artery was found to be blocked by ultrasonography after one month, and the anticoagulant was continued. Despite medical treatment, her liver functions worsened, and the patient came to our hospital for further treatment. The second time, her mother was the donor and she recovered after the Living Donor Right Lobe Liver Graft re-transplantation in adult right lobe liver graft re-transplantation. It has not been reported in China, and the treatment experience is summarized. It is hoped to provide useful reference for clinical colleagues.

P-279

Anastomosis of portal vein and bile duct anomaly in living donor liver transplantation

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Introduction: We report our experiences of type 2 portal vein and bile duct anastomosis during living donor liver transplantation.
Case: Forty-four years old man was admitted for generalized weakness. He suffered from CVH-B for 20 years and 2years ago diagnosed LC with HCC. Primary HCC was treated by percutaneous RFA and recurred HCC was by TACE twice. After TACE generalized weakness, ascites were progressed. Hepatic encephalopathy was developed. Living donor liver transplantation was decided. Donor was 27-year-old son. GRWR was 1.48. Preoperative donor abdomen CT scan was revealed trifurcation of portal vein and low-lying right posterior hepatic duct. Middle hepatic vein branches were double in S5 and single in S8 level. Donor hepatectomy was performed as modified extended right hepatectomy (weight = 850gm). During bench operation neo-middle hepatic vein was reconstructed by use of iliac vein allograft. Lumens of graft portal vein were double. So left saphenous vein autograft patch was fenced to the graft portal veins for making single lumen. Graft was transplanted to recipient from right hepatic vein, portal vein, neo-middle hepatic vein and then right hepatic artery. Bile ducts were make common cannel in manner of V-shaped plasty then anastomosed to recipient bile duct. Total operation time was 632 minutes cold ischemic time was 40 minutes for bench operation. Maximal AST/ALT was 230/207IU/ml at POD #1 then normalized at POD #5 and #15 each. Postoperative abdomen CT revealed patent portal vein, neo-middle hepatic vein and hepatic artery. There was no congestion area in the transplanted liver. Patient was discharged at POD #34.
Conclusion: In the living donor liver transplantation, there were many anatomical difficulties in anastomosis due to anatomical variation especially in portal vein and bile duct. Portal vein fencing and bile-ductoplasty can be a good choice.

Poster Round I, Session 1, 2, 3: Machine Perfusion

P-280

Viability testing and transplantation of marginal donor livers (VITTAL) Trial: Metabolomics of normothermically perfused livers discloses molecular signatures predictive of graft viability and postoperative outcomes

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Background and Aim: Donor organ shortage has led to increased reliance on high-risk livers for transplantation. Furthermore, emergence of machine perfusion has led to a paradigm shift in organ preservation from functional suppression to full ex vivo metabolic support. The recently completed VITTAL trial demonstrated that normothermic machine perfusion (NMP-L) provides an opportunity to objectively assess graft quality and functional integrity to safely transplant high-risk livers rejected by all transplant centres. This study investigated the potential of metabolic profiling to elucidate molecular signatures during NMP-L predictive of graft viability, post-reperfusion syndrome (PRS) and early allograft dysfunction (EAD) in these discarded livers.
Methodology: All livers were deemed marginal according to established high-risk criteria, and rejected by all transplant centres. 31 livers underwent NMP-L for a minimum of four hours, at which point a decision was made to transplant based on established viability criteria. Perfusate aliquots from graft perfusion commencement to 4-hour time point were collected. Samples were centrifuged and the supernatant subjected to an untargeted metabolomics analysis using Ultra High Performance Liquid Chromatography-Mass Spectrometry.
Results: 22 livers were transplanted after achieving viability criteria. Univariate statistical analyses revealed more than 20 metabolites ($q < 0.05$) differentiating liver metabolic profiles according to viability criteria fulfilment following 4 hours of perfusion. Key changes were detected in metabolites relating to lipid, phospholipid and sphingolipid metabolism, notably upregulated in the non-viable group. In transplanted cohort; after 4 hours of perfusion 52 metabolites distinguished EAD(n=7) from non-EAD livers(n=15) and PRS group(n=10) revealed changes in 36 metabolites compared to non-PRS group(n=12).
Conclusion: This study reveals a metabolic signature of high-risk livers that correlates with VITTAL criteria for graft viability for transplantation during NMP-L. It also demonstrates the potential of NMP-L metabolic profiling as a clinical tool to objectively assess the quality and predict functional integrity of these livers pre-implantation.

P-281

Initial report of siRNA uptake during normothermic and hypothermic liver machine perfusion: a promising new therapy

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Background: RNA interference (RNAi) is a natural gene modulation process that was recently approved for clinical use and has great potential for treatment of many pathological conditions. The surface receptor FAS and tumor suppressor p53 are implicated in ischemic liver damage. Both may be silenced via RNAi with limited off-target effects. We determined the efficiency of FAS siRNA delivery with lipid nanoparticles during normothermic (37°C) and hypothermic (4°C) ex vivo machine perfusion. We also show silencing p53 via siRNA reduces inflammation and caspase expression during liver ischemia.
Methods: Rat portal veins were cannulated (Fig. 1A) and perfused at 10mmHg on a closed-loop pump circuit regulated by circulating water bath (Fig. 1B). Controls were perfused with Williams E+10U insulin and lipid nanoparticles (Fig. 1C). Normothermic livers were perfused with medium plus nanoparticle/FAS-siRNA complex with 3'-AlexaFluor-555 modification at 37°C. Hypothermic livers were perfused similarly at 4°C. Biopsies were collected at 4 hours, formalin fixed, stained, then imaged with confocal microscopy. For p53 studies, siRNA was delivered 24 hours before hilum clamping. Tissue/blood was collected 3 days after siRNA injection.
Results: Compared to empty vector controls (Fig. 2A-D), normothermic (Fig. 2E-H) and hypothermic livers (Fig. 2I-L) perfused with FAS siRNA demonstrate diffuse uptake in sinusoids and surrounding central veins. SiRNA is observed together in sinusoid membranes and in hepatocyte cytoplasm. Livers pretreated with p53 siRNA showed reduced cellular infiltration, vacuolization, and fewer caspase-3 positive cells.

Conclusions: By incorporating RNAi into preservation solutions or delivering before procurement, we may reliably improve the quality of livers during the ischemic period. It will be important to determine the ideal perfusion temperature. Further studies will quantify uptake with peptide-nucleic acid hybridization at both perfusion temperatures and the degree of FAS or p53 silencing in a transplant model.

Figure 1:

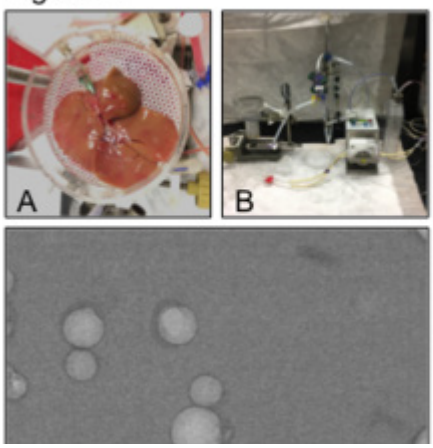
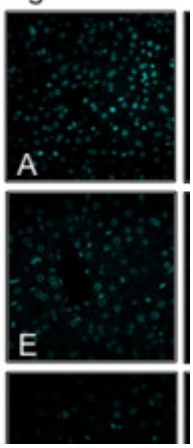


Figure 2:



[FAS Data Figure]

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Normothermic ex situ liver perfusion of donation after cardiac death grafts improves mitochondrial function

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Background: The Normothermic ex vivo liver perfusion (NEsLP) technique reduces reperfusion injury of donation after circulatory death (DCD) grafts and improves post-transplant outcomes. We aimed to understand the mechanistic basis of this improvement using high-throughput metabolomics.
Methods: Pig livers from 8 DCD donors with 30 minutes of warm ischemic time were preserved for 8 hours at cold static storage (CS, n=4) or perfused for 5 hours on NEsLP machine (n=4). Grafts were then transplanted into recipients, and animals sacrificed at day 7 post-transplantation. Liver tissues were collected at: 8 hours following preservation (T0) and 2 hours following liver transplantation (T1). Snap-frozen tissue was processed and analyzed by Sciex 6600 Q-TOF high resolution mass spectrometer. Three platforms of metabolites were compared atT1 vs T0 for both Cold storage and NEsLP: Fatty Acids, Amino Acids and Pentose Phosphate/TCA/Glycolysis Pathway. Data analysis was performed using MetaboAnalyst 4.0, with ANOVA-Simultaneous Component Analysis and Multivariate Empirical Bayes Analysis.
Results: A total of 50 statistical relevant metabolites were identified in the time course analysis obtained in NEsLP compared to COLD grafts **(Table 1)**. Lactate and acyl fatty acid derivative esters of carnitine were most significantly decreased following transplantation with NEsLP versus COLD organs. Tryptophan and alpha-ketoglutarate were significantly higher in NEsLP versus COLD group over time **(Figure 1)**.
Discussion: Compared to cold stored preservation, NEsLP-preserved DCD grafts have lower lactate and Acyl Carnitine-related metabolite concentrations following transplantation, indicating better mitochondrial function and β-oxidation. Additionally, tryptophan and alpha-ketoglutarate production were significantly increased in NEsLP organs, reflecting improved amino acid metabolism leading to protein synthesis. This high-throughput metabolomics study clearly provides a mechanistic rationale for NEsLP in improving graft function in DCD grafts as compared to cold storage alone.

Figure 1: Changes in Abundance of Metabolites Over Time

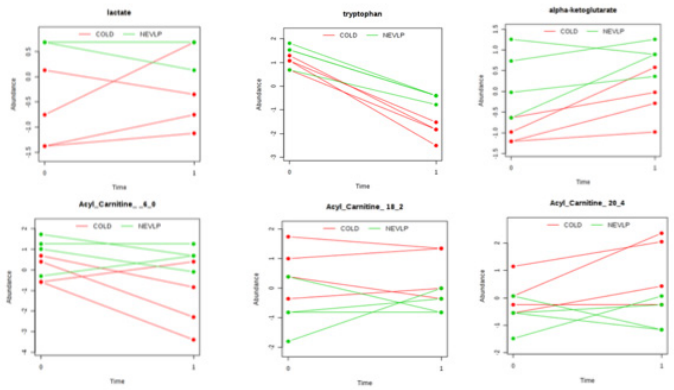

Table 1: Top 50 features identified by MEBA

	Compounds	Hotelling-T2
1	lactate	15.7192
2	tryptophan	15.34322
3	alpha-ketoglutarate	12.06549
4	Acyl_Carnitine_ _6_0	10.86261
5	Acyl_Carnitine_ 18_2	9.03194
6	Acyl_Carnitine_ 20_4	8.74487
7	phenylalanine	6.5822
8	Acyl_Carnitine_ 22_5	6.03624
9	4-aminobutyrate	5.97618
10	lysine	5.93937
11	tyrosine	5.75745
12	arginine	5.68636
13	dihydroxyacetonephosphate	5.53434
14	Acyl_Carnitine_ C4-OH	5.50636
15	Valeryl _Carnitine	5.32356
16	ornithine	5.22639
17	Propionyl _Carnitine	5.08382
18	leucine	4.97065
19	Acyl_Carnitine_ C5DC	4.84827
20	Acyl_Carnitine_5_1	4.81208
21	malate	4.33057
22	Acyl_Carnitine_ 18-OH	3.81352
23	glutamate	3.52683
24	Acyl_Carnitine_ 18_3	3.31857
25	Hydroxy-Palmitoyl _Carnitine	3.22837
26	proline	3.04153
27	phosphoenolpyruvate	3.00638
28	3-phosphoglycerate	2.86685
29	isoleucine	2.86198
30	2-Hydroxygluterate	2.80692
31	citrulline	2.72672
32	Acyl_Carnitine_ 16_1	2.63376
33	ribose-5-phosphate	2.53454
34	methionine	2.45862
35	fructose-6-phosphate	2.22689
36	alanine	2.07741
37	valine	1.91406
38	Acyl_Carnitine_ 10_0	1.89921
39	Acyl_Carnitine_ 18_1	1.57521
40	serine	1.19755
41	_Carnitine	1.05521
42	Hypoxanthine	1.05377
43	Acetyl_Carnitine	0.89599
44	Palmitoyl _Carnitine	0.87803
45	threonine	0.7078
46	Pipecolic Acid	0.69802
47	Butyryl _Carnitine	0.66416
48	Acyl_Carnitine_ 20_0	0.62729
49	Stearoyl _Carnitine	0.33799
50	succinate	0.28704

[figure 1]

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Viability testing and transplantation of marginal donor livers (VITTAL) trial outcomes: bile duct injury assessment during the normothermic machine perfusion of discarded livers

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Background: Histological evidence of donor bile duct injury (BDI) prior to transplantation is known to correlate with development of post-transplant biliary complications. We aimed to analyse BDI on discarded donor livers that were transplanted following viability testing by normothermic machine perfusion (NMP) in the VITTAL clinical trial.
Method: Bile duct (BD) biopsies from 22 livers were obtained before NMP and post-reperfusion prior to abdominal closure. The assessment consisted of grading the injury to the deep peribiliary glands, stromal and arterial necrosis, thrombi and haemorrhage (Op den Dries 2014, Hansen 2012) and the overall score (0 no injury, 1 minimal, 2 mild, 3 mild to moderate, 4 moderate, 5 moderate to severe, 6 severe;) was correlated with development of post-transplant biliary strictures.
Results: The 22 transplants consisted of 12 livers from donors after brainstem death (DBD) and 10 from donors after circulatory death (DCD). Ten recipients (45%) developed BD irregularities seen on magnetic resonance cholangiogram performed 6 months following transplantation. Over a 297-day median study follow-up period, 5 (23%) patients remained clinically asymptomatic, 1 (5%) patient developed an anastomotic stricture successfully managed by stenting and 4 (18%) patients developed non-anastomotic strictures (NAS) requiring re-transplantation. Of these, three were in recipients of DCD livers (n=3) and one in a DBD recipient who developed early hepatic artery thrombosis. Pre-NMP and post-reperfusion BDI correlated with the development of biliary strictures (p< 0.001) and BDI increased significantly in post-reperfusion biopsies in those patients who subsequently developed strictures (p=0.003).
Conclusions: Current BDI scores apply to livers undergoing viability assessment and the degree of injury during NMP could predict grafts at risks for development of NAS. Analysis of perfusate and bile samples may yield biomarkers related to BDI.

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Biliary bicarbonate, pH and glucose are suitable biomarkers of biliary viability during ex situ normothermic machine perfusion of human donor livers

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Background: Ex situ normothermic machine perfusion (NMP) can be used to assess viability of suboptimal donor livers prior to implantation. Our aim was to assess the diagnostic accuracy of bile biochemistry for the assessment of bile duct injury (BDI).
Method: In a preclinical study, 23 human donor livers underwent 6 hours of end-ischemic NMP to determine biomarkers of BDI. Livers were divided into groups with low or high BDI, based on a clinically relevant histological grading system. During NMP, bile was analyzed biochemically and potential biomarkers were correlated with the degree of BDI. Receiver operating characteristics curves were generated to determine optimal cut-off values. For clinical validation, identified biomarkers were subsequently included as viability criteria in a clinical trial (n=15) to identify transplantable liver grafts with low BDI.
Results: Biliary bicarbonate and pH were significantly higher and biliary glucose was significantly lower in livers with low BDI, compared to high BDI. The following cut-off values were associated with low BDI: biliary bicarbonate >18 mmol/L (P=0.002), biliary pH >7.48 (P=0.019), biliary glucose < 16 mmol/L (P=0.013), and bile/perfusate glucose ratio < 0.67 (P=0.013). In the clinical trial, 11 out of 16 livers met these criteria and were transplanted successfully. One patient developed post-transplant cholangiopathy. During NMP, this graft, along with the other non-transplanted livers, had a low delta between biliary and perfusate bicarbonate and pH.
Conclusion: Biliary bicarbonate, pH, and glucose during ex situ NMP of liver grafts are accurate biomarkers of BDI and can be easily determined point-of-care, making them suitable for the pre-transplant assessment of bile duct viability. Results from the clinical study showed that a low delta between biliary and perfusate bicarbonate and pH may be even better suited for predicting low biliary viability. These biomarkers may improve graft selection and decrease the risk of post-transplant cholangiopathy.

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The synthesis of coagulation factors during normothermic machine perfusion of livers is impaired by ischemia in pigs and might predict graft viability

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Normothermic Machine Perfusion (NMP) allows to test liver viability during preservation. Coagulation factors (F) are synthetized by the liver, hence are candidate markers of function. We evaluated the production of F during NMP, tested if ischemia alters their synthesis, and correlated their levels with markers of hepatocyte damage (AST) and sinusoidal endothelial injury [Hyaluronic acid (HAc)]. Porcine livers exposed to 60min Warm Ischemia (WI60, n=5) or not (WI0, n=5) were NMP perfused for 6h. The concentration of FV, FVIII, and FX was measured at 15, 30min, 1, 2, 3, and 6h of NMP and compared within and between groups. Levels of AST and HAc were correlated to FV and FVIII. Mean ±SD is given. FV increased over time in both groups, although a peak was reached at 2h of NMP in WI0 only. FV concentration was inferior in WI60 vs. WI0 (p< 0.0001). FVIII raised in both WI0 and WI60, reaching a peak at 3h only in WI0. FVIII concentration was inferior in WI60 vs. WI0 (p=0.006). FX increased over time in WI0 and its levels were higher than in WI60 (p=0.001). The area under the curve of AST was greater in WI60 (3077) vs WI0 (405.3, p=0.0006). FV was inversely and strongly correlated to AST at all time points (r:-0.93, p=0.001 at 1h NMP). HAc levels increased in both groups but were higher in WI60 vs WI0 (p=0.004). FVIII was inversely correlated to HAc at 1h (r:-0.58, p=0.02) and 2h (r:-0.59, p=0.03). Coagulation factors are synthesized by hepatocytes and sinusoidal cells during NMP of porcine livers and their synthesis is impaired by WI. Measuring FV and FVIII during NMP can provide additional information about hepatocellular and sinusoidal function and may help discriminate functioning from failing livers within few hours of NMP before transplantation.

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Ischemia-free liver transplantation protects bile duct from ischemia reperfusion injury

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Background: Ischemic-type biliary lesions, are a major source of graft loss after liver transplantation, which mainly due to the ischemia/reperfusion injury (IRI) of biliary tree. Ischemia-free liver transplantation (IFLT), based on normothermic machine perfusion and innovations in surgical technique, can provide continue blood supply from procurement to implantation that would avoid IRI of bile duct. We aimed to investigate whether IFLT reduces IRI injury of the bile duct, by accessing bile duct epithelial cell morphology and function in human liver transplantation.
Method: Fifteen livers from donation after brain death (DBD) were transplanted by IFLT and 15 matched DBD livers transplanted by SCS served as controls. Bile duct biopsies and bile samples were collected before transplantation and after reperfusion/re-vascularization. Histological severity of biliary injury was compared according to an established semiquantitative grading system. Biliary epithelial cell function was assessed by measuring pH, bicarbonate and glucose concentration in bile. The concentrations of GGT and LDH in bile were measured as biomarkers of biliary injury.
Result: Results of the histological grading of bile duct injury demonstrated significantly minor injury of the biliary epithelium and peribiliary glands in IFLT (Figure 1). In IFLT, bile continually produced throughout procurement, preservation and implantation, however, bile almost produced after hepatic artery reperfusion in SCS. The biochemical parameters of bile were significantly different in two groups. The bile pH, bicarbonate, bilirubin and bile acid were significantly higher but the biliary glucose was much lower in IFLT, compared to SCS. LDH in bile of SCS was hundreds or even thousands of times higher than IFLT, which can serve as a sensitive marker of biliary injury.
Conclusion: This study suggests that the innovate technique IFLT keep physiological function during transplantation and significantly reduces the injury of bile ducts in liver transplantation.

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Viability testing and transplantation of marginal donor livers (VITTAL) trial outcomes: effectiveness of the lactate clearance-based viability criteria to discriminate hepatobiliary injury and post-transplant complications

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Background: The VITTAL clinical trial validated criteria for transplantation based primarily on lactate clearance. The aim of this study was to correlate lactate clearance with the degree of hepatobiliary injury during normothermic machine perfusion (NMP) and to identify other criterion that could help predict post-transplant outcomes.
Methods: The viability of discarded high-risk donor livers was assessed during 4 hours of NMP principally based on lactate levels ≤2.5mmol/L. The livers were supplied with taurocholic acid and the perfusion performed on the OrganOx Metra® device. Perfusate transaminases, bile production and bile properties were assessed and correlated with several post-operative complications.
Results: Twenty-two (71%) out of 31 livers met the criteria and were then transplanted (12 DBDs and 10 DCDs). Non-transplantable livers exhibited higher release of transaminases, suggesting more severe hepatobiliary injury, with peak median ALT 9,667 vs. 2,410 IU/L, p< 0.001; AST 14,033 vs. 4,760 IU/L, p=0.001; GGT 142 vs. 118 IU/L, p=0.051. Perfusate transaminase levels did not predict early-allograft dysfunction (EAD), post-reperfusion syndrome (PRS) or non-anastomotic biliary strictures (NAS) post-transplantation, but there was a trend between peak ALT during NMP and the recipients' peak post-transplant ALT ([Spearman's]r=0.445; p=0.063). Eight (36%) patients had non-anastomotic bile duct regularities on MRCP performed at 6 months after transplantation. Over the 297 days median study follow-up, 4 (18%) of these remained asymptomatic and 4 (18%) developed NAS requiring re-transplantation. All severe NAS occurred in recipients of DCD livers (n=3) except one in DBD graft associated with hepatic artery thrombosis. There was a trend towards a lower bile pH in patients with NAS 7.61 (7.50-7.92) vs. 8.00 (7.87-8.00), p=0.006, bile pH cut-off 7.75, AUROC 0.82 (0.49-1.00), p=0.068.
Conclusion: Transaminases levels corelate with lactate clearance during NMP; however, neither predict post-transplant complications. In perfusions with taurocholic acid supplementation, bile pH< 7.75 might predict development of NAS biliary strictures.

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A systematic review and meta-analysis of machine perfusion versus static cold storage of liver allografts on transplant outcomes: the future direction of graft preservation

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Background: Machine perfusion (MP) and static cold storage (CS) are currently the two prevalent methods. The aim of this study was to systematically review the published evidence and conduct a meta-analysis to enhance understanding of the benefits of MP preservation compared with CS preservation.
Methods: Clinical articles exploring the efficacy of MP for liver grafts were searched from the Pubmed, EMBASE and Cochrane Library databases. The primary outcome was early allograft dysfunction(EAD), primary non-function (PNF) and biliary complications, especially ischemic cholangiopathy(IC). Secondary outcomes included hepatic artery thrombosis(HAT), one year graft and patient survival.
Results: A total of 10 studies were eligible for the review, including 1 RCT(222 livers) and 9 prospective cohort study(490 livers). The peak level of aminotransferase with MP preservation was significantly lower in 6 studies(including the recent RCT), but no difference could be observed in the rest 4 studies. The overall incidence of EAD was significantly reduced with MP preservation than CS (OR=0.39; 95% CI, 0.25-0.62; P< 0.0001). There was a lower rate of biliary complications(OR0.53; 95% CI, 0.32-0.87; P=0.01) and ischemic cholangiopathy (OR=0.26; 95% CI, 0.10-0.69; P=0.007) in recipients with MP preservation grafts compared with CS grafts. However, no significant differences could be detected between the two preservation methods in the incidence of PNF, HAT, one year patient survival or one year graft survival.
Conclusion: MP can improve short-term complications for human liver transplantation, with a less clear effect in the longer-term. MP preservation of liver grafts is superior to CS in terms of reducing post-transplant EAD rates, biliary complications and IC. However, MP preservation was not associated with the improvements in incidence of PNF, HAT, one year graft survival or one year patient survival.

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Hypothermic oxygenated machine perfusion enables 24-hour ex situ preservation of porcine donation after circulatory death livers

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Background: End-ischemic hypothermic oxygenated machine perfusion reduces ischemia-reperfusion injury of donor livers during storage and transplantation. However, it is unknown whether this

technique also supports an extension of the ex situ preservation time. We aimed to determine whether liver grafts from donation after circulatory death (DCD) porcine donors can be effectively preserved up to 24-hours using dual hypothermic oxygenated machine perfusion (DHOPE).
Method: Porcine DCD livers were subjected to 2h static cold storage (SCS), followed by 2, 6, or 24 hours DHOPE (n=6 per group), using Belzer UW solution. Hepatocellular and bile duct viability were tested during 4h normothermic ex situ reperfusion with autologous blood. DCD livers preserved by 24h SCS (n=2) served as controls.
Results: In all three study groups, portal venous and arterial flows remained stable during DHOPE. After normothermic reperfusion, there were no significant differences in lactate clearance, blood pH, glucose and alanine aminotransferase levels among the DHOPE-preserved livers. All DHOPE livers produced bile and there were no significant differences in biliary HCO_3^-, pH, and LDH between the groups at 4h after reperfusion. Moreover, levels of malondialdehyde and HMGB-1 (markers for oxidative stress) in serum and liver parenchyma, were similar for all DHOPE-preserved livers. Levels of cell-free DNA, a marker of cell death, were similar between the three groups. Histological analyses of bile ducts and liver parenchyma also revealed no differences. In contrast, livers preserved by 24h SCS did not produce bile after reperfusion and turned bluish with reducing portal and arterial flows, representative for a non-viable liver. Histology revealed massive cellular necrosis.
Conclusion: While 24h SCS preservation of porcine DCD liver grafts leads to primary non-function after warm reperfusion, DHOPE enabled successful ex situ preservation of donor livers up to 24h. If confirmed with human liver grafts, this technique can facilitate logistics of allocation and transplantation.

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First Italian experience with *OrganOx Metra* Normotermic Machine Perfusion used on discarded extended criteria donor livers

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Background: Because of donor shortage, about 20% of potential liver transplant (LT) recipients still die during waiting list. In order to increase donor pool, use of Extended Criteria Donors (ECDs) became a widespread practice. Ex situ Normothermic Machine Perfusion (NMP), preserving organ in a functioning, physiological status, avoids damages caused by current standard static cold storage on marginal grafts.
Methods: At Tor Vergata University, Rome, from January to November 2018, five consecutive regional discarded liver grafts from brain death donors [median age: 58 (range: 41-88) years, median BMI: 27 (range: 21-32), median Donor Risk Index (DRI): 1.5 (range: 1.2-2.0)] underwent NMP with OrganOx Metra. Primary aim of the study was to assess viability and safety of NMP used on regional discarded liver.
Results: Four grafts fulfilled viability criteria and were transplanted. One fatty 3.5 kg liver graft was not considered eligible for LT after OrganOx Metra perfusion and split liver procedure was performed during NMP for research purpose only, in order to prove surgery feasibility. AST peak during first 7 days after LT was 1401 U/L (range: 69-1442). All recipients experienced Early Allograft Dysfunction *(Olthoff et al, Liver Transplantation 2010)*. The median Intensive Care Unit stay was 3 days (range: 2-28), median hospital stay was 14 days (range: 9-70). One patient developed hepatic artery thrombosis on 2nd post-operative day that required re-laparotomy and successful thrombectomy. The median follow-up was 4 months (range: 2-4). The 60-days patients and graft survival were 80%; one patient developed Primary Non Function (PNF) and died during re-transplant.
Conclusion: This is first Italian experience with OrganOx Metra NMP; we finally recruited 80% national discarded liver that finally showed acceptable feasibility and safety profile. Although it represents a preliminary experience and need further validation it could be considered an option for well-compensated recipients allowing minimization of waiting list time in organ-shortage era.

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Early and newly introduced viability criteria for liver graft evaluation during normothermic machine perfusion

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Background: The use of normothermic-machine-perfusion (NMP) opens new frontiers in graft evaluation. The bed-side used viability criteria are derived from clinical routine experience and do not offer a complete quality evaluation. The aim of our study is to optimize graft evaluation and to explore new clinically applicable criteria.
Method: We applied NMP to pig liver grafts form cardiac death (n=6) and brain death donors (n=7). NMP was primed with blood-enriched

perfusion fluid, added with heparin and citrate as anticoagulant. After 240 min of perfusion (45min of rewarming) we divided the grafts according to Mergental et al. criteria (transplantable (LT) and non-trasplantable (n-LT)) plus a sub-optimal (SuO) category. Release ratios are calculated: $(C_{end}-C_{start})/C_{start}$. Results are expressed as mean±standard-deviation.

Results: After 240 min of NMP, 4 graft were classified as n-LT, 5 as SuO and 4 as LT. Hepatocellular damage (AST,lactates,LDH) was increased in n-LT compared to the other groups (Tab.1). Cholangiocellular (ALP) damage was only showed in n-LT. Citrate metabolism, Ionized-Ca, possible expression of citrate metabolism, increased in LT and SuO grafts (Tab.1). Glucose concentration showed a downstream trend in LT and SuO. NMP-parameters during the 45min of rewarming were subsequently evaluated. Glucose release ratio was 0.47±0.14Lt, 1.57±0.12SuO and 0.05±0.8nLT (p< 0.001), lactates release ratio was -0.76±0.21LT-G, -0.36±0.26Sb-G and 0.33±0.41nLT (p=0.022). Potassium release ratio in the two transplantable groups (LT+SuO) was -0.45±0.18 while 0.001±0.43 (p=0.47) in nLT-G.

	LT	SuO	nLT	p
AST, U/L	896 ± 197	1164 ± 830	22315 ± 3559	0.001
LDH, U/L	1039 ± 163	2176 ± 2018	14237 ± 1617	<0.001
Lactates, mmol/L	1.53 ± 0.15	4.5 ± 1.2	18 ± 2	0.024
Ca ratio	0.95±0.24	1.21±0.33	0.17±0.15	<0.001
ALP, U/L	41 ± 3	48 ± 24	311 ± 20	0.018

[Tab.1 NMP variables]

Conclusion: In our study, NMP evaluation allowed us to stratify grafts quality into three categories. Citrate metabolism could be used as novel marker of graft quality. We showed that rewarming graft metabolism characterization enables early graft evaluation with comparable results to 240min NMP. Organizational and safety aspects are clear advantages of early-evaluation strategy.

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First four cases of ante situm resection with hypothermic machine perfusion

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Hepatic tumors in close proximity or infiltrating the IVC and the suprahepatic veins might be resectable only by using high risk techniques such as ante-situm in vivo resection. Hypothermic oxygenated machine perfusion could be superior to standard hypothermic flushing in this setting, as it allows a more widespread diffusion of cold perfusate and oxygen, meanwhile allowing continuous monitoring of vascular resistance and temperature of the organ.

We report the first four cases of ante-situm resection of tumours of the hepatocaval confluence and suprahepatic vein reconstruction, with the assistance of in situ hypothermic oxygenated machine perfusion by LiverAssist. Three patients were affected by intrahepatic cholangiocarcinoma and one by adrenal carcinoma; total vascular exclusion time was always expected to be prolonged due to tumour localization and surgical technique.

Machine perfusion time ranged between 30 and 120 minutes; inflow temperature was 8 °C and outflow mean temperature was 12.4°C; mean PV pressure was 4 mmHg with mean portal flow of 272 ml/min. In all cases we observed fast decrease of ALT, AST, LDH and total bilirubin levels in the first week after surgery. Ninety days mortality rate was 0%; major complications (Clavien >IIIa) included stricture of the suprahepatic anastomosis (2/4), thrombosis of the IVC (2/4), hematoma or abscess on the transection plane (2/4). One patient showed recurrence of disease three months after surgery.

Ante situm resection is associated with high morbidity and mortality rates and should only be proposed to super-selected patients. Hypothermic oxygenated machine perfusion has proven to be useful in improving viability of cold stored organs for transplantation, and its use could be extended to in vivo ex situ surgery, as it decreases the risk of ischemic damage, especially in chemotherapy-injured livers, allowing longer and safer operating time.

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Do liver transplant candidates support clinical research using normothermic machine perfusion (NMP) of livers?

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Introduction: Multiple transplant centers are actively engaged in research using NMP of liver allografts with innovative devices that have yet to complete Food and Drug Administration (FDA) approval. The attitudes of patients to machine perfusion of livers has not been studied. We examined the response of patients at our institution to request for consent in order to assess their support of research using this new technology.

Methods: Our institution began enrollment of recipients in normothermic liver perfusion research in April 2017. Patients were approached by a trained, research coordinator in various settings,

including:
(1) outpatient clinic setting;
(2) inpatient setting—day of transplant; and
(3) inpatient setting—during expedited evaluation for liver transplantation.
Reasons for refusal to enter the trial were collected. Patient demographic data were examined.
Results: 62 patients were approached. Responses were generally very positive - 56 consented to enrollment, while 6 refused (90% acceptance rate). Reasons for refusal included, lack of interest (3, 50%), family uncomfortable (1, 17%), insufficient time (1, 17%), only one patient (17%) feared a negative outcome. An outpatient setting was most likely to lead to participation (28/30, 93%), while discussion at time of expedited inpatient transplant evaluation (16/19, 84%) was less likely. MELD score, gender or recipient diagnosis did not result in greater refusal rates. Spanish-only speaking patients had higher rates of refusal (2/4, 50%).
Conclusion: Very rarely patients expressed concern that NMP might damage their future liver. Patients are overall supportive of this novel approach to organ preservation and are most enthusiastic when approached in an outpatient setting with time for detailed informed consent.

		Agreed (56)	Refused (6)
Age of recipient	18-30	3	0
	31-50	10	1
	51-60	15	1
	61-70	24	4
MELD	0-12	4	0
	12-18	7	1
	19-35	35	3
	>35	10	2
Outpatient		28	2
Inpatient			
Expedited evaluation		18	3
Day of transplant admit		10	1
Spanish-speaking only		2	2

[Characteristics of patient approached for participation stratified by response]

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The study on preservation effect of new organ preservation fluid based on tetramethylpyrazine on rat donor livers with 24 hours ex-vivo HMP

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Objective: Tetramethylpyrazine is the main component of traditional Chinese medicine chuanqiong, and it has been found to have antioxidant and anti-apoptotic effects, we hypothesis that this component can help reduce ischemia reperfusion injury(IRI) in organ transplantation. Therefore, a new organ preservation fluids based on tetramethylpyrazine have been developed by us, and are compared with HTK fluid and normal saline by 24 hours hypothermic machine perfusion(HMP) on rar donor liver, with the aim of determining the opti for investigating the preservation effects of new preservation fluid.
Methods: SD rats(male, 280g±50g) were divided into 3 groups (n=6): tetramethylpyrazine group; HTK group; saline group. Rat donor liver were subjected to 24h of HMP with five kinds of fluids in vitro, and the perfusion fluids were collected (0h,3h,6h,9h,24h) to measure liver function [alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH)], and at 24h, liver tissue was preserved by fixing in 10% neutral formalin for subsequent histological study (histopathology).
Results: Tetramethylpyrazine group were better than normal saline group ($P < 0.05$), HTK group in terms of the degree of edema; and tetramethylpyrazine group's ALT, AST, LDH levers were similar with HTK group all the time, lower than saline group($P< 0.05$) at 24h; in terms of HE staining, the hepatic cords were closely arranged and orderly with complete structure in tetramethylpyrazine group and HTK group, and many hepatocytes were damaged and the hepatocyte gap was significantly enlarged in saline groups.
Conclusion: In vitro HMP, organ preservationm fluid based on tetramethylpyrazine has the best performance in various properties, similar with HTK and better than normal saline. Therefore, this fluid can effectively reduce ischemia reperfusion injury and has great potential in organ preservation.

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Both hypothermic and normothermic perfusions fail to reduce the magnitude of cancer growth in a prolonged ischemia, donation after cardio-circulatory death liver transplant model

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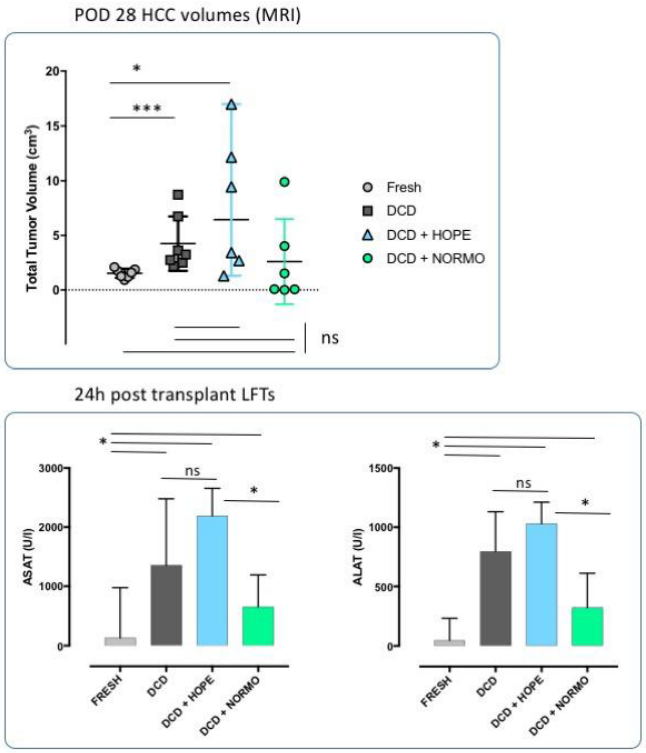
Background: Ischemia/reperfusion injuries facilitate tumor engraftment and growth, as proved by many pre-clinical studies. On the other hand, both hypothermic and normothermic *ex vivo* liver perfusions claim to promote organ recovery in donation after cardio-circulatory death (DCD). We tested whether these perfusions could reduce the risk of post-transplant hepatocellular carcinoma (HCC) growth in 1h-DCD rat livers.
Methods: 1h DCD time in the donors was measured from the onset of ventricular fibrillation after bilateral incision of the diaphragm. Grafts were machine perfused for 2 hours either with hypothermic oxygenated perfusion (HOPE) or normothermic blood-based perfusion (NORMO), then implanted into syngeneic recipient rats. Right after arterial reperfusion $5x10^5$ HCC cells were injected into the vena porta. 28 days after transplant, grafts were explanted and tumour volume measured by MRI. Controls were rats transplanted with fresh or non machine perfused DCD livers.
Results: Survival after transplantation was similar in the four groups and all animals developed HCC nodules. Total tumor volume was lower in the fresh liver recipients compared to the DCD and DCD+HOPE recipients (p=0.0006 and p=0.014 respectively). DCD+NORMO recipients developed both very small and large nodules. Apoptotic and necrotic foci in the post-perfusion DCD+HOPE and DCD+NORMO grafts were as extended as in the non perfused DCD grafts. On the other hand, DCD+NORMO recipients showed faster recovery and better transaminases on day 1 after transplant.
Conclusions: This experiment confirms that ischemia/reperfusion injuries promote HCC "recurrence" after DCD liver transplantation. In a prolonged ischemia model, both 2h hypothermic and normothermic *ex-vivo* perfusions were non- or marginally effective in reducing such risk.



[HCC growth 28 days after transplant and Transaminases 1 day after transplant]

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Pharmacological enhancement of bile duct preservation and function during ex-situ normothermic machine perfusion

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Background: Whilst ex-situ normothermic machine perfusion (NMP) of the liver limits the ischaemic injury to the organ, benefits for biliary complications post-transplantation are not yet clear. Pharmacological enhancement of the hepatic lipid metabolism during NMP was shown to mitigate oxidative mediated inflammatory tissue damage. This study aims to assess whether this treatment improves biliary cell function and enhances its preservation during NMP.

Method: Eight discarded human donor livers were randomly allocated to two experimental groups: the control group and the treatment group (n=4), wherein the perfusate was supplemented with the drugs. Liver tissue, perfusate and bile were sampled systematically. Common hepatic duct biopsies (beginning and end of perfusion) were assessed for injury markers (damage to the lining epithelium, epithelial superficial/deep peribiliary glands, stromal necrosis, mural bleeding and thrombosis). Immunohistochemistry was performed for cytokeratin (CK)19, for integrity of the epithelial cells, and for cluster of differentiation (CD)31, for the endothelial cells.
Results: The experimental groups are comparable in terms of donor type, warm and cold ischaemia time. Treated livers exhibit increased bile production (1.7[1.6-2.6]vs. 0.6[0.7-1.7]ml/h,p=0.021) and improved bile quality- bile pH (7.8[7.7-8.0]vs. 7.3[7.1-7.6],p=0.030). Histologically, at the end of the perfusion, bile ducts from the treated livers demonstrated less injury to the biliary epithelial cells (CK19+;p=0.024) and endothelial cells (CD31+;p=0.005) when compared to the controls. There is a strong correlation between the decreased activation of inflammatory cells (CD11b+) and the reduction in injuries to the biliary epithelial ([Spearman]r=0.813,p=0.042) and endothelial cells (r=0.703, p=0.05). Organs exhibiting better preserved biliary epithelial cells tend to produce higher volumes of bile (r=0.624,p=0.099), as well as better quality bile (r=0.620,p=0.100).
Conclusion: This study suggests the possibility of pharmacological enhancement of bile duct preservation during NMP, potentially via mitigation of the inflammatory mediated injury. This finding might guide studies aiming to further improve biliary complication rates following NMP.

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Analysis of clinical features and countermeasures in elderly patients undergoing ischemia-free liver transplantation

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Objective: To investigate the clinical features of elderly patients undergoing ischemia-free liver transplantation and to propose nursing strategies.
Methods: The clinical data of 28 patients with end-stage liver disease who underwent ischemia-free liver transplantation at the Organ Transplantation Center of the First Affiliated Hospital of Sun Yat-sen University from July 2017 to October 2018 were retrospectively analyzed. Seven patients aged over 60 years old were enrolled in the elderly group and 21 patients less than 60 years old as the control group.
Results: Seven patients recovered smoothly after operation. No complications such as infection, hemorrhage and biliary fistula occurred. There was no significant difference between the postoperative hospital stay and the control group (P>0.05%).
Conclusion: Corresponding nursing measures were taken according to the hysiological and psychological characteristics of elderly patients undergoing ischemia-free liver transplantation, which are combined with psychological symptoms, prevention of infection, monitoring of circulatory system, diet guidance, medication care, etc. Targeted perioperative nursing work and reduction of complications are the key to the success of elderly liver transplantation.

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Use of normothermic machine perfusion (NMP) with marginal donors: variation across regions

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Introduction: NMP has been proposed for use in marginal liver allografts. We wished to examine the early experiences using NMP with marginal donors across the US and to profile each regions approaches.
Methods: NMP liver donors were identified using the Scientific Registry of Transplant Recipients (SRTR) database. Donor data were examined and stratified by UNOS regions. Donor risk index (DRI) was calculated for NMP livers. Donor risks factors included: donation after cardiac death (DCD) status; donor age >60 years; macrosteatosis (>30%), elevated donor transaminases (>500 units/L) and Hepatitis B or C infection. A p-value < 0.05 significant.
Results: 101 livers underwent NMP starting in 2016. Region 10 had most NMP livers (n=30, 29.7%), while region 9 had no recorded utilization. Donors were more likely to be local (n=90, 91.8%) with no nationally shared donors. Mean distance to transplant center was universally < 100 miles. 18 NMP livers were DCD, (8/30, 27%) inRegion 10; Regions 2, 4, 5, and 6 have yet to use a DCD liver on NMP. When examining donor age, Region 7 had the oldest donors (54.7 years) while Region 10 had the youngest donors (42.3 years). Region 6 had donors with the highest BMIs (40.2 kg/m2); Region 8 had the lowest BMI (27.7 kg/m2). When examining use of livers with steatosis, Region 11 had the highest content (13%) while Region 1 had the lowest (6%). Region 7 utilized donors with the highest SGOT (235 units/L);

Region 6 had the lowest SGOT (24 units/L). DRI was highest in region.
Conclusion: Analysis of early experiences with NMP suggest a cautious approach to marginal livers utilization. Interestingly, different regions utilize livers with different marginal characteristics. Each region likely has or will develop expertise in marginal characteristics in utilization of livers with NMP.

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Liver viability assessment for machine perfusion with flow distribution visualization methods using a thermography

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Background: Almost all studies of liver viability assessment used biochemistry method and there are few studies to consider flow distribution conditions. In machine perfusion, the graft is preserved by perfusion. Therefore, it is extremely important to access flow distribution conditions in order to confirm organ viability during preservation. In our research, we proposed noninvasive assessment method of liver flow distribution condition during machine perfusion using a thermography.
Method: Porcine livers were procured under warm ischemia time (WIT) of 0 or 60 min. The livers preserved by subnormothermic machine perfusion (SNMP). Temperature distribution of the liver during SNMP was measured by a thermography. The liver area of the image was extracted and these number of pixels were defined as initial area index I_0 and the total amount of pixel of each perfusion time t s and the local graft temperature T °C were defined as I_{tT}. Here, one of the normalized index of temperature distribution η_{tT} was calculated as I_{tT} divided by I_0. This index can predict that the area at low temperature quickly decreased in good flow condition because perfused flow quickly to the whole liver and the temperature of perfused transfer to the liver.
Results: In the liver of WIT60, η_{tT} is 0.58 at t=0 s and T=11-13 °C and η_{tT} is 0.32 at t=60 s and T=11-13 °C. On the other hand, in the liver of WIT0, η_{tT} is 0.65 at t=0 s and T=10-12 °C and η_{tT} is 0.19 at t=60 s and T=10-12 °C. η_{tT} of WIT0 was decreased more than η_{tT} of WIT60. We consider it is important to measure temperature distribution in a short time because heat transfer from perfused is bigger than that from only liver.
Conclusion: The potential of liver viability assessment method was investigated using liver preservation experiment during the SNMP.

P-300

Progress of extracorporeal membrane oxygenation associated with liver transplantation

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Background: Extracorporeal membrane oxygenation (ECMO) is a life-saving method for critical care medicine, and has been widely reported to be associated with liver transplantation. However, a systemic review about the connection between ECMO and liver transplantation need to be well illustrated.
Method: Case reports, retrospective studies and prospective researches concerning ECMO and liver transplantation were collected, and categorized by grafts' function, recipients' outcome, animal studies and challenges.
Results: Increasing evidences supported that ECMO was able to expand donor pool and improve grafts' qualities whether donated after brain death or cardiac death. And ECMO could serve as a powerful bridge and safe treatment to cardiopulmonary dysfunction in preoperative and perioperative period, also a good assistance to solve the complications happened after operation. Animal studies suggested initiate time points and duration time for ECMO used in LT. Meanwhile, a few ethical issues remained to be discussed, which required the ECMO procedure should be carefully conducted with special consent.
Conclusion: ECMO plays an important role as organ-preserving, life-supporting and complication-solving treatment in liver transplantation. Transplant surgeons and physicians should be aware of indications, management, complications, and challenges of ECMO.

Poster Round I, Session 1, 2, 3: Pediatrics

P-301

Living donor liver transplantation for methylmalonic acidemia and propionic acidemia

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Backgrounds: Methylmalonic acidemia (MMA) and propionic acidemia (PA) comprise the most common organic acidemias, which are both autosomal recessive disorders. Liver transplantation (LT) is considered to be a therapeutic option for MMA and PA due to provision of partial enzyme replacement. However, outcomes of living donor liver transplantation (LDLT) using heterozygous parental liver grafts for MMA and PA were rarely reported.
Methods: Between Nov 2016 and Jun 2018, 21 children with MMA (all were vit B12 unresponsive with MUT gene mutation) and 10 children with PA underwent LDLT in Ren Ji Hospital, Shanghai, all of whom received liver grafts from their parents. Clinical data were retrospectively reviewed from our prospectively collected database.
Results: There were 19 boys and 12 girls, with a median age of 29 months (range from 6 to 104 months) at transplant. The median body weight was 11kg (range from 7 to 23kg). The median GRWR was 2.0% (range from 1.2 to 3.5%). All children had pretransplant histories of acute metabolic decompensation or metabolic stroke, and most of them had varying degrees of developmental retardation and movement disorders. LDLT brought forth obvious serum and urinary metabolic improvement (Table 1) as well as catch-up growth. No children experienced any episodes of acute metabolic decompensation or metabolic stroke after LT. Surgical complications were observed in 3 patients (1 hepatic arterial thrombosis, 1 biliary stricture and 1 intestinal perforation). The graft survival rate was 100% with a median follow-up duration of 11.0 months (range from 5.4 to 24.8 months).
Conclusions: LDLT using parental grafts could be a good therapeutic option to improve the metabolic control and the quality of life for MMA and PA patients, and it should be considered during infancy to minimize risks of nonreversible neurological damage.

Table 1. Serum and urinary metabolite levels before and after LT

Variables	MMA (n=21)		PA (n=10)	
	PreLT	3m PostLT	PreLT	3m PostLT
Serum C3 (umol/L)	27.6 (7.0-76.6)	23.2 (15.4-34.3)	49.1 (23.3-69.3)	28.8 (14.0-38.1)
Serum C3/C2	0.79 (0.32-1.74)	0.66 (0.34-1.05)	1.3 (0.6-2.9)	1.2 (0.7-2.1)
Urinary MMA level	417 (135-1184)	329.3 (3-629)	/	/
Urinary 3-OH-propionate level	24.5 (0.41-69.3)	4.3 (0.5-14.9)	132 (32-760)	28.6 (2.32-36.4)
Urinary methylcitric acids level	10.2 (2.1-36.2)	4.9 (1.6-19.7)	27.1 (11.9-39.9)	9.8 (1.1-33.3)

C3, propionylcarnitine; C2, acetylcarnitine; MMA, methylcitric acid; LT, liver transplantation.

[Table 1. Serum and urinary metabolite levels before and after LT]

P-302

Pediatric living donor liver transplantation in the United States: a retrospective review of the national experience

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Background: The aim of this study is to compare graft survival of pediatric deceased donor liver transplantation (DDLT) and living donor liver transplantation (LDLT).
Methods: The UNOS database was retrospectively reviewed for all primary pediatric liver transplants between March 2002 and September 2016. Baseline characteristics were compared using a two-tailed t-test or chi-square test as appropriate. Characteristics significantly associated with graft survival upon univariable Cox regression were entered into a multivariable Cox regression.
Results: 6,700 pediatric liver transplants were performed during the study period and met the inclusion criteria. 852 (12.72%) were LDLT. LDLT recipients had significantly lower age, weight, BMI, bilirubin, albumin, creatinine, sodium, and cold ischemia time, and higher MELD/PELD, donor age, and donor BMI (Table 1). A greater percentage of LDLT recipients had previous abdominal surgery, biliary atresia, ascites, and a lower percentage of hepatoblastoma or metabolic disease, status 1, outpatient status at allocation, and dialysis. 1-year, 5-year, and 10-year survival of LDLT was 90%, 84%, and 82%, respectively, compared to 88%, 82%, and 75% among DDLT (p = 0.002). Multivariable Cox regression demonstrated that LDLT had a significantly decreased risk for graft loss compared to DDLT, with an adjusted HR = 0.63, 95% CI 0.51-0.78.
Conclusion: LDLT incurs a significant independent survival benefit compared to DDLT in children.

Variable	Deceased Donor Liver Transplant (n = 5,848, 87%) Mean/quantity	SD/%	Living Donor Liver Transplant (n = 852, 13%) Mean/quantity	SD/%	P-value
Age, years	5.40	6.01	3.38	5.06	**< 0.001**
Male	2859	48.89	421	49.41	0.775
Weight, kg	24.14	22.51	16.61	16.41	**< 0.001**
BMI, kg/m²	18.35	4.12	17.32	3.15	**< 0.001**
Previous abdominal surgery	2569	43.93	453	53.17	**< 0.001**
Diagnosis:					
Extrahepatic biliary atresia	1855	31.72	390	45.77	**< 0.001**
Hepatoblastoma	398	6.81	31	3.64	**< 0.001**
Metabolic	863	14.76	69	8.10	**< 0.001**
Acute hepatic necrosis	754	12.89	94	11.03	0.127
Bilirubin, mg/dL	10.39	11.34	11.99	10.77	**< 0.001**
INR	1.97	2.19	2.02	1.87	0.516
Albumin, g/dL	3.20	0.79	3.10	0.75	**0.001**
Creatinine, mg/dL	0.47	0.54	0.37	0.44	**< 0.001**
Sodium, mmol/L	138.54	5.28	137.45	5.05	**< 0.001**
MELD/PELD score	14.64	14.64	17.07	13.78	**< 0.001**
Status 1	1983	33.91	178	20.89	**< 0.001**
Location at allocation:					
Home	3571	61.06	460	53.99	**< 0.001**
ICU	1359	23.24	189	22.18	0.495
Days on waiting list	151.70	338.44	139.16	408.44	0.329
Ascites	3656	62.52	609	71.48	**< 0.001**
Portal vein thrombosis	214	3.66	25	2.93	0.286
TIPS	65	1.11	8	0.94	0.650
Life support	609	10.41	80	9.39	0.358
Mechanical ventilation	541	9.25	71	8.33	0.385
Dialysis	239	4.09	10	1.17	**< 0.001**
Donor age, years	12.82	13.13	32.41	8.37	**< 0.001**
Male donor	3460	59.17	368	43.19	**< 0.001**
Donor BMI, kg/m²	20.05	4.75	25.14	3.85	**< 0.001**
Cold ischemia time, hours	7.29	3.33	2.83	5.01	**< 0.001**

[Table 1. Recipient and Donor Characteristics of Living Donor and Deceased Donor Liver Transplants]

P-303

Liver transplantation for urea cycle disorders in Saudi Arabia

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Introduction: Urea cycle disorders (UCDs) are a group of monogenic inborn errors of hepatic metabolism that often result in life threatening hyperammonemia. Defects in the urea cycle pathway lead to a propensity for hyperammonemia and its consequent neurological damage. Ornithine transcarbamylase (OTC) deficiency is by far the most common UCD, followed by AL (Argininosuccinic Aciduria-ASA) and AS deficiencies (Citrullinemia-CITR). Except for OTC deficiency, UCDs are autosomal recessive in inheritance. Here we analyze our outcome in liver transplantation (LT) mainly live donor liver transplant in treatment of UCDs.
Material and methods: Thirteen children (median age 41 months) underwent liver transplantation at our institution from January 1, 2011 to September 30, 2018. Of these 10 had ASA, two with citrullinemia, and there was a single patient with OTC deficiency. Twelve grafts were donated from living relatives who were heterozygous carriers for the child's disease; a single deceased donor LT was performed. 4 of 13 grafts were ABO-incompatible.
Results: Despite the absence of dietary restriction or ammonia chelation therapy, no hyperammonemic episodes or elevations in amino acid chromatography levels were noted in any LT recipients. Electron microscopy showed particular macroscopic mitochondrial features. 31% (n=4) developed acute cellular rejection but the actuarial graft and patient survival is 100%.
Conclusions: Apart from neonatal onset of OTC deficiency which represents a clear indication for LT, in all other UCD's conditions the indication is based on the failure to maintain metabolic compensation with medical treatment. Our experience utilizing LT is very promising with excellent graft and patient survival. Utilizing heterozygotic donors appears to be a safe practice for both the recipient and donor.

P-304

Customized reconstruction of hepatic vein in pediatric living donor liver transplantation using lateral left segment grafts

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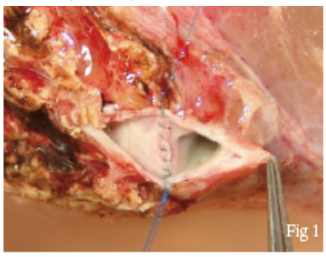
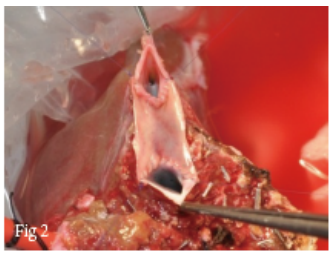
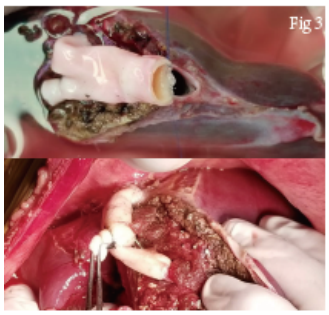
Background: The anatomic variation of segment II and III increases the risk of outflow complication in pediatric living donor liver transplantation (LDLT) using lateral left segment (LLS).
Methods: We share our experience on hepatic vein reconstruction in a consecutively cohort of LDLTs with different anatomy variations.
Results: From Jan 2017 to the end of Dec2017, 381 pediatric LDLTs were performed in our center, among which 365 cases used the LLS graft with or without size reduction. The hepatic vein of grafts were classified into three types based on the number and location of orifice: single orifice (type I, n=258, 70.7%); two adjacent orifices (type II, n=41, 11.2%); and two wide spaced orifices (type III, n=66, 18.1%). For the type II and type III cases, unification venopalstic techniques

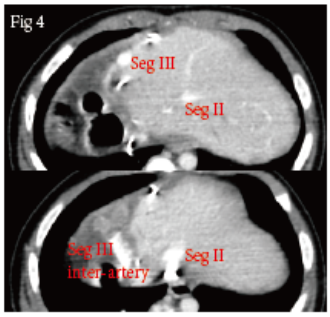
were performed including wedged unification (figure1, n=90) and wedged unification with a vessel patch (figure2, n=12). Notably, a novel interposition unification venoplasty using cryopreserved iliofemoral artery (figure3, n=5) was performed by one single surgical group in type III cases with two spaced orifice > 20mm distance. Briefly, hepatic vein of segment III on the cut surface was anastomosed to one oblique end of iliofemoral artery, followed by unification of its another end with Segment II. During median follow up of 8 month (3-15 month), no hepatic vein complications of hepatic vein occurred. For the 5 cases receiving the interposition unification venoplasty, there is no hepatic vein complication. The interpositional arteries were patent one month after transplantation in CT scan (figure4).

Conclusion: Customized strategy is required for LLS graft with complex outflow vessels to achieve satisfactory outcomes. Our novel interposition unification venoplasty using cryopreserved iliofemoral artery is safe for cases with two wide spaced orifices, although long term follow-up results are still required.









Different venoplastic techniques of hepatic vein of LLS graft:
Fig1, wedged unification venoplasty was performed in 90 cases;
Fig2, wedged unification with a vessel patch was performed in 12 cases.
Fig3, interposition unification using cryopreserved iliofemoral artery was used in 5 cases.
Fig4, CT scan revealed patent flow in both segment II and artery-interposioned segment III.

[Figures]

P-305

Pediatric liver transplantation for metabolic disease

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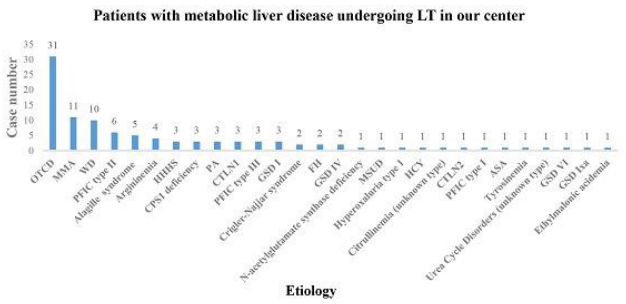
Traditional treatment for some Metabolic Disease results in variable but suboptimal outcomes, An ideal therapy would be enzyme replacement, achieved by organ and cell transplantation, or gene therapy.

Methods: All pediatric cases underwent LT in our center from June 2013 to October 2018 were enrolled in our study. The etiology, type of transplant, postoperative complications and prognosis in patients with liver-based metabolic disorders disease were retrospectively analyzed.

Results: There were total 104 children with liver-based metabolic disorders disease (21.0%) among the 496 children who underwent LT in our center. The median age was 49.0 months (range, 3.4-193.2months) and the median follow-up time of was 15.4 months (range 0.8-65.0 months). Living donor liver transplantation(LDLT) was performed in 75cases, deceased donor liver transplantation (DDLT) in 34 cases and domino liver transplantation in 5. Of the 104 patients, 44 cases (42.3%) were urea cycle disorder, 15 cases (14.4%) were organic acid metabolism disorder, 10 cases (9.6%) were Wilson´s disease, 10 cases (9.6%) were progressive familial intrahepatic cholestasis, 7 cases (6.7%) were glycogen storage disease. Blood ammonia level drops to normal after LT in children with urea cycle disorders. It showed marked reduction in propionyl carnitine (C3) and C3/C2 level and the mean urine MMA was reduced by 81.7% (P< 0.01) in patients with methylmalonic acidemia (MMA). Clinical symptoms associated with neurological damage are gradually relieved in almost all cases. The overall 1-, 2- and 3-year cumulative survival rates of recipients were 98.0%, 96.2% and 96.2%. The graft cumulative survival rates were 97.1%, 95.3% and 92.4%. Three patients underwent re-transplantation due to graft failure.

Conclusion: LT is a valuable option for children with metabolic disorders disease and has gained favorable prognosis although the role of pediatric LT in the management of metabolic disease remain to be further explored.



[Patients with metabolic liver disease undergoing LT in our center]

P-306

Pediatric reference values for the total psoas muscle area (tPMA)

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Background: Sarcopenia, the unintentional loss of skeletal muscle mass, is often ascertained by cross-sectional (CT) imaging of the psoas muscle area (PMA) in adults, and is associated with poor outcomes in end-stage liver disease. Research efforts in pediatrics are hampered by a lack of consistent quantitative definitions for PMA in children. Our goal was to generate pediatric reference values for PMA at two intervertebral lumbar levels, L3-4 and L4-5.
Methods: We analyzed abdominal CT scans of children presenting to the emergency department of a large Canadian tertiary care center who required abdominal CT imaging between 01/01/2015 to 31/12/2015 after trauma. Children with a documented chronic medical illness or an acute spinal trauma at presentation were excluded. Total PMA (tPMA) was measured as the sum of left and right PMA (mm^2) at L3-4 and L4-5 levels. Age- and sex- specific tPMA percentile curves were modeled using quantile regression, and an online app was created to easily calculate age specific z-scores and percentiles.
Results: CT images from 800 children between the ages of 1-16 years were included in the analysis. Values of tPMA at L4-5 were significantly larger than at L3-4 at all ages, with excellent correlation for girls (r=0.95) and boys (r=0.98). For girls tPMA at 50th percentile ranged from 365mm^2 (447mm^2) to 2336mm^2 (2704mm^2) at L3-4 and L4-5. For boys tPMA at 50th percentile ranged from 394mm^2 (498mm^2) to 3050mm^2 (3513mm^2) respectively. Interrater correlation coefficients were excellent at L3-4 (0.97, 95% CI 0.94 to 0.981) and L4-5 (0.99, 95% CI 0.986 to 0.995).
Conclusion: We provide novel pediatric age- and gender- specific growth curves for tPMA at L3-4 and L4-5 levels. Together with a freely available online tool, these reference curves will enable earlier identification and targeted intervention of sarcopenia in children with chronic medical conditions including end-stage organ disease.

P-307

Outcomes of liver transplantation for Alagille syndrome after Kasai portoenterostomy; Alagille syndrome with agenesis of extrahepatic bile ducts at porta hepatis

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Background: Alagille syndrome (ALGS) is an autosomal dominant disorder, characterized by a paucity of intrahepatic bile ducts, resulting in significant cholestasis, and peculiar extrahepatic features. Some ALGS patient shows a considerable overlap with biliary atresia (BA), and they can undergo Kasai procedure. The purpose of this study is to show the manifestations of BA overlapped ALGS cases in our institution, and to compare the outcomes of AGS patients following liver transplantation (LT) between those who previously underwent Kasai surgery (ALGS-Kasai group) and those who did not (ALGS-non-Kasai group).
Methods: Medical records of ALGS patients who underwent LT in Kyoto University Hospital, Japan from January 1992 to March 2018 were analyzed. ALGS diagnosis was determined according to physical, radiologic, and histopathological findings.
Results: Thirty-one patients were ascertained (ALGS-Kasai: 4 males and 5 females vs. ALGS-non-Kasai: 14 males and 8 females, p=0.43). Of 31 ALGS patients, 96.8% of children had pulmonary artery stenosis, 54.8% showed facial features, 29% revealed skeletal anomalies and 9.7% demonstrated ocular anomalies. The age at LT was significantly younger in ALGS-Kasai than ALGS-non-Kasai group (1.47 [interquartile range (IQR), 0.75-1.92] vs. 5.1 [IQR, 1.4-9.29] years; p=0.038). Overall patient survival did not significantly differ between ALGS-Kasai (88.9%) and ALGS-non-Kasai patients (86.4%) (p=0.84). Furthermore,

the 1-year, 5-year, and 10-year patient survival rates for ALGS-Kasai group were 100%, 88.9%, and 88.9%, respectively, whereas those for ALGS-non-Kasai group were 90.9 %, 90.9%, and 86.4%, respectively, with *p*-values of 0.36, 0.90, and 0.84, respectively.
Conclusions: BA overlapped ALGS cases had neonatal progressive cholestasis which prompted Kasai procedure, and early liver dysfunction after Kasai led to performing LT. The ALGS-Kasai patients undergo LT at earlier ages than the ALGS-non-Kasai patients, however, overall patients' survival rates are similar between groups. Overall ALGS patients' survival rate after LT is considered high.

P-308

Open-labeled, prospective observational study of immune cell function assays in the diagnosis and monitoring of infection in pediatric liver transplant patients

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Purpose: The Cylex™ Immune Cell Function (ImmuKnow) Assay can be used to assess cell-mediated immunoreactivity in immunocompromized patients based on peripheral CD4+ T cell adenosine triphosphate (ATP) activity. We applied such test in young Chinese pediatric liver transplants (PLTs) to evaluate its clinical application in diagnosis and monitoring of their immune status post-surgery.
Methods: In this two-center, prospective observational clinical trial, we enrolled pediatric (under 3-years-old) Chinese liver transplant recipients (PLTs) to evaluate the clinical application of the assay in the diagnosis and monitoring of immune status post-surgery from April 2017 to June 2018. Detailed clinical records including drug dosage, biochemical and imaging exams were collected at all visiting points. Patients were allocated to stable, infection, or rejection groups according to clinical diagnosis. Detailed clinical records, including ImmuKnow assay results, were collected at all time-points.
Results: A total of 225 PLTs were selected and Finally, 216 PLTs were enrolled with an infection incidence of 76.1% (n = 160). In the stable status group, the ImmuKnow values ranged from 167-371 ng/mL. In addition, the median ImmuKnow value in the infection group was significantly lower than that in the stable group (135 vs. 236 ng/mL, $P < 0.001$), and could be used to diagnose infection (AUC = 0.784, 95% CI: 0.720-0.848). ROC curve analysis revealed a cut-off point of 152 ng/ml with sensitivity and specificity of 57.3% and 95.5%, respectively. And ImmuKnow values showed no correlation to immunosuppressive drug dosage or concentration, nor immune cell numbers.
Conclusion: ImmuKnow ATP were significantly lower in infected PLTs and showed its diagnostic value in transplant related infections, implying that it may assist in immunosuppressive drug monitoring in young child post-LT.
Keywords: Liver transplantation, pediatric, immune function assay, infection

P-309

Posttransplant lymphoproliferative disorder in Chinese pediatric liver transplant recipients: a single-center experience and retrospective study

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Background: Posttransplant lymphoproliferative disorder (PTLD) is a heterogeneous group of lymphoid malignant neoplasms arising after liver transplantation (LTX). Several factors such as nature of immunosuppressive therapy, Epstein-Barr Virus (EBV) serological status have been reported to contribute to the development of PTLD.
Methods: A retrospective analysis was performed of all pediatric LTX patients from January 2017 to September 2018, a detailed record of immunosuppressive treatment, Epstein-Barr virus infection status and PTLD incidence has been conducted. The immune function assay was applied to measure the differences of immune status between PTLD and non-PTLD patients.
Results: 708 pediatric patients were included by effective follow-up. Among them 402 (56.8%) patients have been affected by EBV. The incidence of PTLD was 3.39% (n = 24) in pediatric LTX patients. An episode of EBV infection occurred in 24 (100%) patients with virus load varying from 1.25E+3 to 5.9E+6 copies/ml. The Immune function assay values in PTLD patients were significantly lower than non-PTLD patients (85 vs 223 ng/ml, $P < 0.0001$). Immunosuppressant reduction or stop combined with the anti-CD20 monoclonal antibody (Rituximab) would be treated for PTLD patients. One (4.2%) patients died as a result of PTLD progression.
Conclusion: PTLD following pediatric LTX is often associated with EBV infection in the context of iatrogenic immunosuppression. A development for management based on EBV viral load and routine monitoring of EBV-specific immune responses may promise further improvement in outcomes with EBV positive PTLD in children.
Keywords: Post-transplant lymphoproliferative disorder, Epstein-Barr virus, liver transplantation, pediatric,

P-310

Effect of liver transplantation for children with Niemann-Pick disease type B

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We evaluated the efficiency of liver transplantation for children with Niemann-Pick disease (NPD) type B. From October 2006 to October 2018, 7 of 1512 children that received liver transplantation at Ren Ji Hospital were diagnosed as NPD type B through genetic testing of *SMPDI* mutation, ASM activity measurement and characteristic clinical findings. The median age at diagnosis is 12-month with initial presentations of hepatosplenomegaly, growth retardation, repeated pneumonia and diarrhea. Even after comprehensive supporting treatment, all patients developed liver dysfunction, severe interstitial pulmonary disease, compromised lung function and hypersplenism following time, as well as hypertriglyceridemia in four patients. They were transferred to our hospital for transplantation (median age 6.5-year-old). Among them, 4 patients received living donor liver transplantation and 3 received orthotopic whole liver transplantation. Splenectomy was conducted spontaneously. All patients are alive with a median follow-up of 10 months (5-53 months). Liver function returned to normal within 3 weeks after transplantation and maintained stable during the follow-up. Thrombocytopenia and leukopenia were cured, as well as hypertriglyceridemia. Pulmonary disease was relieved after transplantation, as evidenced by resolution of interstitial lung disease and restored lung function. Bronchitis only occurred one time in two patients with a quick recovery during follow-up. Catch-up growth was observed in all patients, especially in one male patient as his height z-score increased from -3.9 to -1 4-year after transplantation. Patients with follow-up longer than 9 months indicated significant psychomotor activity improvement. Meanwhile, hypotonia was relieved in four patients after transplantation. However, intelligence development delay still exists in four patients during the follow-up. Three of them have been receiving intelligence recovery therapy under the instructions of pediatrists and neurologists, while the long-term effect needs more investigations. In conclusion, liver transplantation is a safe and effective treatment for NPD type B patients with severe liver and pulmonary dysfunction.

P-311

Liver transplantation for tyrosinemia in the nitisinone era

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Background: Liver transplantation (LT) serves as a definitive treatment of the defective metabolic pathway along with other serious disease manifestations such as liver failure and hepatocellular carcinoma (HCC) in type 1 tyrosinemia. This study aims to evaluate outcomes of 15 patients with type 1 tyrosinemia who underwent LT in nitisinone era and discuss its effect on prevention of HCC.
Methods: A LT database of 1042 patients was reviewed. Data from 15 patients with type 1 tyrosinemia were retrospectively analyzed. There were 8 male and 7 female patients and the average age was 5.4 years (median= 1.5 years, range 4 months - 26 years). Liver failure was evident in 11 patients (73.3%). Liver nodules suspicious for HCC were observed in 10 patients (66.6%). Rickets (n=3) and Fanconi's syndrome (n=1) were relatively rare. The average MELD (Model for End-Stage Liver Disease) / PELD (Pediatric End-Stage Liver Disease) score was 9.6 (range -11 to 44).
Results: All the patients except one were treated with nitisinone prior to LT. A total of 7 patients (46.7%) proved to have HCC on their pathologic specimen. Mortality rate was 20% (n=3). These patients succumbed to death following a prolonged complicated postoperative course on their postoperative 22nd, 39th, and 40thdays. All the patients with HCC are alive and disease free after an average of 54.1 months (range 6 - 108 months) of follow-up.
Conclusion: Nitisinone treatment has opened new horizons in the management of type 1 tyrosinemia but LT still remains the only option for the refractory patients developing liver failure and in the event of HCC. Close monitoring of the patients with a multidisciplinary approach can help to prevent possible delays for LT.

P-312

A retrospective study for the early stage cytomegalovirus prevention after pediatric living donor liver transplantation

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Background: This single center, retrospective study investigate the effectiveness of different preventive strategies for the prevention of early stage cytomegalovirus infection after Pediatric living doner Liver Transplantation.
Methods: The records of the children who underwent living-related liver transplants between 2015 and 2016 were retrospectively analyzed.According to the situation of postoperative medication, the patients were divided into prophylaxis group and preemptive treatment group.Ganciclovir was given to prevent giant cell infection in the preemptive group postoperatively.In the preemptive treatment group, no drugs were given to prevent cytomegalovirus infection postoperatively, only ganciclovir was given when cytomegalovirus DNA was positive.Cytomegalovirus infection was compared between the two groups within 180 days after surgery.
Results: 146 living-related liver transplants recipients in Tianjin First Center Hospital were enrolled,including 74 in the prophylaxis group and 72 in the preemptive treatment group.74 patients received postoperative intravenous ganciclovir.CMV infection was detected in 58 recipients (39.73%) after transplantation, concomitant abnormal liver function was seen in 8 patients and gastrointestinal symptoms was observed in 1 patient.All patients recovered from CMV infection with ganciclovir treatment, no recipients death was seen in this study. CMV infection rate was 41.89% in prophylaxis group and 37.50% in preemptive treatment group. There was no statistical difference in cytomegalovirus infection rate and infection time between the two groups.
Conclusion: In this study,the antivirus prophylaxis could not reduce the infection rate of cytomegalovirus. preemptive treatment is an effective methods in the prevention of cytomegalovirus, which can avoid unnecessary drug use, reduce the burden of patients´ families and avoid drug side effects.

P-313

Combined liver-kidney transplantation for hyperoxaluria type 1: monocentric experience in adult and pediatric recipients

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Background: Combined liver-kidney transplantation(CLKT) is a therapeutic option for different pathological status as hyperoxaluria(PH1). Kidney graft loss is major complications expecially in pediatrics recipients related to oxalate high serum levels.
Methods: Between 9/2001 and 7/2018, 13 CLKT out of 2306 liver transplantation (0,6%) were performed for PH1 with graft from cadaveric heart-beating donors, 6 in pediatric and 7 in adult recipients. In all patients whole liver grafts were used. The population was divided in two groups,
group_1: recipients with kidney graft loss and
group_2: recipients with kidney graft alive.
Results: Median recipient age[IQR] was 33.3[12.2-42.5] years; median donor age 28.3[12.0-33.2]years while median donor weight was 68[40-76]kg. During a median[IQR] follow-up of 5.7[1.4-8.7] months, only one (8%) liver graft was lost due to multiple organ failure, whereas 3 (23%) kidney grafts were lost, all in pediatric recipients, in 2 cases due to primary non function, with oxalate renal accumulation, despite haemodialysis, in 1 case due to chronic rejection. Donor's age and weight and recipient's age at CLKT were significantly lower in group_1 (p=0.01). At multivariable logistic regression no risk factors for kidney loss were identified. 5-years liver and kidney graft survival was respectively 92% and 85%. One patient received a new kidney transplant 2 years after, whereas the other 2 are still in haemodialysis.
Conclusions: Nevertheless the small sample, in our experience, as well as in the literature reports, kidney graft loss was the major complication after CLKT for PH1. Our data suggests the relationship between donor age and weight, recipient age and kidney graft loss. Pre-emptive liver transplantation whit sequential kidney transplantation may be a better therapeutic strategy to reduce kidney loss due to high serum oxalate level in children.

P-314

Simultaneous partial splenectomy during liver transplantation in pediatric patients for the prevention of persistent severe hypersplenism posttransplant

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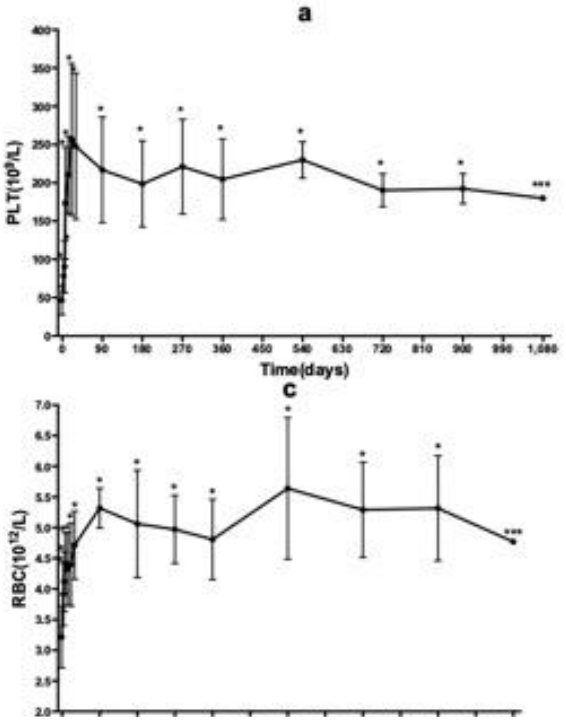
Introduction: Some liver transplant recipients would remain persistent severe hypersplenism posttransplant, which may put recipient at a higher risk of serious bleeding and infection. And splenomegaly may persist for a long time after liver transplantation, and an enlarged, congested spleen is susceptible to traumatic injury, especially in pediatric patients.
Methods: Between January 2015 and August 2018, seven pediatric patients with severe hypersplenism and splenomegaly underwent simultaneous partial splenectomy during liver transplantation at our institution, which has not been reported before. Hematological data including platelet, leukocyte, and erythrocyte counts, as well as hemoglobin were collected from medical records retrospectively, while the length and thickness of spleen were determined by abdominal ultrasound.
Results: The simultaneous partial splenectomy during liver transplantation was successfully performed in all 7 patients including 5 boys and 2 girls. Their mean age was 8.4years(5-15years). The median total operation time was 495minutes (320-768minutes), the medianintraoperative blood loss was 350mL(300-1300mL),and the median hospital stay was19days(14-55days). Patients werefollowed for 7.0-36.6 months(median13.5months). The length and thickness of thespleen decreasedimmediately from 18.89±1.77cm to 11.13±2.28cm(P< 0.001) and from 6.31±0.53cm to 4.97±1.29cm(P< 0.05), respectively, preoperatively to postoperatively. During the follow-up of 6 months, the mean platelet and leukocyte counts increased from 46.71±18.91×10^9/L to 198.57±56.34×10^9/L(P< 0.001) and from 1.59±0.42×10^9/L to 4.71±1.36×10^9/L(P< 0.001), respectively. In the long-term postoperative period, peripheral blood cell counts remained within the reference ranges. All patients survive to date with no procedure-related complications or occurrence of traumatic spleen injury.



[Follow-up data of a.PLT, b.WBC, c.RBC, d.HGB, e.splenic length and f.thickness]

Conclusion: The simultaneous partial splenectomy during liver transplantation in pediatric patients with severe hypersplenism is a feasible option for the prevention of persistent severe hypersplenism posttransplant, achieving a satisfactory long-term hematological response and eliminatingthepotential risk of traumatic spleen injury.

P-315

Reducing lateral segment grafts medially improves outcome in liver transplant for infants less than 10 kgs of weight

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Background: Liver transplants in babies < 10 kgs of weight and particularly in those with biliary atresia are often complicated by portal vein thrombosis(PVT). Many strategies have been suggested to avoid this complication namely: reducing laterally and inferiorly,

using a conduit from superior mesenteric vein to donor portal vein, and monosegment grafts. In our pediatric program, we have reduced the graft medially by transecting to the left of the falciform ligament by baring and lowering it where the graft is thick and does not at the long and slim lateral part.
Patients and methods: This technique was introduced in 2015. The normal left lateral segment is harvested by transecting to the right of the falciform ligament in order not to damage the vascularity of the left lateral segment graft. However, the graft is thickest at this point and moving the transection line to the left will reduce the graft weight markedly. By not dissecting in the space between the left hepatic artery and left bile duct, vascularity can be maintained. The graft can then be fixed using the left triangular ligament.
Results: Between 2015 to 2018, a total of 45 pediatric transplants were performed in children weighing less than 10 kgs, out of which 16 grafts underwent medial reduction. The CT volumetry reported an average graft volume of 256 g and after medial reduction, the average graft volume was 219 gm. PVT was noted in 2 patients out of 16 with medial reduction and in 3 patients out of 29 with left lateral segment grafts. Overall 11 out of 45 patients died in the first year post transplant.
Conclusions: Amongst the various techniques suggested for graft volume reduction, medial reduction reduced graft volume more predictably and reduced the incidence of PVT in our series. The one year survival was 75.6%.

P-316

Hepatic artery reconstruction with interposition of donor's right gastroepiploic artery graft in pediatric living donor liver transplantation for metabolic disease

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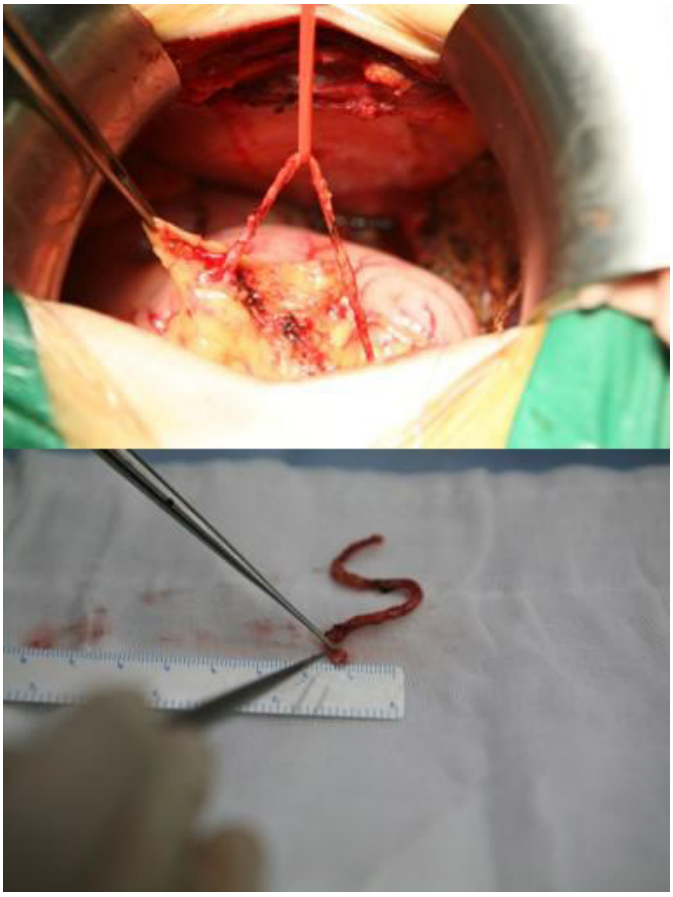
Objective: Most children with metabolic diseases have no signs of liver cirrhosis, and the diameter of hepatic artery is tiny. The incompatibility of artery caliber between grafts and recipients make arterial reconstruction more difficult. We introduce the indications, technique, results of our experience using donor's right gastroepiploic artery (RGEA) as interposition vessel to solve the problem in pediatric living donor liver transplantation(P-LDLT).
Methods: A retrospective analysis of P-LDLT for patients with metabolic diseases from June 2013 to November 2018 in our center was carried out. The arterial conditions, reconstruction methods and prognosis were analyzed.
Results: The donor's RGEA was utilized in 5 cases. There were 3 children with OTCD and 2 children with CPS1 and maple syrup urine disease respectively. In three cases, the grafts' left hepatic arteries were anastomosed with the recipients' proper hepatic arteries(PHA) using donors' RGEA as interposition vessel. In other two cases, the donors' RGEA were interposed between graft's middle hepatic artery (MHA) and the recipient's bifurcation of PHA and gastroduodenal artery(GDA). No arterial complications occurred in children using RGEA with follow-up time 5±3.4m.
Conclusion: In P-LDLT for patients with metabolic diseases, the application of right gastroepiploic artery as an interposition vessel can solve caliber mismatch and short arteries problems and achieve good results.



[RGEA]

P-317

Evaluation of new-onset acute diarrhoea after liver transplantation in children using nested PCR multiplex panel

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Introduction: Diarrhoea after liver transplantation (LT) is seen in 10-43% recipients. The diagnostic tests currently used, lack sensitivity, specificity. The FilmArray panel is a nested PCR that evaluates for 22 diarrheagenic pathogens in the faces. We planned to determine the incidence of infectious diarrhoea in our cohort and determine the etiological profile.
Patients and methods: 50 consecutive LT recipient children between May 2017 & December 2018 were included. FilmArray was performed on stool sample of children having either >/=3 liquid stools/day for >48 hours. The sample was collected, transported and analysed as per manufacturer's instructions. Demographic, clinical and laboratory data were collected as per pre-designed format.
Results: 13 of 50 (26% - incidence) had acute diarrhoea and for whom FilmArray test was done. 8 of 13 (61%) had infectious diarrhoea. 14 organisms were detected among the 8 cases of infective diarrhoea as 3 cases had more than one identified pathogen. Bacteria were detected 9 times, of which E coli was seen in 6 (2 Entero-pathogenic E.Coli (EPEC), 1 Entero-adhesive E.Coli (EAEC) and 3 Entero-toxigenic E.Coli (ETEC)), and Vibrio, Plesiomonas, Campylobacter were each detected one time. Virus were detected 5 times, of which twice was Rotavirus and once each Astrovirus, Adenovirus F40/41, Norovirus. No difference was seen between infectious and non-infectious diarrhoea recipients for - portal hypertension severity, PELD score pre LT, primary liver disease, non-bile flow in the intestine pre-LT, CMV, EBV viremia, type of anastomosis and diet diversification prior to the LT.
Conclusion: Diarrhoea post-LT was observed in 26%, infectious causes being identified in 60% of them, wherein most often these are viruses and self-limiting. The profile of the diarrhoea causing organisms among the LT recipient children mimicked community acquired diarrhoea. FilmArray helped in better antibiotic stewardship and has been included in our clinical practice as a diagnostic modality.

P-318

Significance of intrapulmonary vascular dilatations in paediatric candidates for liver transplan

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Background: Intrapulmonary vascular dilatations (IPVDs) frequently are detected during pre-liver transplant (LT) assessment of children, using the delayed appearance of micro-bubbles at contrast- enhanced echocardiography. We aimed to determine the predisposing factors for IPVD development and their impact early post-LT events.
Methods: 50 consecutive paediatric LT recipients were screened of which 13 were excluded due to obstructive or restrictive lung disease, intra-cardiac shunting, inadequate data or early mortality. All underwent pulse oximetry, contrast-enhanced echocardiography and ABG evaluation. Children were divided in two groups - with IPVD (groupA) and without IPVD (groupB). Characteristics compared between the two groups were age of LT, underlying liver disease, PELD score, duration of mechanical ventilation post-LT, duration of ICU stay, acute cellular rejections and early mortality.
Results: 10 out of 37 (27%) included children had IPVD and were classified as group A, remaining 27 without IPVD as group B.
Only one child in group A satisfied criteria for hepato- pulmonary syndrome. Only age at LT was significantly different, 32 months Vs 68 months, in group A and B respectively. No significant differences were seen in PELD score (18Vs17), pulse oximetry readings, duration of mechanical ventilation (1.6 vs 2.4 days), duration of hospital stay (21 vs 22 days), frequency of ACR and early mortality.
Conclusions: IPVD is seen in significant number of pre-LT candidates (27%). The clinical significance of diagnosing IPVD pre-LT remains uncertain as there no difference in pulmonary associated morbidity.

P-319

Living donor liver transplantation using reduced segment 2 monosegment graft in an infant

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Background: In pediatric LDLT, monosegmental grafts is used to overcome size discrepancies between adult donors and pediatric recipients. However sometimes problems related to large-for-size graft are encountered even when using such grafts. The reduced monosegmental graft has been introduced to address this problem. Herein we report a 5 month old, 5 kg infant with acute on chronic liver failure and underwent LDLT by using reduced S2 monosegment graft from his father.
Case report: 5 month old male infant with past medical history of elevated liver enzymes and INR since 40 days old presented with jaundice and lethargy and referred to our center for treatment of acute liver failure. As he was unresponsive to supportive therapy and daily plasmapheresis and his condition deteriorated, the decision to proceed with LDLT from father was made. The predictive GRWR of LLS graft was larger than 4, therefore the use S2 monosegment graft was decided after analyzing intrahepatic vasculature with 3D computer-generated model of the donor liver. S2 graft weighting 240gr was harvested by insitu resection of S3.Further lateral reduction of the S2 graft to 160gr was done on back table. The left hepatic vein of the graft was anastomosed to the common orifice of hepatic veins. PV and HA anastomoses was done in a standard fashion. The bile duct of the graft was anastomozed to the recipient's main bile duct. Postoperative course was uneventful and the patient is doing well at 5 months of follow up.
Conclusion: LDLT using monosegment grafts offers a safe and useful option for treating smaller infants. Although it is technically more challenging, S2 monosegment grafts are better for reducing graft thickness. Brief understanding of intrahepatic vascular anatomy of the donor and careful preoperative planning is crucial for successful monosegment LDLT.

P-320

Management of portal vein anastomotic stenosis after pediatric liver transplantation: evaluation of single center experience

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Introduction: Late onset portal vein anastomotic stenosis (PVAS) is a frequent complication in pediatric liver transplantation. For clinical relevant PVAS percutaneous transluminal angioplasty (PTA) is the first option. When PTA is not feasible or not successful to obtain portal vein patency, a surgical Meso-portal shunt (MPS) can be performed. Our aim was to evaluate the characteristics of pediatric patients with post-transplant PVAS and the results of our management of these patients.
Methods: We retrospectively studied all patients after liver transplantation aged ≥18 years that underwent a therapeutic intervention (PTA or MPS) procedure between 2014 and 2018. We evaluated primary patency of the PTA and MPS and secondary patency after the complete therapeutic intervention process.
Results: At our center, 18 (11%) of 165 patients underwent a therapeutic intervention procedure for PVAS, of whom 72% had biliary atresia as the primary diagnosis, 72% were transplanted under 1 year of age and 67% received a living donor graft. The median post-procedural follow-up time was 1.4 years. Twelve patients underwent a primary PTA, of whom one patient underwent two PTA's and one patient three PTA's in total. 10 patients received a MPS of whom four patient had MPS after PTA. Primary patency was 67% for the first PTA, 0% for the second and third and patency after MPS was 80%. Secondary patency was 89% for the complete therapeutic approach.
Conclusion: In 11% of our cohort of pediatric transplantation patients portal vein anastomotic stenosis is a significant problem especially in recipients with biliary atresia, transplantation below 1 years of age and after living donor transplantation. Based on our results we do not support a second PTA if the first PTA fails. Our combined treatment strategy with PTA and MPS has a good clinical outcome with a secondary patency of 89%.

P-321

Evaluation of spleen volume with computed tomography after liver transplantation in pediatric recipients

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Introduction: We planned to investigate the outcome of splenomegaly after liver transplantation (LT) in children.
Methods: Thirteen patients (8 female) were included in the study. We calculated the spleen volumes (SV) and spleen volume/standard spleen volume (calculated as SSV [cm^3]=0.7+(4.7 x bodyweight [kg]) (SV/SSV) of the patients by computed tomography (CT) before transplant (SV0), at first week posttransplant (SV1) and after two years posttransplant (SV2). We recorded hemoglobin, white blood cell and thrombocyte levels and liver function tests concurrently.
Results: Mean age at time of LT was 6.2±5.3 years (0.5-15.7 years). The CTs after two years posttransplant were performed at a mean time of 3.85±1.07 years (2-5 years) posttransplant. The mean SV0, SV1 and SV2 were 378±285.5 cm^3, 348.5±266.5 cm^3 and 354.6±253.6 cm^3, respectively. The mean SV/SSV0, SV/SSV1 and SV/SSV2 were 3.91±1.83, 3.51±1.94 and 2.3±1.38, respectively. The patients were divided into two groups: group 1 (11 patients, 84.6%) had an improvement of splenomegaly which was demonstrated by a decrease in SV/SSV ratio and group 2 (2 patients, 15.4%) who had an increase in SV/SSV ratio over time. The SV2 and SV/SSV2 ratio were significantly lower in group 1 compared to group 2 (p=0.048 and 0.03, respectively). There was no significant difference among SV0, SV1, SV/SSV0 and SV/SSV1 between two groups. The white blood cell count and thrombocyte count after posttransplant 2 years were significantly lower in group 2 compared to group 1 (p=0.03 and 0.03, respectively).The liver function tests (transaminases, bilirubin and albumin levels) did not differ between two groups at any time, while INR level after 2 years posttransplant were significantly lower in group 2 (p=0.03).
Conclusion: Splenomegaly tends to improve regardless of pretransplant spleen size in pediatric patients who underwent LT. This improvement is not prominent in the postoperative early period and requires time to demonstrate.

P-322

Impact of short term intravenous ganciclovir prophylaxis vs pre-emptive therapy for prevention of cytomegalovirus and associated complications in paediatric liver transplant

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Introduction: Cytomegalovirus (CMV) infection is common worldwide, after primary infection it becomes latent. The aim of this work was to determine the impact of short term intravenous (IV) ganciclovir prophylaxis for 2 weeks (CMV D+R-) from week one post-transplant versus pre-emptive therapy for 3 weeks or longer commenced according to clinical status (CMV D+R+, D-R+, D-R-) in paediatric liver transplant (LT) recipients.
Materials and methods: Single institute retrospective review of primary LT in children (< 16y) between 2008-2011 (n=180) with data extracted from a prospectively maintained transplant database, electronic patient records and microbiology database. Follow-up data over 2 years was analysed. CMV infection was assessed on CMV DNA PCR. All available graft biopsy data was reviewed for histologically confirmed hepatitis and graft rejection episodes. Statistical analysis was with IBM SPSSv25.
Results: There were 180 LT in children (89 male and 91 female). Median age at transplant 1.5 years (2 months - 18 years). The most common indication for LT was chronic liver disease (n=134, 74%) followed by acute liver failure (n=26, 14%), non-cirrhotic metabolic (n=17, 9.4%) and hepatoblastoma (n=3, 1.6%). Patients with CMV D+R- status (n=54) had lower symptomatic infection at 20.37% compared to 25% in D+R+ (n=36) and 52.5% in D-R+ (n=40). Pre-emptive treatment reduces CMV related symptoms albeit infection remains present (p=0.001). Otherwise there was no significant difference in the occurrence of graft rejection or length stay between groups.
Conclusion: Patients who receive pre-emptive treatment for CMV infection in LT have better outcome in terms of reduced CMV related symptoms.

P-323

Deceased donor predictors for pediatric liver allograft utilization and outcome of the use of paediatric donor livers in adult recipients

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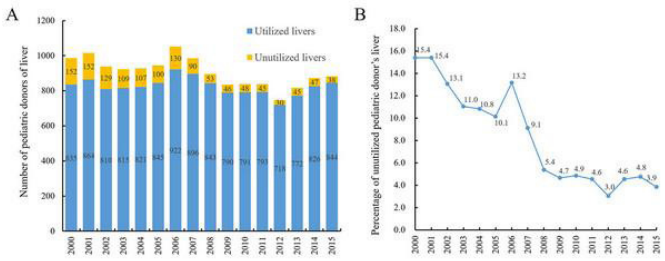
Background: The number of pediatric deceased organ donors has recently declined. Pediatric liver allografts sometimes were allocated to adult recipients when there are no suitable pediatric recipients. We determined to find out the utilization rate, identify risk factors for graft discard and analyse the outcomes of adult liver transplants using pediatric livers.
Methods: We used data from the SRTR database from 2000 to 2015. The trends of pediatric liver donors and utilization rates were analyzed. Donor risk factors that impacted the graft use of pediatric livers were measured.
For clinical outcome, we used the data from our center. Records from adult recipients undergoing liver transplant between 2011 and 2016 who received grafts from paediatric (≤18 years) donors and deceased adult (>18 years) donors were collected and analysed.
Results: For utilization analysis, we identified 14506 eligible pediatric liver donors. A total of 1321 authorized liver grafts did not recover or recovered without transplantation. Based on the multivariate analysis, factors including donation in the years of 2000-2005, death of anoxia, lack of heartbeat, HBsAg positivity total bilirubin >1 mg/dl, Creat >1.5g/land BUN >21 mg/dl were significantly related to graft non-utilization.



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For clinical outcomes analysis, we found that most baseline demographics of recipients were comparable. Pediatric donor livers were much smaller in size. The 3-month, 1-year, and 3-year recipient survival rates were 92%, 85%, and 82% in the pediatric donor group, which were not significantly different from adult donor group (93%, 87%, and 83%, P=0.863). There was no difference in early allograft dysfunction, primary non-function, biliary complications, vascular complications between the two groups.
Conclusions: The pediatric liver allograft utilization rate and risk factors for non-utilization of grafts were determined. Using pediatric donor livers in well-selected adult recipients is a safe procedure.

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Assessment of disease-specific HRQOL in pediatric liver transplant recipients with the PeLTQL: a quality improvement project

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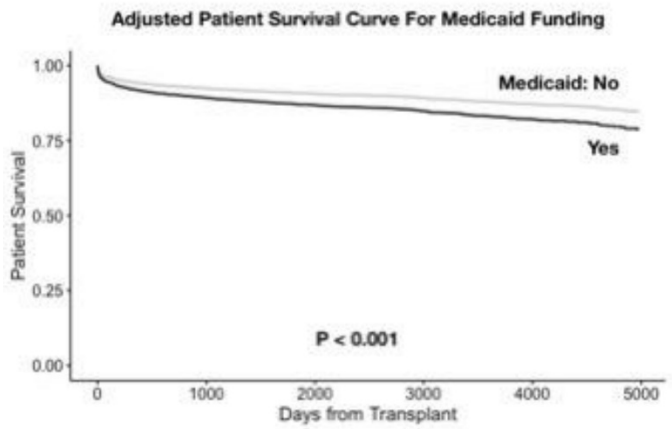
Introduction: Patient-reported outcome measures are not yet utilized broadly in standard clinical follow-up of pediatric liver transplant (LT) recipients. Understanding of the patient´s perspective can complement traditional outcome metrics. Since 2013, the Pediatric Liver Transplant Quality of Life (PeLTQL) tool, the first disease-specific health-related-quality of life (HRQOL) tool for pediatric LT recipients, has been incorporated into clinical practice. This quality improvement project aimed to assess targeted HRQOL subdomains important to long-term pediatric LT survivors.
Methods: We reviewed patients with current age >8 years, post isolated pediatric LT performed ≥12 months ago, and completion of PeLTQL assessment between 2013-2018. Higher total PeLTQL scores indicate better HRQOL (range 0-100) with total scores: < 62.5 indicating probable anxiety and < 49.3 probable depression. Subdomains scores were also evaluated.
Results: A total of 86 pediatric (45% male, median age range 10-12 years-old, 51% biliary atresia, 68% 6+ years post-LT) LT recipients completed 82 self- and 80 parent- PeLTQL versions. 17% of patients scored < 62.5, and 10% of adolescents scored < 49.5. Adolescent (age 13-18 years) patients self-reported lower total self-PeLTQL scores (71±10.71) and subdomain scores: Coping and Adjustment (66±14.52), Future Health (71±13.41), and Social-Emotional Functioning (75±14.39), compared to younger (age 8-12 years) LT recipients (74±12.51, 69±13.12, 75±20.61, 78±13.42 respectively). Similarly, parent-reported PeLTQL scores were lower across all domains for adolescent-aged patients. Overall, subdomain scores for Coping and Adjustment were most impaired.

Conclusion: Despite being many years post-transplant, patients who have undergone LT as an infant or child are at risk for challenges with coping and adjustment. Specific themes include the ongoing need for surveillance medical care, impact on family members and altered self-image. Results highlight the value of routine assessment of HRQOL even in children without identified issues, towards the goal of targeted interventions to help adolescents adapt to stressors associated with LT.



[Adjusted Patient Survival Curve for Medicare Funding]

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Impact of insurance status on pediatric patients undergoing first time liver transplantation

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Background: Socioeconomic status has been associated with inferior outcomes after multiple surgical procedures. The impact of socioeconomic status on the outcomes of liver transplant in the pediatric population is not well studied. We sought to evaluate the impact of insurance status, as a proxy for socioeconomic status, on patient and allograft survival in pediatric patients undergoing first time liver transplantation.
Methods: We conducted a retrospective analysis of the UNOS data base from January 2002 through September 2017, which revealed 6997 pediatric patients who underwent first time isolated liver transplant. A mixed Cox proportional hazards model was performed to adjust for donor, recipient, and program characteristics in order to determine the relative risk(RR) for insurance status on allograft and patient survival. All results were considered significant with a P-value < 0.05. All statistics were performed using R version 3.5.1 and package coxme 2.2-10.
Results: Medicaid status had a significant negative impact on long-term survival after controlling for multiple covariables. Pediatric patients undergoing first time liver transplant with Medicaid has a RR of 1.42 (CI: 1.18 -1.60) of dying post liver transplant.
Conclusion: Pediatric patients undergoing first time liver transplantation have multiple risk factors that may impact long-term survival. Having Medicaid insurance almost doubles your chances of dying post liver transplant. Maybe these patients need more global support post-transplant to improve their long-term survival.

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Live donor liver transplantation for type 1 Citrullinemia

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Introduction: Argininosuccinate synthetase deficiency or type 1 citrullinemia is an autosomal recessive disorder that has variable clinical manifestations. It is the second most common urea cycle defect that leads to hyperammonemia and if left untreated it can be fatal. Liver transplantation (LT) for urea cycle defects is well documented in the literature, however, there are very few reports solely on citrullinemia. This study aims to present a single center experience about LT for citrullinemia children transplanted from their parents.
Methods: Among 292 pediatric LT recipients between July 2009 and October 2018, two were transplanted for citrullinemia.
The first patient was a 7-month-old, 7 kg boy presented with hyperammonemia crises, frequent ICU admissions, and the requirement for dialysis. His PELD score was 28 mostly due to prolonged INR of 3.6. The second one was a 19-months-old, 10 kg girl with poorly controlled metabolic status resulting in frequent hyperammonemia attacks and mild motor and mental retardation. Her PELD score was 9 and her liver functions were within normal limits.
Results: Both patients received LT from their parents; one from his mother and one from her father. The postoperative courses were

uneventful and they were discharged home on postoperative 26th and 27th days. The ammonia levels returned to normal and measured between 30 to 40 µmol/L within 10 days following surgery. They were allowed normal diet after surgery and hyperammonemia did not occur at all. Their motor and mental developments were comparable with their peers. Currently, both of the patients are alive and well with normal ammonia levels and liver functions after 56 and 100 months of follow-up.
Conclusion: LT is an established method for the treatment of citrullinemia. Using grafts from heterozygotic does not have a negative impact on either donors or recipients.

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Live donor liver transplantation for hepatoblastoma

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Introduction: Liver transplantation (LT) combined with chemotherapy provides excellent outcomes for patients with unresectable Hepatoblastoma (HB) (PRETEXT stages III and IV). This study aims to evaluate the results of live donor LT for this group of patients in a single center.
Material and methods: An LT database of 1042 patients transplanted in our institution between July 2009 and November 2018 was reviewed. Among 292 pediatric recipients, 13 of them were transplanted for hepatoblastoma (7 male and 6 female). The mean age was 2,5 years (range: 6 months and 7 years). All were transplanted with left lateral sector grafts (segment 2 and 3) and 3 of these grafts were further reduced in size. Duct-to-duct anastomosis was preferred in all cases except one.
PRETEXT stage was 4 in 11 patients and 3 in 2 patients. All patients received chemotherapy according to SIOPEL protocol while 3 of them had previous liver resection prior to LT as well.
Results: Among 13 patients there was no perioperative mortality. The mean follow-up was 48 months (range: 6- 97months). Recurrence was observed in 4 patients (30%). There were 3 mortalities (23%) due to recurrent and advanced disease at 12th, 21stand 22ndmonths while one patient is alive with lung metastases 65 months after transplant. Remaining 9 patients are disease-free with stable liver function tests. Actuarial survival and disease-free survival rates at 5 years are 76 and 69% respectively.
Conclusion: LT offers optimum treatment for advanced HB. Live donor allows optimal timing of transplantation after chemotherapy in countries with limited access to grafts from deceased donors. Excellent results can be achieved by a multidisciplinary approach following proper radiological assessment combined with resection, chemotherapy, and liver transplantation.

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The risk of arterial complication in pediatric living donor liver transplantation: importance of the arterial blood flow intensity

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Background: Hepatic artery thrombosis (HAT) is one of the most severe complications leading to a high morbidity and mortality especially in pediatric liver transplantation. We evaluated the risk factors associated with HAT following pediatric living donor liver transplantation (LDLT).
Methods: Sixty-five pediatric cases of LDLT experienced at Hokkaido University hospital between July 1998 and February 2017 were analyzed.
Results: The hepatic artery was reconstructed with 8-0 nylon interrupted sutures under surgical microscope in 61 (93.8%) or under magnifying loupes in 4 (6.2%). HAT occurred in 6 cases (8.2%) within 38 days after the operation, and all cases were those performed under surgical microscope. A multivariate logistic regression analysis showed that the smaller recipient's artery (less than 2.0mm in diameter; P = 0.0027), selection of variant recipient's hepatic artery such as hepatic artery off from superior mesenteric artery or from left gastric artery, and anastomosis by using an interposition graft (P=0.0006) were independent risk factors for HAT. Additionally, hepatic artery flow velocity less than 30 cm/sec after re-arterialization was identified as a predictor of HAT development (P = 0.0034). While, there were no significant differences in primary diseases, recipient age, recipient body weight, MELD score, GRWR, episode of acute cellular rejection, and cold / warm ischemia times between cases with and without HAT. Discrepancy in calibers between recipient and graft arteries: graft hepatic artery smaller than recipient's, was neither independent risk factor. Of the 6 cases with HAT, re-transplantation was carried out in 3 in whom one died after the operation. Other 3 cases were rescued without re-transplantation by re-entry through collaterals.
Conclusion: Meticulous surgical planning including the selection of appropriate hepatic artery with good blood flow would contribute to the successful outcome after pediatric LDLT.

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Living donor vs. deceased donor liver transplantation for pediatric patients with metabolic liver disease

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Purpose: Liver transplantation has been accepted as the appropriate treatment option for pediatric metabolic liver disease and the most common methods used are LDLT and DCD. Due to the low incidence of liver-based metabolic disease and low acceptance rates of LDLT in some countries, little research has been performed to compare the outcomes of the two operation methods for metabolic disease.
Methods: Clinical data of 89 patients undergoing liver transplantation for the treatment of liver-based metabolic disorders were reviewed. pre- and peri-transplant demographics, post-transplant survival rate, early allograft dysfunction (EAD), virus infection, severe complications and laboratory test data were collected and analyzed.
Results: For the 89 patients, only 2 of them died by the end of the last follow-up. The post-transplantation EAD rate and severe complications were different for LDLT and DCD. There was no significant difference between LDLT and DCD for the incidence of viral infections and the onset time of EBV and CMV infections either. In terms of laboratory indexes, the recovery time of PLT, AKP and AST levels were significantly different. Among the different types of metabolic disease, there was no significant difference found in viral infection, EAD, laboratory indexes, severe complications or duration of hospital stay.
Conclusions: LDLT shows a lower incidence rate of EAD and complications, while it also shows a 1-year survival rate and incidence of viral infections compared similar to that of DCD. LDLT is the better treatment option of pediatric liver transplantation for metabolic liver disease compared with DCD.

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Early referral to transplant centers is a prognostic factor influencing outcomes of pediatric liver transplantation

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Introduction: Liver transplantation (LT) is the only curative treatment for children with end-stage liver transplantation. LT outcomes are influenced mainly to the recipient clinical status at the time of transplantation and the optimization of the management of children candidate to LT is essential to achieve good outcomes.
Aim: To analyse the long-term outcomes of pediatric LT and to identify the prognostic factors associated with patient/graft survival.
Material and methods: Retrospective analysis of LT performed in a pediatric transplant center between September 2008-December 2017. Recipient, donor, surgical characteristics were analysed. Exclusion criteria included LT combined with other organs, domino LT and re-transplantation.
Results: Out of 200, 181 children [age: 19 (0-222)months; body weight: 10(3-45)Kg] underwent LT for cholestatic disease (n=131,72.4%), metabolic disorder (n=30,16.6%), tumors (n=14,7.7%), acute liver failure (n=6,3.3%). At the time of LT, the median Pediatric End-Stage Liver Disease (PELD) was 20(0-63), 36(20%) patients were hospitalised and 20(11%) were urgency. 135(75%) grafts were from deceased donors [whole(n=37,21%); split (n=87,48%); reduced(n=11,6%)], 46(25%) from live-donors. The post-transplant intensive therapy stay was 5(1-45) days and the total hospital admission 24(1-264)days. The median cold ischemic time was 7(0.8-13)hours, and 40% >8 hours. Patient survival was 96% at 1-year and 95% at 5-years. Graft survival was 96% at 1-year and 94% at 5-years, with re-transplantation rate of 1.1%. Post-operative morbidity occurred in 65(36%) cases: 35(54%) [17(48.6%) biliary/18(51.4%) vascular] complications were treated by radiological intervention and 30(46%) required re-operation. At multivariate analysis, early referral to transplant center($p < 0.0001$), PELD>30($p=0.043$) and hospitalization($p=0.035$) at the time of LT were risk factors for graft failure.
Conclusion: Long-term LT outcomes are excellent. Patient and graft losses occur mainly within the first 3 months after transplantation, primary related to recipients' poor clinical status. Early referral of children with end-stage-liver disease to pediatric transplant centers is essential to achieve good results.

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Pediatric liver transplantation using hyper-reduced left lateral segment graft

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Shortage of donor resources is an important factor limiting the operation of liver transplantation. Split liver transplantation is an important method to relieve the shortage of donor resources. Because of the uncertainty of donor conditions, the weight of donor liver and recipient often does not match, especially in children. In this case, reduced-size liver transplantation is particularly important for critical child recipients. One case of over-reduced volume splitting liver transplantation was successfully completed in the organ transplantation center of Tianjin First Central Hospital. The recipient underwent splitting liver transplantation for biliary atresia and acute liver failure. The donor´s left lateral lobe weighed 560 g and the recipient´s body weight was 5.5 Kg. The graft weight was 120 g after over-reduction and the operation proceeded smoothly. The patient´s liver function returned to normal 2 weeks after operation, and the blood flow of the transplanted liver remained normal. This case report aims to provide more clinical experience for reduced-size liver transplantation in children.

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Outcome of a left lateral section variant graft in small children less than 10kg: a comparison study between split and living donor liver transplantation

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Background: A variant graft of left lateral section (vLLS graft) was innovated to overcome a large for size syndrome in pediatric liver transplantation, especially in living donor liver transplantation (LDLT) for a small children. However, the outcome of a vLLS graft was not established in split liver transplantation (SLT).
Methods: We divided 36 pediatric recipients less than 10 kg in to 4 groups according to a graft type; LDLT with a LLS graft (Group 1; n=11), LDLT with a vLLS graft (Group 2; n=5), SLT with a LLS graft (Group 3; n=8), and SLT with a vLLS graft (Group 4; n=12). Surgical complication and graft outcome were compared among 4 groups.
Results: Primary abdominal closure was done in all patients. Surgical complications were noted as follows; 3 hepatic vein complications (8.3%, each one in Group 2, 3, and 4), 3 portal vein complications (8.3%, 1 in Group 1; 2 in Group 4), 2 biliary complications (5.6%, 1 in Group 1; 1 in Group 4), and no hepatic artery complications. However, there was no significant difference among 4 groups (P>0.05). There were 3 graft failures in Group 2 (n=2) and Group 4 (n=1) which was primary graft non-function in fulminant hepatic failure patients (8.3%).
Conclusion: A vLLS graft was safely used without increased risk of surgical complication in small children who underwent a SLT.

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Posttransplant lymphoproliferative disorder in pediatric liver transplant recipients: a single-center experience

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Objective: This study was conducted to analyze the clinical characteristics ,treatment and outcome of posttransplant lymphoproliferative disorder (PTLD) in liver transplant recipients.
Methods: This study includes a retrospective data analysis of nine pediatric liver transplant recipients with PTLD who were treated at the our center from Jun 2013 to Aug 2018. Demographic,clinical, treatment data and outcome were collected.
Results: The primary diseases were biliary atresia, cryptogenic cirrhosis and ornithine transcarbamylase deficiency (OTCD). Eight patients received living donor liver transplantation (LDLT). One patient received liver transplantation from donation after cardiac death (DCD) donors. All the patients were diagnosed by pathology. Four cases were classified as early lesions of PTLD. One case was polymorphic PTLD. Two cases were burkitt lymphoma. One case was diffuse large B cell lymphoma and one case was classical Hodgkin lymphoma-like PTLD. The patients had different clinical manifestations mainly including fever, anemia, diarrhea, enlargement of lymph nodes or hepatosplenomegaly, jaundice, intestinal obstruction and even intestinal perforation. All the patients had positive EB-DNA in serum. After the diagnosis, immunosuppressants were reduced or discontinued. All the patients received anti-CD20 (Rituximab) theraphy. Four cases were treated combined with chemotheraphy (R-CHOP, ABVD, COPP/ABV). One case was treated combined with radiotherapy. Two cases received surgical treatment due to intestinal obstruction. Eight patients

achieved complete response and were alive at the time of review. One patient died of relapse of PTLD.
Conclusion: PTLD is one of the most serious and fatal complications after liver transplantation. The detection of EB-DNA load and imaging examination can provide clues for diagnosis. Definite diagnosis can be made based on histopathology. Treatment varies according to differet classifications, and basically including immunosuppression reduction, anti-CD20 antibody, operation, radiotherapy and chemotherapy. Early detection and early-stage treatment are needed to rescue patients who have suffered from PTLD.

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Simultaneous anatomical subtotal splenectomy during liver transplantation for the prevention of persistent severe hypersplenism posttransplant: a case with 3-year follow-up

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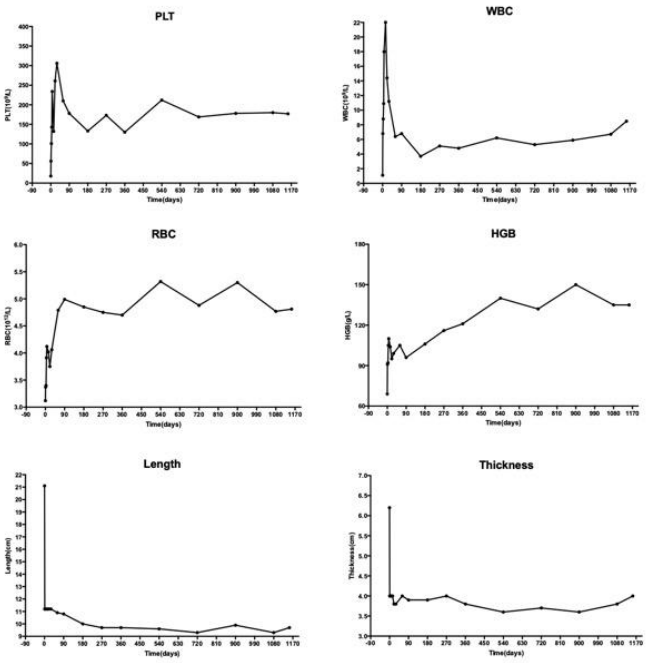
Introduction: Some liver transplant recipients would present with persistent severe hypersplenism posttransplant,which may put immunosuppressed transplant recipients carry a higher risk of serious, even life-threatening bleeding and infection. Additionally, preoperative massive splenomegaly may also persist for a long time after liver transplantation.
Methods: We retrospectively analyzed the clinical data of 6-year-old girl with biliary atresia, portal hypertension, severe hypersplenism and massive splenomegaly, who received a living donor liver transplantation and simultaneous anatomical subtotal splenectomy on August 28, 2015. To our best knowledge, simultaneous anatomical subtotal splenectomy during OLT has not ever been performed in pediatric patients to prevent the persistence of posttransplant severe hypersplenism, and this is probably the first case report of its type described in the medical literature.
Results: The living donor liver transplantation and simultaneous anatomical subtotal splenectomy were successfully completed. The normalization of platelet and leukocyte counts observed in this patient within the third and first day of the transplant were maintained within the reference ranges during the long-term follow-up period. Additionally, immediately posttransplant there was a significant reduction in the length and thickness of the spleendetermined by abdominal ultrasonographic examination. The volume of the remnant spleen calculated by using the 3-D imaging system was 258.58 cm^3, 215.39 cm^3, and 237.56 cm^3at 14 days, 138 days, 1154 days posttransplant, respectively. There was no occurrence of procedure-related complications and traumatic spleen injury during the whole follow-up period.
Conclusion: The experience of our patient shows that for pediatric patients with preoperative severe secondary hypersplenism and massive splenomegaly, simultaneous anatomical subtotal splenectomy during OLT may be an effective and feasible treatment for the prevention of persistent severe hypersplenism, achieving a long-term desired hematological response and eliminating the potential risk of traumatic splenic injury.



[Evolution of PLT, WBC, RBC, Hemoglobin, Splenic length and thickness throughout follow-up.]

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Transitional care in pediatric liver transplantation: do we need to structure a personalized program?

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Background: The transition of young liver transplant recipients (LTR) from the pediatric to the adult department is generally characterized by the resistance toward the new health care personnel. This might be caused by the perception of a less "user friendly" setting. An unguided transition might represent a significant risk of reduced compliance. With possible impact on the transplant outcome. The objective of this study is to identify both criticalities and needs in order to develop a formal transitional program.
Method: Young LTR approaching he transition age have been profiled for compliance, and clinical and sociological variables: age, sex, transplant indication, graft status, hospital admissions, current transplant center of reference (TC), autonomy from the caregiver.
Results: 159 LTR (77M/82F) age 21.92 (21.87M e 21.97F). LTR were grouped as follows: Gr. A, 50 (32%) LTR currently actively followed by original TC; Gr. B, 53 (33%) LTR currently followed by different TC but we have info; Gr. C, 30 (19%) LTR currently followed by different TC but we don´t' have info, Gr. D 26 (16%) LTR currently "in transition". The autonomy of the caregiver during the transiction was graded Great/Good vs Low/Insufficient: 68% vs 32%.
Conclusion: An "Unguided transition" represents real risk factor for loss of compliance, bearing the possibility to compromise the transplant outcome. Our initial descriptive analysis support this hypothesis. Therefore, based upon our profilation of both LTR and caregivers we have currently developed a "transitional clinic" with the presence of a pediatrician, a transplant physician and the psychologist: a personalized follow-up program shall be designed for each LTR based upon their socio-clinical condition ad hoc psychological testing profilation.

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Early vascular complications after pediatric liver transplantation and the role of antithrombin and therapeutic anticoagulation

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Background: Anticoagulation after pediatric liver transplant is a common practice to prevent graft-threatening vascular thrombosis events such as hepatic artery thrombosis (HAT) and portal venous thrombosis (PVT). No consensus guideline exists to direct this practice. Our tertiary care children's hospital utilizes anticoagulation and antithrombin replacement after liver transplant. The purpose of this study is describe the bleeding and clotting complications of our study population.
Methods: Patients who received a liver transplant from October 2017 to October 2018 were included. Demographics, reason for transplantation, labs, medication data, imaging, and bleeding or thrombosis complications were collected for the inpatient time period after transplant. Basic statistical analyses were used to describe the cohort. Patients received either heparin or enoxaparin post-operatively, with a transition to aspirin at discharge.
Results: The study institution performed 20 liver transplants during the study period. 9/20 (45%) were transplanted for biliary atresia. Median recipient weight was 17.5 kg. 12 patients received a whole graft, 8 received segmental grafts. Patients were anticoagulated per surgeon preference using institutional protocols, with 16 receiving therapeutic enoxaparin, 1 receiving prophylactic enoxaparin, 3 receiving therapeutic heparin. All patients had antithrombin replaced for levels < 70%. No patients had HAT or PVT. One patient had partial thrombosis of an accessory artery. 6 patients had bleeding complications with 3 returning to the OR. Bleeding complications occurred in 4/8 patients (50%) who had overlap of therapeutic enoxaparin and aspirin.
Conclusions: Dual therapy with therapeutic enoxaparin and aspirin appears to carry greater risk of bleeding without benefit of thrombosis reduction. Antithrombin replacement, combined with therapeutic anticoagulation seems to be effective at preventing vascular graft thrombosis in our study population. The adherence to anticoagulation protocols after liver transplant is likely an important component for successful management of this patient population and should be studied in a multicenter trial.

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Social and psychological impacts of having a child with liver transplant

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Introduction: Liver transplantation is a chronic stressor as with all other solid organ transplants.In this study,we aimed to evaluate the social and psychological impact of liver transplantation on the parents of pediatric liver transplant patients who require a lifetime of protection,care and medical support.
Materials and methods: Between December 1988 and November 2018 we performed 611 liver transplantation procedures at our

centers of which 284 were pediatric transplants.Of the 284 pediatric patients,44 patients who received liver transplants at Baskent University from February 2011 to February 2017 were included in this study.All patients have normal liver functions and have at least 1 year follow up period. The data collection was done via questionnaires. We evaluated the demographic data. The social and psychological impacts of liver transplantation on the parents were evaluated with family impact scale (FIS), Nottingham health scale (NHS) and Beck depression scale (BDS). The collected data was analyzed with suitable statistical methods.
Results: The age range of 44 pediatric liver patients was 4 months-17 years. The total FIS score of the parents was much more higher than the normal population (72.54±10.98). With this finding, liver transplantation was shown to have economic, psychological and social effects on parents.The total score of BDS also showed that parents have depressive findings (11.43±9.63).The evaluation of NHS data of the parents showed that they have lower emotional reaction scores (30.29±27.60) and social isolation values (27.68±31.68) than the normal population.As the follow up periods after liver transplantation get longer, the impact of parents and depressive findings significantly decreased. However, emotional reaction and social isolation did not change (p< .05).
Conclusion: It is well known that both children and their parents experience strains in orientation of communal living and fulfilling their daily requirements after liver transplantation.Social and medical support should be planned for the parents also.

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The use of split liver transplantation from deceased pediatric donor: a single center experience in China

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Background: The use of split liver transplantation (SLT) from deceased pediatric donor is rarely reported. This study analyzed the outcomes of SLT from pediatric donor at a single center in China.
Material and methods: From 2017 to 2018, we performed 24 SLTs from 12 deceased pediatric donors using splitting technique. We investigated the results of SLT from pediatric donor.
Results: 12 pediatric donors were 8 male and 4 females. The age of the donors ranged from 4 years to 16 years with a median age of 10.5±4.5 years. The graft weight was from 457-1330g with a median weight of 980±295g.9 liver grafts were splited and received by two pediatric recipients, another 3 liver grafts were slpited and received by an adult and a pediatric recipient. 12 recipients included 3 adult and 9 children received extended right lobes (ERL). Another 12 children received left lateral segments (LLS) Further reduction of the LLSs was required in five smaller infants, who finally received reduced-LLS grafts. The mean age of the recipients received LLS was 6.8±2.8 months excluded 1 child was 4 years old, while 9 children received ERL was 5.6+4.6 years. Graft and patient survival rates were 83.3% and 83.3%, respectively, at both 1 year and 2 years. There were 2 cases of biliary complication and 1 cases of portal vein stricture, but no incidence of arterial complication or small-for-size graft syndrome.
Conclusions: The use of split liver transplantation from deceased pediatric donor is a feasible option to expand door pools, especially for infant recipients. careful manipulation and reasonable recipient selection may achieve a satisfactory result.

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Right-sided diaphragmatic hernia after pediatric living donor liver transplantation: a review of 3 cases study

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Background: Right-sided diaphragmatic hernia (DH) is a rare, but complicated, pathophysiological condition associated with pediatric living donor liver transplantation (LDLT). It is a potentially life-threatening condition in the absence of early recognition and surgical treatment.
Method: In this report, we describe three cases of children who developed right-sided DH after LDLT and the risk factors related with this condition.
Result: The primary disease in all LDLT patients, as performed using a left lateral segment graft, was biliary atresia. The DH was diagnosed by chest X-ray or CT at fifty-five days to six months post-transplant. Defects were located in the right posteromedial region of the diaphragm and secured by primary interrupted suture closure with no recurrence. To our knowledge, this represents the first description of a right kidney and Roux limb herniating into the thoracic cavity and the potential anatomical mechanisms.
Conclusion: Risk factors for right-sided DH in pediatric LDLT include, bile leakage, refractory pleural effusion, as well as surgical trauma, excessive diathermy and pressure gradient differences between abdominal and thoracic regions. Once DH is identified, surgery should be performed immediately.

P-340

Methylmalonic and propionic acidemia among hospitalized pediatric patients: a nationwide report

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Background: Methylmalonic acidemia (MMA) and propionic acidemia (PA) are the most common organic acidurias. The epidemiological data on these two rare disorders in China are limited. The aim of our study is to determine the proportion, characteristics and form of payment of MMA and PA among hospitalized pediatric patients with liver diseases in China.
Methods: Data were obtained from a national inpatient database in China from 2014 to 2017. We extracted patients with diagnosis of MMA and PA, identified using The International Classification of Diseases, 10th Revision (ICD-10 codes). Demographic characteristics, hospital locations, total costs and health insurance were further analyzed.
Results: Among all hospitalized pediatric patients with liver diseases, there were increasing trends in the proportions of individuals diagnosed as having MMA or PA from 2014 (1.10% for MMA; 0.26% for PA) to 2017 (1.61% for MMA; 0.32% for PA). For both MMA and PA, the medians of total payments per hospitalization have been generally stable. However, the data showed that less pediatric patients pay for their own hospitalization expenses (MMA: 41.87% to 31.70%; PA: 40.38% to 35.66%) and most of them still went to tertiary hospitals in 2017 (MMA: 80.96%, PA: 76.21%). Moreover, the hospitals in Beijing and Shanghai received a majority of MMA or PA pediatric patients from other districts.
Conclusion: Our study is the first nationwide-based study to provide epidemiological information of MMA and PA among hospitalized pediatric patients with liver diseases. Less proportion of self-paying were observed, while the healthy resources have been still relatively centralized.

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Customized reduction of left lobe/left lateral graft in pediatric LDLT recipients: outcomes of a prospective study

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Background: Graft size rather than GRWR has more significant bearing on outcome in Pediatric LT. Disproportionate liver grafts are associated with complications such as intra-abdominal hypertension, portal venous thrombosis(PVT), and requirement of mesh for abdominal closure. We present our results following use of reduced-graft customized to the size of diaphragmatic recess for each patient.
Method: Patients undergoing LDLT were entered into prospectively maintained database. Patients with weight ≤10 kgs, undergoing LDLT between March-2017 till November-2018 and a minimum follow-up of 28-days post-surgery were included in the study. Patients were categorized according to the use of reduced graft and were reviewed for pre-operative factors, peri-operative complications, incidence of PVT and overall outcome.
Results: There were 55 pediatric LDLTs during the study period. 40 patients(21 females,52.5%) fulfilled the study criteria and were included. Mean preoperative weight was 6.3 Kgs. Mean PELD score was 23.6 with 55% having PELD between 11-20 and 35% with PELD>20. There were no intraoperative mortalities. 36/40(90%) patients received reduced left-lateral or left-lobe graft. Mean graft-weight after reduction was 132.9 gms, mean reduced volume was 117.1 gms and mean GRWR was 2.1%. Five patients(12.5%) had PVT in postoperative period attributable to technical factors. Additionally, 1 patient developed PVT due to sudden post-operative hypotension. All cases required reoperative intervention. There were 4 PVT cases following reduced-graft(11.1%) while 1(25%) without reduction(P=0.42). Patient with reduced-graft had significantly lower duration of ascitic drainage(P=0.005), biliary complications(P=0.023) and time to normalization of INR(P=0.011). Further, there were higher wound related morbidity in patients without reduced-graft(P=0.06). Mesh was required for abdominal closure in 3/4(75%) patients without reduction and in none following reduction. There was no significant difference in hospital stay, ICU stay or in-hospital mortality between two groups.
Conclusion: Customized reduced graft is ideal procedure to reduce incidence of PVT and other complications in pediatric LDLT recipients.

P-342

Prevalence of infections in infants within first six months of liver transplantation

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Introduction: Infections a major cause of morbidity and mortality after pediatric liver transplantation especially in young children.
Methods: We conducted a retrospective study at Baskent University in Turkey between March 2005 to September 2018. Cases of death within the first 6 months were excluded. The standard immunosuppressive regimen after liver transplantation consisted of tacrolimus, mycophenolate mofetil and steroids. Ampicillin and cefotaxime were administrated intravenously and continued 72 hours after surgery. Prophylactic regimen was consisted of oral trimetoprim-sulfomethoxazol, flucanazole and valgancyclovir.
We evaluated causative organisms in bloodstream, subclavian catheter, urine and intra abdominal drainage fluid cultures. We also evaluated EBV and CMV infections by polymerase chain reaction in all recipients.
Results: Thirty-four cases whose median age was 8 months (4-12 months) at the time of liver transplantation were evaluated. 26 of 34 (76%) cases had biliary atresia. There were 26 bacteria isolated from the blood cultures (19/34; 55%), 9 bacteria (12/34, 35%) isolated from the subclavian catheter cultures, 5 bacteria (12/34, 35%) isolated from the urine and 9 bacteria (16/34, 47%) and 1 fungus (2/34, 6%) isolated from the intraabdominal drainage fluid cultures within the first six months of liver transplantation. Klebsiella pneumonia was the most common isolated bacteria from bloodstream and abdominal catheters and urine cultures. Staphylococcus epidermidis was the most common isolated bacteria from subclavian catheter cultures. Only one recipient had CMV infection during this period.
Conclusion: At least one pathogenic organism was isolated from the cultures of 27 out of 34 patients within first six months of liver transplantation. The most common infections were bloodstream and intraabdominal infections due to Klebsiella pneumonia.

P-343

Predictive factors of T cell mediated rejection after pediatric liver transplantation.

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Background: Liver biopsy is a gold standard for diagnosing T cell mediated rejection (TCMR) after liver transplantation (LT) although the procedure is invasive. The purpose of this study was to determine clinical factors to predict TCMR after pediatric LT.
Method: We retrospectively examined all patients who underwent liver biopsy within one month after LT in our institution between October 2016 and September 2018. We excluded patients with high-dose methylprednisolone prior to the biopsy. We examined patient characteristics, blood biomarkers, abdominal ultrasound parameters within three days prior to the biopsy that can predict the presence of TCMR. TCMR was defined as 4 points or more in the rejection activity index (RAI) in the Banff criteria.
Results: 48 patients were included in this study. The median age was 12.1 months (range, 2-160). The indications for LT were cholestatic liver disease (n=27, 54%), metabolic liver disease (n=11, 22%), and acute liver failure (n=6, 12%). 25 patients (52%) had TCMR (RAI4-5:11, RAI6-7:11, RAI8-9:3). TCMR patients showed significantly higher absolute eosinophil count, white blood cell count, amount of bile, hepatic vein velocity, change in the amount of ascites, and cold ischemia time. The area under the receiver operating characteristic curves for predicting TCMR was 0.80 for absolute eosinophil count, and 0.74 for hepatic vein velocity (less than 0.75 with the other factors). For absolute eosinophil count, the threshold value of 241 / μL showed a sensitivity of 88% and a specificity 65%. For hepatic vein velocity, the threshold value of 72 cm/s showed a sensitivity of 58% and a specificity of 78%.
Conclusion: Absolute eosinophil count and hepatic vein velocity may play the role of predictors for TCMR after pediatric LT. To reduce unnecessary liver biopsy, further investigations are needed to evaluate the appropriate cut-off values and the combination of these factors.

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Short and long term outcomes of pediatric liver transplantation (LT) in a single institution

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We present the results of a pediatric liver transplant series combined with an adult program over a 27 year period.
Patients and methods: From 1991 to 2010, 160 LT were performed in 151 pediatric recipients with a mean age of 5±4.9 years and a mean weight of 18±14 kg using 54 whole grafts and 106 partial grafts (55 split, 43 living donor and 9 reduced-size grafts) after a mean waiting time of 106±190 days and a mean follow-up of 14.2±7.7 years (range : 0-27.6).
Results: There were 3 main indication groups for LT, cholestatic diseases (n=117), liver failure (n=23) and metabolic diseases (n=18) including 14 combined liver-kidney transplantations. Recipient's age and weight were significantly lower in those receiving a partial graft. Post-operative main surgical complications included 4 PNF, 2 hepatic artery thromboses, 17 portal vein thromboses, 36 biliary stenoses, leading surgical revision in 83 patients and 9 patients were retransplanted. Medical complications accounted for 10 PTLD, acute and chronic rejections in 80 and 16 patients respectively and 11 secondary kidney transplantations. Mean eGFR and staging of fibrosis (METAVIR score) on protocol liver biopsies were 109, 100, 97 and 0.82, 1.43, 1.48 at 1, 10, and 20 years after LT respectively. Comparing whole and partial liver transplantations, there were significantly more surgical complications in the later group. In univariate analysis, portal vein thrombosis was associated with poorer graft survival and biliary stenosis with increased graft fibrosis. Overall patient and graft survival was 84.7% and 79.3% respectively. Whole and partial graft overall survival was 86.7% and 75.7% respectively (p=0.07), moreover overall partiel graft survival dramatically improved in the second half of the series at 94.5%.
Conclusions: Learning curve and combining both pediatric and adult LT led to improve expertise and results.

Poster Round II, Session 1, 2, 3: Acute Liver Failure

P-345

Molecular analysis of rejection and injury in liver transplant biopsies: the INTERLIVER STUDY

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Background. Distinguishing T cell-mediated rejection (TCMR) from other sources of inflammation in liver transplant biopsies by histology has been challenging. Recent progress in molecular assessment of kidney, heart, and lung transplants suggests that microarray biopsy phenotyping would provide novel insights for liver transplantation.

Method. We prospectively studied 102 liver transplant biopsies (90% for indications) from USA, Canada, Europe, and Australia with gene expression microarrays (INTERLIVER ClinicalTrials.gov NCT03193151). We used 453 kidney-derived rejection-associated transcripts (RATs) in unsupervised archetypal (AA) and principal component analyses (PCA).

Results. Every liver biopsy yielded abundant high quality RNA for microarray analysis. In PCA, principal component 1 correlated with transcripts associated with inflammation (e.g. PTPRC/CD45), TCMR (e.g. Granzyme A) and interferon-gamma effects (e.g. GBP5), and with histologic portal triaditis; PC2 correlated with injury-induced transcripts (e.g. SERPINB8).

AA identified 3 archetypes (A1, A2, and A3) and scored every biopsy for similarity to each: $S1_{normal}$, $S2_{TCMR}$, and $S3_{injury}$ (Figure 1, with biopsies colored by highest score). Biopsy groups were studied for expression of previously annotated transcript sets (Table 1). $S1_{normal}$ biopsies lacked rejection, inflammation, and injury. $S2_{TCMR}$ biopsies had high expression of rejection- and IFNG-inducible transcripts. $S3_{injury}$ biopsies had increased transcripts reflecting injury and cellular damage (e.g. DAMPs), and were early post-transplant i.e. had donation-implantation injury.

Additional 5-archetype analyses suggested a small subclass of late biopsies with plasma cells and mast cell transcripts, which in other organs are associated with fibrosis. No biopsies manifested molecular changes suggesting ABMR.

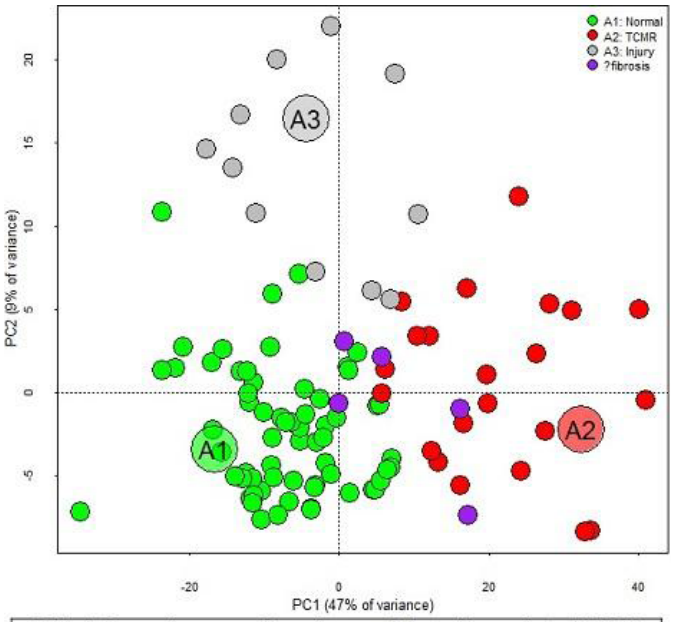

Table 1. Comparing scores for pathogenesis-based transcript set (PBTs) among 102 liver biopsies

Biological processes	Mean transcript set score* in biopsies grouped by highest archetype score	$A1_{normal}$ (N=66)	$A2_{TCMR}$ (N=25)	$A3_{injury}$ (N=11)	Possible fibrosis subset (N=5)**
Time of biopsy post-transplant (TxBx) in days		1148	295	4	1188
TCMR-related and T cell infiltrate	TCMR-RATs	-0.20	**0.59**	-0.12	0.30
	QCATs	-0.19	**0.64**	-0.30	0.37
All rejection/injury	GRITs	-0.16	**0.34**	0.18	0.15
	All-rejection-RATs	-0.26	**0.70**	-0.03	0.18
ABMR	DSASTs	0.00	0.02	-0.07	**0.13**
	ABMR-RATs	-0.18	**0.45**	0.05	0.16
	ENDATs	-0.03	0.04	0.10	**0.33**
Parenchymal injury	AKI transcripts	-0.14	0.13	**0.52**	0.45
	DAMPs	-0.05	0.05	**0.16**	-0.05
	IRIT5	-0.06	0.13	0.07	**0.38**
Mast cell and plasma cell transcripts	MCATs	0.08	-0.07	-0.33	**1.07**
	IGTs	-0.12	0.43	-0.28	**0.71**

*The gene sets were empirically derived in human cell lines, human transplants, and mouse models. They reflect biological processes relevant to rejection and injury. The gene set score is a ratio between mean gene set expression in each cluster and the full reference set.
** These 5, which were subclassified in a new AA, were previously classified as 2 normal, 3 TCMR.

[Figure 1 and Table 1]

Conclusion. Molecular phenotyping classifies liver transplant biopsies as normal, TCMR, and early injury. The incidence of biopsies with TCMR-like changes (25%) was higher than in other organ transplants which raises the possibility that immunoregulatory mechanisms such as T cell exhaustion may be operating.

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LncRNA HOTAIR deficiency protects livers from ischemia reperfusion injury by facilitating M2 macrophage differentiation

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Background: The role of LncRNA HOTAIR in hepatic ischemia/reperfusion (I/R) injury remains unknown. Here, we comprehensively examined the role of LncRNA HOTAIR in hepatic I/R injury.
Method: In the current study, we analyzed the function of lncRNA HOTAIR in regulating tissue inflammatory immune response in mice liver partial warm ischemia model. The regulatory effects of HOTAIR on inflammatory responses, cytokine and chemokine release, apoptotic and anti-apoptotic responses during hepatic I/R injury were identified by real-time PCR, Western blot, immunohistochemistry.
Results: The expression of HOTAIR was increased during hepatic I/R injury in vivo and in hepatic Kupffer cells. HOTAIR deficiency reduced the extent of liver injury by decreasing macrophage and neutrophil infiltration, preventing cytokine and chemokine release and alleviating hepatocyte apoptosis during hepatic I/R injury. At the cellular level, knocking down HOTAIR in Kupffer cells and peritoneal macrophages isolated from WT mice expressed higher levels of M2 markers and produced lower TNF-α and higher IL-10 in response to LPS than did their control group.
Conclusion: LncRNA HOTAIR deficiency protects livers from ischemia reperfusion injury by facilitating M2 macrophage differentiation.

P-347

ARRB1 protects against hepatic ischemia-reperfusion injury via TRAF3 suppression

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Background: The hallmarks of hepatic ischemia/reperfusion (I/R) injury, a common clinical problem that occurs during liver surgical procedures, include severe cell death and inflammatory responses that contribute to early graft failure and a higher incidence of organ rejection. Unfortunately, effective therapeutic strategies are limited. β-arrestins are multifunctional proteins that mediate receptor desensitization and serve as important signaling scaffolds in numerous physiopathological processes. Here, we showed that only ARRB1 was upregulated in I/R-injured liver tissues, we examined whether ARRB1 is protective or detrimental against hepatic I/R injury.
Methods: We overexpressed ARRB1 in the liver of C57BL/6 mice using an ARRB1 adenovirus. Wide-type and ARRB1 knockout mice were subjected to a partial (70%) hepatic ischemia for 45 minutes, followed by various periods of reperfusion. Isolated hepatocytes from wild-type and ARRB1 knockout mice were subjected to hypoxia-reoxygenation injury to determine the in vitro effects of ARRB1. The function of ARRB1 in I/R-induced liver damage and the potential underlying mechanisms were investigated through various phenotypic analyses and biological approaches.
Results: Mice subjected to I/R injury showed typical patterns of hepatocellular damage. Prior injection with ARRB1 adenovirus reduced cell death, inflammatory cell infiltration, and cytokine production in both in vivo and in vitro hepatic I/R models, whereas hepatic ARRB1 knockout resulted in the opposite effects. Mechanistically, ARRB1 directly interacts with TRAF3, which prevents the activation of the downstream NF-Kb and JNK pathways. Importantly, inhibition of TRAF3 almost completely reversed the ARRB1 overexpression-mediated protection function of I/R injury.
Conclusion: ARRB1 is a novel I/R mediator that protect liver damage and reduce inflammation via TRAF3 mediated activation of JNK and NF-kB pathways.

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Hyperglycemia aggravates acute liver injury by promoting macrophage NLRP3 activation via AMPK/mTOR-dependent autophagy inhibition

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Background: The detrimental effects of diabetes mellitus/hyperglycemia include an increase in the oxidative stress response and an enhanced inflammatory response. Despite an increased understanding of the pathophysiology of toxin-induced liver injury, the role and underlying mechanism of hyperglycemia in regulating thioacetamide (TAA) induced liver injury remains unclear.
Methods: Type I diabetes was induced by streptozotocin treatment. Hyperglycemic mice (STZ) and control group mice (CON) were subjected to TAA-induced acute liver injury model. Liver injury and NLRP3-mediated innate immune response were evaluated. RAW 264.7 cells were cultured with low (LG) or high glucose medium (HG), and the signaling pathways in regulating autophagy and NLRP3 activation were analyzed.

Results: Compared to the CON group, STZ mice exhibited a significant increase in liver injury and intrahepatic inflammation post TAA treatment. HG RAW 264.7 cells showed much higher levels of TNF-α, IL-6 and NLRP3 activation. In contrast, autophagy were inhibited in HG RAW 264.7 cells. AMPK/mTOR signaling was found to be involved in inhibiting autophagy activation by high glucose treatment. Autophagy induction by mTOR-siRNA or AMPK agonist inhibited NLRP3 activation in HG RAW 264.7 cells.
Conclusion: Hyperglycemia aggravated TAA-induced liver injury by autophagy inhibition, leading to NLRP3 activation in macrophages. These findings demonstrated APMK-mTOR dependent autophagy is a novel regulator of innate immunity in toxin-induced liver injury in diabetes mellitus.

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Markedly increased p-JNK expression is associated with increased necrosis and decreased autophagy in cholestatic liver

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Background: Clinically, liver fibrosis and cholestasis are two major disease entities, ultimately leading to hepatic failure. Although autophagy plays a substantial role in the pathogenesis of these diseases, its precise mechanism has not been determined yet.
Materials and methods: Mouse models of liver fibrosis or cholestasis were obtained following the serial administration of thioacetamide or surgical bile duct ligation (BDL), respectively. Next, after obtaining liver specimens at specific time points, we compared the expression of apoptotic (cleaved caspases), necrotic (phospho-c-Jun N-terminal kinase [p-JNK] and CD68), and autophagy markers (microtubule-associated protein light chain 3B [LC3B] and p62) in the fibrotic or cholestatic mouse livers, using polymerase chain reaction, western blot analysis, immunohistochemistry, and immunofluorescence.
Results: Following BDL, although there was a time-dependent increase of necrotic markers (p-JNK and CD68), no significant expression changes were detected in pro-apoptotic markers (cleaved cascades) over time. In addition, autophagy marker studies indicated that whereas autophagy was upregulated in fibrotic livers, it was downregulated in cholestatic livers. We also observed mild to moderate activation of p-JNK in fibrotic livers, whereas cholestatic livers demonstrated a significantly higher p-JNK activation.
Conclusions: Whereas fibrotic livers exhibited a mild to moderate increase in p-JNK expression related with the induction of autophagy and apoptotic cell death, cholestatic livers exhibited a marked increase in p-JNK expression which might be associated with the reduction of autophagy and a subsequent increase in necrosis.

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Liver transplantation for genotype 4 HEV related acute-on-chronic liver failure

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Background: Hepatitis E virus (HEV) is one of the common cause of acute hepatitis. Usually, Its infection is characterized by acute, self-limiting, and benign course, but when it occurs in patients with chronic liver disease(CLD), acute-on-chronic liver failure(ACLF) could develop and require liver transplantation. Most of the reports of HEV-related acute liver failure (ALF) and ACLF were genotype 3, and genotype 4 HEV related ALF and ACLF were fairly reported.
Method: This is a retrospective chart review study. HEV related ALF or ACLF patients who were admitted to our hospital between November 2015 to November 2018 were analyzed in this study.
Results: During the study period, four HEV related acute hepatitis patients were admitted to our hospital. Diagnoses were made by viral RNA detection in serum samples, and they all had genotype 4 HEV. One patient did not have any CLD, whereas the other three patients had CLD. Pre-existing liver disease of these three patients were; one chronic hepatitis B virus infection; two alcoholic liver disease. ALF developed on one patient who did not have any CLD, whereas ACLF occurred on three patients with CLD. ALF patients recovered spontaneously with steroid pulse therapy and apheresis therapy. HEV-RNA became negative on three ACLF patients. However, liver decompensation progressed and all of them were listed for liver transplantation. One patient underwent deceased-donor liver transplantation, and another one underwent living-donor liver transplantation. Both of them are alive and remains HEV-RNA negative. The other ACLF patients died while waiting for liver transplantation.

In summary, 3/3 (100%) genotype 4 HEV-related acute hepatitis patients with CLD developed ACLF and required liver transplantation.
Conclusion: In genotype 4 HEV-related acute hepatitis, the incidence of ACLF were quite high on CLD patients even after HEV-RNA clearance. liver transplantation should be considered on HEV patients with CLD.

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Is liver transplantation (LT) an alternative for acute liver failure (ALF) due herpes simplex virus?

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Introduction: The association between, herpes simplex virus (HSV) infection, acute liver failure (ALF) and hemophagocytic syndrome (HPS) is unusual. Most of the affected individuals are either immunosuppressed or pregnant women. Early diagnosis and prompt specific treatment may improve prognosis, but it is uncertain the impact of positive viremia over it. We describe an unsuccessful case of HSV infection complicated with HPS and ALF who underwent liver transplantation (LT).
Case presentation: Fourty-one years-old female, with steroid-dependent asthma was admitted with 11 days history of fever, odynophagia, jaundice, coagulopathy and encephalopathy. Upon admission, aphtoid ulcerations in the tongue and oral cavity were noted, and acyclovir was initiated. The patient fulfilled the criteria for LT priorization due to ALF. Myelogram was compatible with HPS and the HSV PCR was positive in blood. No other causes of ALF were identified. The patient underwent LT 72 hours after the admission and died 48h afterwards due to recurrence of the HSV infection and multiorgan failure despite of continuous acyclovir. The liver explant pathological analysis revealed massive necrosis with herpetic viral inclusions.
Discussion: Accurate identification of the etiology of ALF and immediate initiation of specific treatment may reduce mortality in HSV hepatitis. HSV should be considered in differential diagnosis in ALF and HFS, particularly if fever is present. In most recent literature the empiric treatment with acyclovir is recommended until de HSV is excluded in patients with unknown etiology, especially immunocompromised. LT appears not an option in the cases of systemic commitment and viremia.

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INR above measurable value of 8.7 but normal ROTEM in acute fulminant hepatic failure due to acetaminophen overdose

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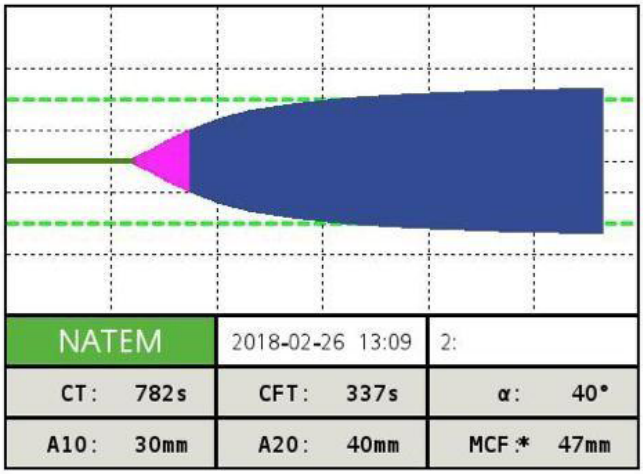
Introduction: Standard coagulation tests abnormalities, like elevated internal normalized ratio (INR), are common in patients with fulminant hepatic failure (FHF). Those laboratory abnormalities do not correlate with clinical bleeding or hemostatic function in liver disease patients. We present a case of a patient in fulminant hepatic failure with an unmeasurably high INR (>8.71) but a normal ROTEM.
Case description: A 36-year-old female was admitted for fulminant hepatic failure due to acetaminophen toxicity (acetaminophen level: 110 mcg/mL, AST/ALT 1900/1800 IU/L, MELD-score: 36 [creatinine: 0.9 mg/dL, INR: >8.71, bilirubin: 3.6 mg/dL]). Laboratory coagulation was; PTT: 30 sec., PT: >100 sec. platelets: 156,000, fibrinogen: 116 mg/dL, factor V activity: 7%. Due to the very high INR and concerns of spontaneous bleeding, a ROTEM analysis was performed to evaluate the clinical coagulation status. All parameters (CT, CFT, alpha-angle, A10, MCF) were within normal limits, figure 1. Despite the normal viscoelastic assay, there were concerns for the patient's severe coagulopathy, indicated by abnormal routine lab results, from the hepatologist and she received 9 units of FFP and 5 units of cryoprecipitate prior to obtaining central venous access for continuous-veno-venous-hemodialysis (CHHVD) and molecular adsorbent recirculating system (MARS).



[Patient's perioperative ROTEM analysis for liver transplantation evaluation]

Conclusion: When evaluating patients with acute FHF, even INR levels that are unmeasurably high do not signify abnormal clinical coagulation based on ROTEM. Therefore, we encourage the use of viscoelasticity such as ROTEM for hemostasis assessment in FHF. FFP and cryoprecipitate transfusion may be used only based on the result of viscoelastic essay if available.

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Liver transplantation for acute liver failure caused by incidental diffuse primary hepatic angiosarcoma

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Background: Rare acute liver failure patients caused by primary hepatic angiosarcoma may be perfomed liver transplantatioin.
Method: A patient with acute liver failure performed liver transplantation was retrospectively analyzed.
Results: The 58-year-old male was transferred to our hospital from a local clinic due to gradually worsening of liver function and suspicion of hepatic venular occlusive disease (HVOD). MRI revealed liver hemangiomatosis, and the patient developed acute liver failure with a Child-Pugh score of 12 points and a Model for end-stage liver disease (MELD) score of 28 points. Emergency liver transplantation was performed for the patient. The pathology of the resected liver suggested primary hepatic angiosarcoma (HAS). The patient's recovery was uneventful. No complications were observed during the postoperative course, and initial immunosuppression included tacrolimus, mycophenolate mofetil and corticosteroids. Due to histological findings, tacrolimus was switched to sirolimus as the main immunosuppressive drug two months after liver transplantation. During the two-month follow-up after liver transplantation, CT scan suggested tumor recurrence and lung metastasis. After 1.6 g/time of gemcitabine was administered for two times, the tumors continued to gradually progress. The patient died of cerebral hemorrhage six months after liver transplantation.

Conclusions: The etiologic disease, which could lead to acute liver failure, should be determined before performing the liver transplantation, and at least primary HAS should be excluded, since it is considered a contraindication to liver transplantation due to its poor outcome. Even though preoperative percutaneous biopsy was not recommended due to risk of bleeding, we suggested intraoperative biopsy for making the definitive diagnosis before liver transplantation was actually commenced during the exploration. If liver transplantation has been performed for incidental HAS, molecular targeted assay should be performed, and new molecular therapies or chemotherapies according to the molecular targeted assay results should be immediately considered after liver transplantation, in order to improve the outcome.

Poster Round II, Session 1, 2, 3: Basic Science/Translational Research

P-355

Epithelial-mesenchymal transition regulated by Wnt/β-catenin signaling promotes tissue formation in hepatic differentiation from mouse ESCs

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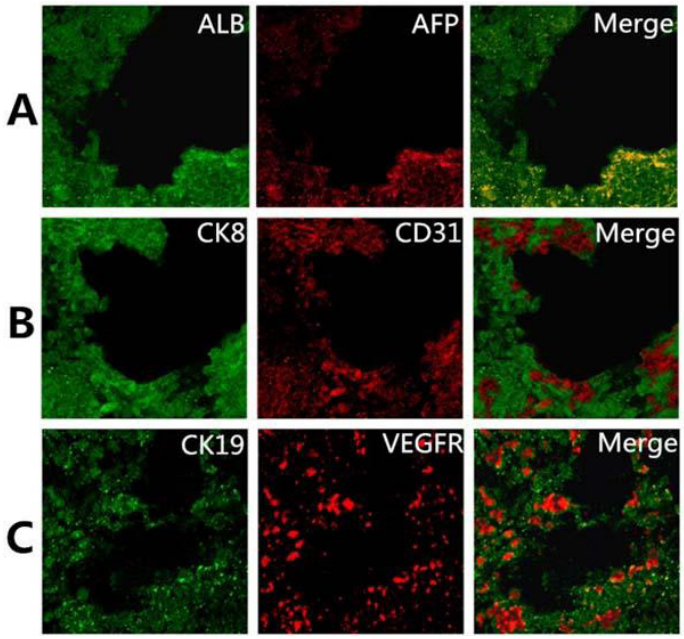
Objective: In embryonic tissue development in vivo, suitable and stable level of epithelial-mesenchymal transition (EMT) play an important role to form the regular and tight tissue structures. In this study, embryonic stem cells (ESCs) were differentiated into hepatic tissue structures by dynamically regulating EMT levels in differentiation system in vitro.
Methods: ESCs from BALB/c mice were induced hepatic differentiation by using hepatic growth factor (HGF) and fibroblast growth factor (FGF) etc in vitro. During this differentiation, the Wnt/β-catenin signaling was dynamically inhibited by sFRP-1 at the middle differentiation stage (13d) and the maturation differentiation stage (17d) to reduce the EMT levels. Finally, differentiated cells growth into three-dimensional tissue structures were observed in vitro and these tissue structures were transplanted into the liver of the BALB/c mice to observe their growth in vivo.
Results: In the early stage of differentiation, the EMT levels were simillar between experimental group and control group. In the middle and late stages of differentiation, the EMT levels in the experimental group were stable and significantly decreased compared with that in control group. Differentiated cells in experimental group maintained growth of 3-dimensional tissue, whereas differentiated cells in control group exhibited single-cell state. The expression of hepatic and vascular cell markers was detected in the experimental group. Immunofluorescence results showed hepatocyte-like cells and vascular structure appearing as dense-layer arrangement and HE staining further revealed formation of hepatic lobule-like structures in experimental group, whereas control group did not show expression of vascular markers(Fig1). These hepatic tissue like structures grew well in mice liver and exhibited good hepatic function.
Conclusion: During ESCs hepatic differentiation in vitro, regulating the EMT into a stable level at the middle and late stages of differentiation could effectively promote ESCs differentiated into hepatic tissue structures.



[Fig 1]

P-356

Pre-operative plasma metabolonics profiling reveals a prognostic fingerprint in liver transplantation for hepatocellular carcinoma

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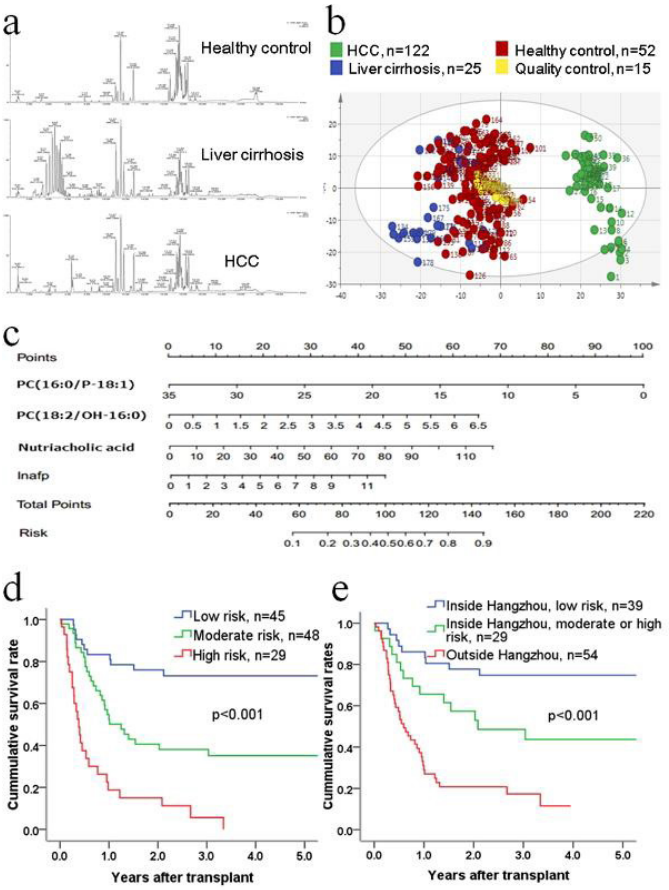
Background: This study aims to identify pre-operative plasma metabolite markers for the prognosis of patients with hepatocellular carcinoma (HCC) undergoing liver transplantation, and further to establish a novel fingerprint to improve the efficiency of recurrence-risk prediction and candidate selection.
Methods: Metabolomics profiling was performed on the pre-operative plasma of 122 HCC patients undergoing liver transplantation, 52 health controls (HC) and 25 liver cirrhosis (LC) patients (Figure 1a and 1b). Prognostic metabolites were identified, and further enrolled to establish a fingerprint/nomogram predicting tumor recurrence after transplantation.
Results: According to univariate cox regression, 5 prognostic metabolite markers were identified ($p < 0.01$), including PC(16:0/P-18:1), PC(18:2/OH-16:0), PC(o-16:0/20:4), nutriacholic acid and 2-Oxo-4-methylthiobutanoic acid. In the HCC group, all the 5 metabolites

were significantly altered compared to the HC group (p< 0.01), while only PC(o-16:0/20:4) and nutriacholic acid were significantly decreased compared to the LC group (p< 0.01). By enrolling the 5 metabolite and blood AFP into multivatiate analysis, we found that PC (16:0/P-18:1), PC(18:2/OH-16:0), nutriacholic acid and AFP were independent risk factors for tumor recurrence (p< 0.01). Therefore, a prognostic fingerprint was established as a nomogram (Figure 1c), which divided the patients into the low-risk group (n=45), moderate-risk group (n=48) and high-risk group (n=29), with discriminated prognosis (p< 0.001, Figure 1d). In the patients fulfilling Hangzhou criteria, the fingerprint/nomogram can also successfully stratify the patients into groups with different recurrence risk (p< 0.05, Figure 1e).

Conclusion: Metabolomics profiling is able to identify novel prognostic metabolite markers in liver transplantation for HCC. The pre-operative plasma fingerprint/nomogram established is efficiency in the prediction of recurrence risk and can facilitate candidate selection in liver transplantation for HCC.



[The prognostic metabolite fingerprint/nomogram in liver transplantation for hepatocellular carcinoma]

P-357

Towards engineering human extrahepatic bile ducts from ductal extracellular matrix and biliary organoids

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Introduction: Bile duct-related complications are a common cause of graft failure after donation after circulatory death liver transplantation. In case of leakage or strictures tissue engineered extrahepatic bile duct (EBD) constructs could be used to repair these complications. Decellularization techniques can remove cells from ductal tissue to generate bile duct extracellular matrix (ECM) which can be used as a scaffold for ductal tissue engineering. The aim of this study is to establish a reproducible method to decellularize bile duct tissue and to explore recellularization with human LGR5+ bile duct-derived organoids.

Methods: EBD tissue is obtained from human donor livers, discarded for transplantation due to steatosis and/or age (N=10). To remove the remaining cells, EBD tissue was treated with Trypsin-EDTA and Triton-x-100. After complete decellularization, ductal tissue was cut open and circular discs were made. Bile duct derived organoids were initiated from healthy human EBD tissue and kept in culture. An organoid-derived cell suspension was added to the luminal side of the ECM and cultured for up to 3 weeks.

Results: The ductal ECM was completely decellularized, while maintaining EBD architecture and ECM proteins. After seeding with organoid cells, an epithelial monolayer formed which covered the entire luminal surface of the ECM. Microscopic analysis showed that these epithelial cells were polarized, similar to large cholangiocytes. Moreover, the cholangiocyte-markers cytokeratin-7 and 19 were detectable at mRNA and protein levels.

Conclusion: This study shows that decellularization of human EBD matrix is feasible. Recellularization with bile duct organoid cells resulted in complete coverage of the ECM with cholangiocyte-like cells and a potential restoring of the barrier function. Further study is ongoing to confirm functionality of these tissue engineered bile ducts.

P-358

Guanine nucleotide-binding protein G(i)α2 aggravates hepatic ischemia-reperfusion injury in mice by regulating MLK3 signaling

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Background: Hepatic ischemia-reperfusion (I/R) injury is a major challenge in liver resection and transplantation surgeries. Previous studies have revealed that Guanine nucleotide-binding protein G(i) α2 (GNAI2) is involved in the progression of myocardial and cerebral I/R injury, but the role and function of GNAI2 in hepatic I/R have not been elucidated.
Method: The hepatocyte-specific GNAI2 knockout ($GNAI2^{hep-/-}$) mice were generated and subjected to hepatic I/R injury. Primary hepatocytes isolated from $GNAI2^{hep-/-}$ and $GNAI2^{flox/flox}$ mice were cultured and challenged to hypoxia-reoxygenation (H/R) insult. The specific function of GNAI2 in I/R-triggered hepatic injury and the underlying molecular mechanism were explored by various phenotypic analyses and molecular biology methods.
Results: GNAI2 expression was significantly increased in liver tissues from liver transplantation patients and wild-type (WT) mice after hepatic I/R. Interestingly, hepatocyte-specific GNAI2 deficiency attenuated I/R-induced liver damage, inflammation cytokine expression, macrophage/neutrophil infiltration, and hepatocyte apoptosis in vivo and in vitro. Mechanistically, upregulation of GNAI2 phosphorylates MLK3 through direct binding, which exacerbated hepatic I/R damage via MAPK and NF-κB pathways activation. Furthermore, blocking MLK3 reversed GNAI2-mediated hepatic I/R injury.
Conclusion: Our study firstly identifies GNAI2 as a promising target for prevention of hepatic I/R-induced injury and related diseases.

P-359

Baseline monocytes as a biomarker to predict sepsis and acute rejection after liver transplantation

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The role of monocyte subtypes in sepsis and rejection remains largely unknown. The aim of this study was to investigate kinetics of bone marrow derived monocyte cells in living donor liver transplant and their impact in sepsis and rejection.
During Jan 2016 - Dec 2017 at ILBS, 28 donor-recipient pairs were studied. PBMC (peripheral blood mononuclear cell) from bone marrow derived monocytes were performed at baseline and on POD (Post Operative Day) 1, 3, 5 and 7. PBMC's were isolated by the Ficoll-Hypaque method and flow cytometry was performed for monocytes characterization for the CD14/CD16 marker. CT volumetry was done on POD7.
There were 50% males in the donor group and 92.86% males in recipient group. Majority of the CLD were ethanol related (64.28%). In healthy donors the remnant liver regenerated from 459.37gm±102.77 to 749.6gm±184.95 and in recipients from 718±128.82gms to 1229.36±207.35 gms on POD7 (p- 0.031). 32.14% (9/28) of recipients had sepsis and 21.42% (6/28) had rejection. The percentage number of monocytes was twice in transplant recipients at baseline compared to healthy donor (controls). The total baseline monocyte population was significantly less in the sepsis group (43.36% vs.51.60 %). This was contributed by the classical monocytes (CD14CD16-) which was significant lower in recipients with sepsis. Between POD 1 and POD 5 there was no significant difference in classical monocytes in both the groups. But on POD7 the circulating classical monocytes again became significantly less only in recipients who later developed sepsis. The overall baseline monocyte population was more in recipients with rejection (59.74% vs., 46.46%), p-0.0003.This was contributed mainly by the non-classical monocyte (CD14-CD16+) sub-population in the rejectors (23.14% vs. 12.48%), p-0.001.
Baseline monocytopenia and low classical monocytes are predictor of sepsis. High baseline non-classical monocytes a potential biomarker of early acute rejection.

P-360

Kupffer cells are critical for inflammation resolution in liver ischemia reperfusion injury via tim-4 mediated efferocytosis

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Innate immune-dominated inflammation drives the pathogenesis of Liver ischemia reperfusion injury (IRI). Although the activation of liver inflammation by IR have been studied extensively, few has been focused on the inflammation resolution in the disease process. In a murine liver partial warm ischemia model, we characterized

the inflammation resolution during IR at histological, cellular and molecular levels. The role of Kupffer cells (KCs) was determined by clodronate-liposome (CL)-mediated depletion, and their functional mechanisms were explored by the inhibition of KC efferocytosis via TIM-4 blocking Abs, during the recovery stage of liver IRI (three doses at 24h, day 3 and day5 post reperfusion). The restoration of liver homeostasis from a 90 min ischemia lasts for 7 days, as defined by: (i) repair of hepatocellular damage, (ii) clearance of infiltrating neutrophils, (iii) downregulation of inflammatory and fibrosis genes, and (iv) recovery of KCs and disappearance of infiltrating macrophages. KC depletion by CLs drastically interfered with all these restoration processes, leading to persistent liver inflammation and fibrosis gene upregulation. As macrophage (MΦ) efferocytosis plays key roles in tissue repair and immune regulation, we studied KCs and infiltrating MΦs in their abilities of efferocytosis. KCs were much more efficient in engulfing apoptotic cells. KCs, but not infiltrating MΦs, expressed TIM-4, and TIM-4-signaling was critical for KC effereocytosis in vitro. In vivo TIM-4 blockade by its antagonist antibodies significantly delayed the repair of liver damages. Furthermore, confocal microscopy of liver macrophages revealed efferocytotic (>2 DAPI positive nucleuses) F4/80 positive cells isolated from ischemic livers at day 3 and 5, but not 6h or sham, post reperfusion. TIM4-4 blockade significantly decreased the numbers of those efferocytotic cells. The study documents key roles of KCs in liver inflammation resolution after IR. The repair of IR-induced hepatocellular damages is dependent on TIM-4- mediated KC efferocytosis.

P-361

MicroRNA microarray-based identification of the suppressor role of miR-181a using a novel high-metastatic hepatocellular carcinoma cell model

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Majority of hepatocellular carcinoma (HCC) patients are not eligible for surgical intervention due to metastasis, which poses a major obstacle to cure. Systemic dissection of the molecular mechanisms underlying metastatic progression of HCC is necessary for the development of new diagnostic and therapeutic strategies for metastases. Huh-7/M8 with enhanced migration and invasion abilities was successfully established by repeatedly collecting and amplifying Huh-7 cells which were able to migrate into the lower transwell chamber. MicroRNA microarray and qPCR revealed that miR-181a was down-regulated in Huh-7/M8. Overexpression of miR-181a inhibited Huh-7/M8 invasiveness, while miR-181a inhibitor promoted Huh-7 invasiveness. HMGB2 was proved to be a direct target of miR-181a, and overexpression of miR-181a led to down-regulation of HMGB2 mRNA and protein translation. miR-181a-HMGB2 axis inhibits metastasis of hepatocellular carcinoma by suppressing epithelial- mesenchymal transition. Upregulation of miR-181a in hepatocellular carcinoma tissues is associated with HMGB2 downregulation. The inverse correlation between miR-181a and HMGB2 mRNA expression was verified by linear regression analysis ($r=-0.523$, $P<0.01$). Low miR-181a expression and high HMGB2 expression correlate with patients' poor survival. In a word, our data demonstrated that miR-181a inhibits metastasis of hepatocellular carcinoma by suppressing HMGB2 mediated epithelial-mesenchymal transition, which asserts miR-181a and HMGB2 as prognostic biomarkers and potential therapeutic targets for the suppression of HCC metastasis.

P-362

Comprehensive and combined transcriptomic and proteomic analysis reveals key factors underlying ischemia-reperfusion injury in human liver transplantation

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Purpose: Ischemia-reperfusion injury (IRI) is a major challenge in liver resection and liver transplantation surgery. Hepatic IRI can seriously impair liver function and even cause irreversible damage, but there are gaps in the literature regarding IRI. Herein, we aimed to explore the possible molecular mechanisms underlying IRI using comprehensive and combined bioinformatics analyses.
Methods: Three Gene Expression Omnibus (GEO) datasets comprising liver transplantation data (GSE15480, GSE14951, and GSE12720) and a dataset constructed by our center (GSE113024) were collected for a comprehensive analysis. The co-regulated differentially expressed genes (DEGs), intersecting pathways and key biological processes were identified and validated in clinical samples. We then performed a proteomic analysis of ischemic and reperfused livers (PXD010812). Differentially expressed proteins, functional enrichment involving GO terms, protein domain enrichment and KEGG pathways were identified. Correlations between the transcriptome and proteome were analyzed, and co-regulated DEGs and co-regulated markers were used to elucidate the core factors underlying IRI.
Results: Ten DEGs were co-upregulated in the 4 GEO datasets, including ATF3, CCL4, DNAJB1, DUSP5, JUND, KLF6, NFKBIA, PLAUR, PPP1R15A, and TNFAIP3. Co-expression of the DEGs in 10 matched

clinical samples was verified by quantitative real-time PCR. Six pathways were co-enriched in all 4 chips, including the NF-kappa B signaling pathway; NOD-like receptor signaling pathway; Influenza A; Legionellosis; Transcriptional misregulation in cancer; and MAPK signaling pathway. The combined analysis demonstrated 10 co-regulated genes/proteins, including HBB, HBG2, CA1, SLC4A1, PLIN2, JUNB, HBA1, MMP9, SLC2A1, andPADI4. The co-regulated DEGs and co-regulated genes/proteins formed a tight interaction network and could serve as the core factors underlying IRI.
Conclusions: Comprehensive and combined transcriptomic and proteomic analyses revealed key factors underlying IRI during human liver transplantation. Further studies are needed to elucidate the detailed mechanisms of these potential key factors in IRI progression.

P-363

Improved engraftment of human hepatocytes in immunodeficient, FAH deficient pigs

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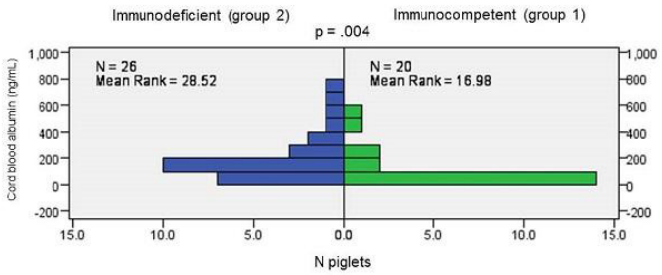
Introduction: We previously reported the livers of fumarylacetoacetate hydrolase-deficient (FAH-deficient) pigs provide a selective advantage for expansion of donor FAH-expressing hepatocytes. However, the immune response against human cells blocks this advantage. We hypothesize the knockout of recombinase activating gene-2 (RAG2) will produce an immunodeficient phenotype and will allow improved engraftment of human hepatocytes.
Methods: We previously described the generation of FAH/RAG2 double-knockout embryos via sequential CRISPR knockouts. At day 35 of gestation, ten-million human hepatocytes were injected into each fetal liver. At Caesarian-section, umbilical-cord blood was obtained for quantification of human albumin via ELISA. Piglets were housed in a bioprotective facility. Immunodeficient and FAH-deficient genotypes and phenotypes were reconfirmed. The same protocol was performed on immunocompetent, FAH-deficient pigs as control. Statistical comparison was performed with the Wilcoxon ranksum test.
Results: Seven litters were delivered in each group yielding 20 immunocompetent, FAH-deficient (group-1) and 26 immunodeficient, FAH-deficient (group-2) piglets. At birth, group-2 had a significantly greater circulating human albumin concentration than group-1 (166 vs 107 ng/ml, p = .004) (Fig. 1). In all piglets, elevated blood levels of tyrosine and succinylacetone were consistent with FAH deficiency. Group-1 demonstrated an immunocompetent phenotype. Group-2 demonstrated an immunodeficient phenotype with variable growth curves and ubiquitous staphylococcal and pseudomonal infections. Flow cytometry of peripheral blood leukocytes confirmed an immunodeficient phenotype. Immunohistochemistry of liver samples revealed no porcine FAH+ hepatocytes. The anticipated knockout sequences were reconfirmed on genotype.
Conclusion: We have produced a large animal model of a FAH/RAG2 double-knockout pig. FAH deficiency provides an intrinsic selective advantage for expansion of normal donor hepatocytes. RAG2 deficiency produces a tolerant state benefiting human hepatocyte engraftment as demonstrated by significantly increased human albumin at birth. This model may be suitable for large scale expansion of human hepatocytes.

Fig. 1: Cord blood human albumin concentration



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P-364

The effects of liver transplantation on changes in the stool microbiome

Victor D., Franco L., Bell S.M., Mobley C., Saharia A., Dorman S., Lunsford K., Egwim C., Ankoma-Sey V., Galati J., Mcfadden R., Ghobrial R.M.

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Background: The microbiome of patients with cirrhosis is altered in comparison to healthy subjects. The composition and role of the microbiome in liver disease is being described. Liver transplantation cures the recipient of cirrhosis. The effects of transplantation on the microbiome have yet to be completely characterized.
Methods: Pre-operative consent was obtained for 27 consecutive liver transplant recipeints. 10 patients were ultimately qualified for this prospective observational study with stool samples collected within one week of transplant. Subsequent samples were collected at one, three, and 6 months. Stool microbiome profiling was done by 16S rRNA gene sequencing to determine the microbiome composition
Results: 38 stool microbiomes were profiled. Eight patient submitted a complete samples. The average age was 60.9 years. The patients were 80% Caucasian and 50% had HCC as the indication for transplantation. 40% had HCV cirrhosis. Baseline microbiome composition was dominated by Proteobacteria, Firmicutes, and Bacteroidetes, marked by an increase the relative abundance of *Citrobacter, Escherichia,* and *Bacteroides* species. At month 1, there was a slight improvement in microbial diversity and communities were marked by a decrease in *Proteobacteria* and an increase in *Bacteroides* and *Blautia*. At 3 months, the relative abundance of *Blautia* continued to increase despite maintaining similar levels of diversity. At month 6, the highest diversity was observed and communities resembled healthy stool microbiomes. In comparing patients who had HCC exception to those who did not the Shannon diversity index was higher in the HCC patients at transplant and it increased for both groups over time.
Conclusion: This pilot study highlighted the shifts in the stool microbiome occuring after liver transplant. Microbiomes turned from being dominated by Proteobacteria to a more balanced community. This effect was mostly seen between 3 and 6 months samples, especially in patients with higher biologic MELD scores at transplantation.

P-365

Identification of new drug targets to prevent ischemia-induced bile duct injury using a human biliary organoid model

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Background: Ischemic cholangiopathy is a severe complication after liver transplantation (LT). It has been hypothesized that hypoxia during transplantation render cholangiocytes more susceptible to bile-salt toxicity, due reduced protection by CFTR-related bicarbonate secretion. Direct evidence is missing since proper bile-duct models are lacking. Liver-derived organoids (LDOs) can be expanded in culture and resemble cholangiocyte-like cells. Thus this study aims to investigate the effect of ischemia on cholangiocyte transport-channels and hypoxia-related biliary injury in LDOs and explore this model for drug-discovery.
Methods: LDOs, cultured from healthy individuals, were analyzed on mRNA- (qRT-PCR) and protein level (Western blot) for cholangiocyte-specific transporters. Channel functionality was tested using an Ussing-chamber assay in 2D-grown organoids (n=42). Hypoxic conditions were achieved by nitrogen gas (95%N2/5%CO2) exposure. To study bile-related toxicity, undiluted bile was added under oxygen and hypoxic conditions. Finally, compounds were tested for the ability to abrogate the hypoxic-induced inhibition of CFTR.
Results: CFTR was expressed in all LDOs on both gene- and protein level. Moreover, CFTR-activity was measured in LDO monolayers after stimulation with Forskolin (cAMP-activator). CFTR-activity was significantly reduced under hypoxic conditions (1.66±0.45 vs. 4.18±0.48, p=0.005). Furthermore, a significant decrease in activity was observed when cells were switched from oxygenated to hypoxic conditions (8.00±1.19 vs.5.89±1.26, p=0.02). Further experiments showed that CFTR indeed secrete bicarbonate in these conditions, confirming that hypoxia reduces apical bicarbonate secretion. When LDO monolayers were exposed to bile, it resulted in more cell death in hypoxic conditions (31.2%±4.32 vs.19.18±4.81, p=0.04). Most importantly, addition of compound C (cAMP-inhibitor) was able to rescue CFTR-activity under hypoxic conditions.
Conclusion: LDOs provide an excellent new model to study cholangiocyte-transporters. We demonstrate that hypoxia inhibits CFTR-related bicarbonate secretion and identified a cAMP-inhibitor can restore this. This encourages further clinical studies to test whether cAMP-inhibitors can prevent hypoxia-related biliary injury during graft preservation and after LT.

P-366

Microencapsulation of HNF4α-MSCs and human primary hepatocytes ameliorates mouse acute liver failure

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Background and aims: Orthotopic liver transplantation improves the survival and quality of life of patients with acute liver failure

(ALF), but this procedure is expensive, complex, and limited by the rarity of donor livers. Mesenchymal stem cells (MSC) and hepatocytes are two attractive sources of cell-based therapies for ALF. The co-transplantation of hepatocytes and MSCs is considered to exert a more effective therapeutic performance than the transplantation of single cells. In our previous study, the overexpression of HNF4a in the MSC has been demonstrated to enhance the expression levels of hepatic-specific proteins and genes. Here, we investigated the effect of HNF4a-MSC on the human primary hepatocytes and the coencapsulation of both on ALF mice.
Methods: ALB and Urea were tested to detect the function of hepatocytes enhanced by HNF4a-MSC. The mRNA levels of ALB, CYP3A4 were also tested. In vivo, microcapsules were transplanted to mice and ALF was induced by injection of LPS and D-gal 2h after transplantation. Liver injuries were assessed by biochemical measurements and histopathology analyses. Macrophage markers of M1 and M2 were observed in the livers to demonstrate the polarization of macrophage. Cell viability was tested in D-gal treated primary hepatocytes and protein chip of the CM was performed to explore the pivotal factors in cytoprotection of HNF4a-MSC.
Results: HNF4a-MSC increased the synthesis and secretion of hepatocytes, and the coencapsulation of HNF4a-MSC and hepatocytes was successful at preventing the release of liver injury biomarkers and promoting M1 to M2 macrophage polarization. The greatest cell vitality was observed in injured hepatocytes treated with CM from the coculture of HNF4a-MSC and hepatocytes. Further studies demonstrated that secretomes derived from the CM play an important role in protection mediated by HNF4a-MSC. Our results reveal that the co-transplantation of HNF4a-MSC and hepatocytes could be a novel strategy for the treatment of ALF.

P-367

Potential mRNA and miRNA are involved in with carcinogenesis of hepatocellular carcinoma by FVII

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Purpose: Our previous studies revealed HCC is associated to coagulation mechanism, and factor VII (FVII), which is a trigger of coagulation cascade, was also mentioned involved in multiple functions of tumorigenesis. Our previous studies observed FVII is usually highly expressed in HCC tissue and correlates to poor prognosis. Many microRNA (miRNA) were recognized that is able to influence cancer process, a recent study also demonstrated that more than 50% of miRNA genes are located in cancer-associated genomic regions, however, there is no previous studies investigate whether FVII would regulate miRNAs in HCC progression.
Materials and methods: Tissues of HCC patient were divided into high or low FVII according to compare their FVII level of tumor part to adjacent normal part itself. Hep3B and HepG2 cell line were transfected with FVII plasmid DNA or siRNA. Next generation sequencing (NGS) was performed for finding FVII-related mRNA or miRNA, and real-time PCR for validation. Interesting mRNA or miRNA were examined the effect in proliferation, autophagy or migration on HCC, and the association with prognosis were assessed to determine the feasibility of chosen mRNA and miRNA to serve as prognostic marker.
Results: The expression of TGFB1, CDKN2A and CDKN2B are opposite while E2F3 is positive correlated with FVII, imply the possible mechanism for promoting HCC proliferation. FVII also regulate the migration-associated mRNAs e.g. E-cadherin, β-catenin and vimentin. Besides, several miRNA such as miR-135a, miR-27a, and miR-141 show significant difference between high and low FVII. QPCR validation and clinical statistics will be further applied.
Conclusion: Our finding develops a FVII-related signal transduction network. In future, it may be applied as a therapeutic target specific for HCC, and provide useful information in HCC treatment.

P-368

Energetic status change during liver graft storage and normothermic machine perfusion in rats

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Background: Liver energetics, that is significantly affected by both cold (CI) and warm ischemia (WI), is generally considered as an indicator of graft quality. Normothermic Machines Perfusion (NMP) is a valuable tool to evaluate and recondition marginal organs before transplantation. Our aim was to investigate liver ATP pool throughout the transplantation process.
Method: Liver ATP content was evaluated in the following groups (N=5 rats each):
1) Native,
2) CI_4°C, 30 minutes cold ischemia;

3) WI_20°C, 30 minutes warm ischemia at 20°C;
4) WI_37°C, 30 minutes warm ischemia at 37°C;
A)NMP-DMEM, 30 minutes CI at 4°C followed by 2 hours of NMP using DMEM as perfusate; B)NMP-RBC, 30 minutes CI followed by 2 hours of NMP using DMEM with human red blood cells (RBC, 15% hematocrit) as perfusate. ATP was evaluated on homogenized biopsies using an ATP-dependent luciferin-based assay; results are expressed as pmol/mg of wet liver tissue.
Results: ATP content in Native group was 1354±109pmol/mg. while in the three groups of liver storage was:CI_4°C 985±102pmol/mg,WI_20°C553±92pmol/mg and WI_37°C179±37pmol/mg. ATP content in all storage groups was statistically lower compared to Native (CI_4°Cp=0,027;WI_20°C and WI_37°C p< 0.001). The decrease in ATP was significantly greater in WI_37°C group compared to both the WI_20°C (p=0,025) and the CI_4°C (p< 0,001) groups.
ATP concentration in livers from the NMP-DMEM group was 327±26pmol/mg (p< 0,001vsNative), while in the NMP-RBC group was 565±56pmol/mg (p< 0,001vsNative). There was also statistical difference between NMP-DMEM and NMP-RBC groups (p=0,010).
Conclusion: The present study confirms that warm ischemia is detrimental for liver energetic status, whereas CI enables to preserve the ATP pool of liver tissue. NMP did not restore the physiological ATP levels. This result indicates that a deeper comprehension of liver metabolism during ex vivo perfusion and a more precise design of perfusion solution composition are mandatory to improve the reconditioning potential of NMP procedure.

P-369

Induction of carbonyl reductase 1 by NRF2 as a therapeutic intervention for hepatic ischemia during liver transplantation

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Background and aims: Carbonyl reductase 1 (CBR1) protects cells against lipid peroxidation. As living donor liver transplantation creates low oxygen conditions that induce oxidative stress, we investigated whether CBR1 transcription is upregulated under ischemic conditions via Nrf2 and attenuate hepatic ischemia reperfusion injury.
Methods: To study CBR1 promoter, we performed luciferase assay. For the CBR1 function study, we established overexpression cell line and performed siRNA treatment. Western blot performed to analyze the expression levels of oxidative stress markers and lipid peroxidation products. Aspartate aminotransferase (AST) and alanine transaminase (ALT) measurements were performed for liver serum chemistry. Immunohistochemistry (IHC) was studied to analyze expression level of CBR1.
Results: We found that Nrf2 induces CBR1 transcription during ischemia reperfusion in mice and humans. Pre-treatment with sulforaphane, an inducer of CBR1 expression, increased expression of the liver function. AST and ALT significantly decreased ischemia reperfusionrelated pathological changes in liver tissue. CBR1 overexpressing cell line showed oxidative stress attenuating. In contrast, CBR1 siRNA treateted cells expressed increasing levels of oxidative stress proteins as compared to the parent cell line. We also observed that human CBR1 is overexpressed during orthotropic living donor liver transplantation via Nrf2. Overexpression of CBR1 prevents hepatic ischemia reperfusion injury by influencing the lipid peroxidation signaling pathway.

P-370

Activation of aldehyde dehydrogenase-2 attenuates hepatic ischemia/reperfusion injury

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Background and aim: Oxidative stress, which plays an essential role in I/R injury, leads to production of reactive aldehydes (*e.g.*, malondialdehydes and 4-hydrononenal, 4-HNE) through lipid peroxidation. This study investigated whether activation of aldehyde dehydrogenase-2 (ALDH2), a mitochondrial enzyme that is responsible for detoxifying aldehydes, ameliorates I/R injury.
Methods: Alda-1 (50 mg/kg, ip), an ALDH2 activator, or vehicle was given 1 h before hepatic ischemia. Male mice underwent 1 h-warm ischemia to 70% of the liver or sham operation.
Results: At 6 h after reperfusion, alanine aminotransferase (ALT) increased from 34 U/L to ~18,000 U/L. Alda-1 treatment decreased ALT release by 65%. Massive necrosis and mild apoptosis also occurred, which were decreased >60% by Alda-1. Inflammation accompanied I/R injury as indicated by increases of TNFμand damage-associated molecular pattern molecule HMGB1 expression, and infiltration of both neutrophils (MPO) and macrophages (F4/80). These inflammatory responses were all blunted by Alda-1. The mitochondrial permeability transition (MPT) plays an essential role in I/R injury. Moreover, oxidative stress causes activation and mitochondrial translocation of c-JUN *N*-terminal kinase (JNK), which promotes onset of the MPT. At 2 h after reperfusion, phospho-JNK increased substantially, whereas total JNK remained unchanged, indicating JNK activation. Widespread mitochondrial depolarization occurred in the liver. Alda-1 blunted JNK activation and mitochondrial

depolarization. 4-HNE adducts increased substantially after I/R. Alda-1 did not increase ALDH2 expression but decreased 4-HNE adducts, indicating Alda-1 works by activation of ALDH2.
Conclusion: Oxidative stress causes mitochondrial dysfunction and liver I/R injury, at least in part, by producing reactive aldehydes. Therefore, acceleration of aldehyde degradation by ALDH2 activation is a novel strategy to protect mitochondria and ameliorate hepatic I/R injury (NIDDK and NIAAA).

P-371

Role of hyperperfusion portal vein flow and ischemia in porcine liver transplantation

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Background: Portal vein flow optimal modulation during liver transplantation (LT) remains debated.
Almost all of the experimental models reproduce hyperperfusion portal vein flow (HPVF) only after partial graft LT or major hepatectomy described as "small-for-size" syndrome (SFSS). The objective of this study was evaluated the impact of HPVF and its early consequences after ischemia-reperfusion in porcine liver.
Method: Nine pigs included in the analysis were divided into three groups according to the experimental model: a HPVF group with creation of a hyperperfusion portal by a calibrated aorto-portal shunt, a hepatic ischemia (HI) group induced by a total vascular clamping of the liver with intrahepatic flushing with a refrigerant preservation solution, and an HI + HPVF group combining the two models.
We analyzed the hemodynamic, biological and histological repercussions over 24 hours.
Results: HPVF was obtained at more than 2 times baseline portal flow in the HPVF group (p=0,045) with 100% survival and in the HI + HPVF group (p=0,0001) with 66% survival. Adaptation by significant decrease in hepatic arterial flow was found in the HPVF (p=0,022) and HI + HPVF groups (p=0,0001). The HI model with a 66% survival reproduced an effective HI with a clamping time of 15 minutes and an intrahepatic flushing of 600mL[550-750], demonstrated by significant increased AST-ALT levels and extensive necrosis on pathology. A significant decrease in inter-mesenteric-renal aorta flow and renal flow was observed and was more important in the HI + HPVF group than HPVF (p=0,046).
Conclusion: This study described for the first time a reproductible and viable HPVF and HI models in a large animal. HI added endothelial and hepatocyte injuries in the HI + HPVF group and aggravated systemic and renal hemodynamic tolerance. However, HI did not influence hepatic adaptation and its ability to regulate increased portal flow at 2 times baseline.

P-372

Loss of FXR exacerbates liver damage by activating NLRP3 inflammasome induced pyroptosis in liver ischemia reperfusion injury

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Background: Farnesoid X receptor (FXR) is a nuclear receptor known to be widely involved in inflammatory diseases. The relationships among FXR, nucleotide-binding oligomerization domain-like receptor family pyrin domain-containing 3 (NLRP3) inflammasome and pyroptosis are largely unknown in liver IRI. We aimed to investigate the mechanism by which the FXR/NLRP3 inflammasome/pyroptosis axis regulates inflammatory responses in a mouse hepatic ischemia reperfusion injury (IRI) model.
Method: A mouse partial (70%) liver warm ischemia (90 min) model was induced in the present study. The expression of FXR, GSDMD, NLRP3, IL-1β, cleaved caspase-1 in clinical liver transplantation samples and mouse IRI livers was detected by Western blot and qRT-PCR. Hepatic necrosis after IRI was detected by H&E staining. The lever of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were detected by a biochemical analyzer.
Results: We showed that induction of pyroptosis in vivo in warm IRI mouse livers. Deletion of FXR exacerbated liver damage, as evidenced by increased levels of serum alanine aminotransferase and aspartate aminotransferase, hepatocellular necrosis, intrahepatic neutrophil trafficking, and the upregulation of pro-inflammatory cytokines. FXR deficiency activated the expression of gasdermin D (GSDMD), which has been identified the pyroptosis executioner. FXR silencing increased pyroptosis and liver damage after hepatic IRI. Blocking NLRP3 inflammasome in FXR knockout mice showed the reduced expression of GSDMD-N, cleaved caspase-1, IL-1β and decreased liver damage.
Conclusions: These findings provide a novel mechanism that FXR regulates pyroptosis through inhibition of NLRP3 inflammasome, leading to ameliorate hepatic IRI.

P-373

Multi-omics approach to identify up- and down-stream regulators in ischemia reperfusion injury leading to early graft dysfuntion in liver transplantation

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Intro: We investigated the role of global DNA methylation (DNAm) patterns on gene expression (GE) during ischemia reperfusion (I/R) injury in liver transplant (LT) patients.
Methods: 92 paired biopsies from 38 DDLT and 8 LDLT were collected at pre-implantation (Pre-Imp) and post-reperfusion (Post-Rep). DD LT patients were sub-classified based on I / R injury severity post-LT as: high (HI, n=21) or low (LI, n=17) I/R injury (based on AST/ALT >< 2,000 IU/L). Live donors liver transplant (LDLT) recipients were used as controls. Methylome and transcriptome were interrogated and interactions were analyzed.
Results: Among HI DDLT recipients there were 6334 Dme CpG sites Pre-Imp and Post-Rep using an FDR< 0.01. From GE using same samples, 2730 DE probe sets between Pre-Imp and Post-Rep samples were observed (FDR< 0.01). When restricting attention to the LI group, there were 1338 DE probe sets Pre-Imp and Post-Rep samples (FDR< 0.01). CGI regions were categorized into CGIs, CGI shelf, shores and non-CGI regions. Distribution of the Dme CpGs was analyzed showing 43% CGI with equal distribution (32%) of Dme CpGs on the promoter and gene body regions. Genes mapped to the Dme CpGs were related to the global GE microarray data. A total of 208 genes in the LI group and 45 genes in the HI group were common between the DNAm and GE datasets. The analysis of these genes showed activation of fibroblast cell proliferation, cell survival, cell cycle progression and inhibition of cell death in LI while cell movement of neutrophils, phagocytosis of blood cells, and cell viability were affected in the HI group.
Conclusion: Hereby, a key effect of ischemia on graft DNAm patterns was identified. It was observed that DNAm patterns play a key role in I/R injury by inducing differential GE changes affecting severity of graft injury and outcome.

P-374

Inhibition of GSK3β protects liver against ischemia/reperfusion injury via activating AMPK-mediated autophagy

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Background: Autophagy has been found to play an important role in hepatic ischemia/reperfusion injury. Our previous study has also clarified that rictor deficiency aggravated hepatic I/R injury by suppressing autophagy. Here, we will explore whether autophagy participates in GSK3β-mediated cytoprotection in liver I/R.
Methods: Mice were administered with SB216763 to inhibit GSK3β before subjected to hepatic ischemia/reperfusion. Liver injury was evaluated by using the liver and blood samples of these mice. Autophagy was measured by detecting expression of LC3B II and ATG-5, as well as the number of autophagosomes by TEM. Primary hepatocytes pretreated with SB216763 for 2 hours were subjected to hypoxia/reoxygenation to induce autophagy. The lactate dehydrogenase level was used to evaluate cell death and survival. Autophagy inhibitors and AMPK inhibitor were administered *in vivo* or *in vitro*.
Results: SB216763 significantly increased the number of autophagosomes and the protein levels of LC3B II and ATG-5 in liver I/R models, which was accompanied a decline of hepatic necrosis and apoptosis. In consistent with the *in vivo* study, autophagy and cytoprotection were induced by the inhibition of GSK3β *in vitro* study. Moreover, autophagy inhibitors pretreatment attenuated the cytoprotective role of autophagy in the GSK3β-treated liver I/R models. Further analysis showed that pretreatment with an AMPK inhibitor increased mTOR activity, decreased autophagy and abrogated GSK3β- mediated liver protection.
Conclusion: Autophagy was induced by GSK3β inhibition through AMPK/mTOR pathway and could substantially ameliorate liver I/R injury. Therefore, our findings strongly renew the therapeutic value of the GSK3β/autophagy axis in the hepatic I/R injury.
Keywords: Hepatic ischemia/reperfusion injury; autophagy; GSK3β; AMPK

P-375

Quantitative proteomics analysis of donor liver provides new insight into the molecular process of liver injury

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Background: Successful orthotopic liver transplantation (OLT) surgery mostly depends on good and functional liver donor, besides of mature transplant technology. The molecular basis of different liver donor with distinct susceptibility to ischemia/reperfusion (I/R) injury during liver transplantation remains undefined. Using isobaric tags for relative and absolute quantification (iTRAQ), we investigated proteomic alterations during early graft reperfusion in human liver transplantation.
Methods: Liver tissue samples were acquired from 15 donor livers, which belongs to three groups: optimal graft function (OGF), early allograft dysfunction (EAD), primary nonfunction (PNF). Each pair biopsy was taken at the start of the retrieval operation, before anhepatic phase and at the end of transplantation. Comparative quantitative proteomics was performed to find differential promoetic among OGF, EAD, PNF and control group. Label-free LC-MRM-MS-based targeted method was further emploied for verification.
Results: A total of 1139 proteins were identified and expressed differentially between those tissue group. 22 proteins were identified to play a centrol role in the ischemia reperfusion injury (IRI) injury process. However, a higher uniformity was noted in the PNF group. More than 160 differentially expressed proteins were detected in PNF group, compared to 54 and 36 proteins in the EAD and OGF groups respectively. The molecular function of these proteins were mainly involved in catalytic activity, binding, antioxidant activity, transporter, molecular transducer, enzyme regulator, etc. Further verification test demonstrated that 15 proteins were found to be related to IRI injury, including decreased expression of CNDP2, PRDX1, HGD, FABPL, THIO, 6PGD, HPPD in PNF group.
Conclusion: This study uncovered new insights into graft function related protein in liver allograft. Dysfunctional liver donor is more sensible to IRI injury companied with more protein changes in biological process and molecular function. The present findings might provide new avenues for evaluation of liver allograft quality.

P-376

The alarmin IL-33 has a key-role in hepatic ischemia-reperfusion in a mouse model

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Background: It has been demonstrated that IL-33 plays a role as an alarmin in the initiation of the inflammatory response in renal ischemia/reperfusion (I/R) injury [1-3].
The aim of this study was to establish whether IL-33 acts also as an alarmin in hepatic I/R.
Method: A model of warm hepatic ischemia with clamping of 70% of the liver was chosen in wild-type mice and IL-33 KO mice with C57BL/6 background. Severity of I/R injury was assessed with serum ALT measurement and histological analysis of clamped liver according to a pre-determined score.
Results: In wild-type mice, IL-33 was constitutively expressed in liver sinusoidal endothelial cells and was released from the ischemia phase and its immediate course into systemic circulation without neo-synthesis. I/R injury was decreased in IL-33 KO mice after 4h and 8h of reperfusion. Therefore, in the first hours after I/R, IL-33 acts as an alarmin and is at least partly responsible for I/R injuries. After 4h of reperfusion, the IL-33 plasmatic concentration decreased and returned to its basal state after 24h, while a neo-synthesis of IL-33 appeared in liver sinusoidal endothelial cells and also in hepatocytes. IL-33 acts here as a cytokine whose biological role remains to be unravelled.
Conclusion: Taken together, these results suggest that IL-33 plays an important role as an alarmin in hepatic I/R injury. A delayed role of IL-33 as a cytokine seems to exist, requiring further investigation.
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P-377

The shifting of hepatic macrophages during the perioperative period of liver transplantation

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Background: Hepatic macrophages (HMs), a key component of non-parenchymal cells in liver, are mainly divided into two major sources. One is the liver-resident population, Kupffer cells (KCs), and the other is the monocyte-derived macrophages recruited from the peripheral blood. The composition and function of HMs in the transplanted liver remains unclear.
Method: We analyzed the shifting of HMs during the perioperative period in a murine orthotopic liver transplantation model. Mice liver expressing systemical eGFP were transplanted to wild type recipients. HMs were acquired from liver grafts after transplantation and analyzed by flow cytometry.
Results: During the first post-transplant month, donor-derived macrophages (DDMs) decreased from 100% to 1.2% of total HMs, whereas the recipient-derived macrophages (RDMs) increased from 0% to 98.8%. Similarly, RDMs were predominant (99.7%) in M1-skewed (CD16/32+) HMs at post-transplant day 30. M1-skewed RDMs sharply increased to a peak at post-transplant day 1. Then they decreased and became relatively steady (M1-skewed RDMs/RDMs: around 20%) after 2 weeks, while M1-skewed DDMs barely changed (M1-skewed DDMs/DDMs: around 20%). RDMs in M2-skewed (CD206+) HMs only accounted for a half at post-transplant day 30. M2-skewed RDMs remained at a low level (M2-skewed RDMs/RDMs: 1%), while M2-skewed DDMs increased sharply and remained at around 50% (M2-skewed DDMs/DDMs) during the first post-transplant month.
Conclusion: RDMs become the new host of the transplanted liver.

P-378

Evaluation of *New Baskent University Preservation Solution* for liver, kidney and intestine graft during cold ischemia: preliminary experimental animal study

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Background: Despite significant advances in organ transplantation, damage caused to organs due to long cold ischemia time and perfusion solutions remains a serious hurdle. The objective of this preliminary experimental animal study was to compare the efficacy of the new Baskent University Preservation Solution (BUPS) with UW, HTK and saline solutions.
Methods: In addition to the electrolytes raffinose, mannitol, N-acetylcycteine, taurine, adenosinei and ascorbic acid were used in BUPS.
50 Male Sprague Downey rats, weighting 350-450 g, were randomized into 4 groups (Group B: BUPS, Group H: HTK, Group W: UW, and Group C: Saline) corresponding to the 3 solutions tested. Under general anesthesia, the rats were perfused with 50 cc (+4 C) BUPS, UW, and HTK perfusion solutions from the distal part by connecting the proximal of the intra-abdominal aorta after laparotomy. To assess cold ischemia injury, both kidneys, liver and intestine were removed and placed in the same solution. Samples were taken from these organs for pathological evaluation at 0, 1, 3, 6, 12, 24 and 48 hours.
Results: Neither group had shown significant cellular injury at 0, 1, 3-hour perfusion. At 6,12, 24 and 48-hour perfusion, the percentage of injured were found to be lowest in Group B and H compared to Group W and C ($p< 0.01$). Also, compared to Group H, the degree of organ damage was most moderate in Group B at 6,12, 24 and 48-hour perfusion ($p< 0.05$).
Conclusion: Cellular damage during ischemic conditions was assessed with various preservation solutions. The rate of cellular injury was lowest in BUPS therefore making it a utilizable perfusion solution.

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Effects of the gut-liver axis on ischaemia-mediated hepatocellular carcinoma recurrence in the mouse liver

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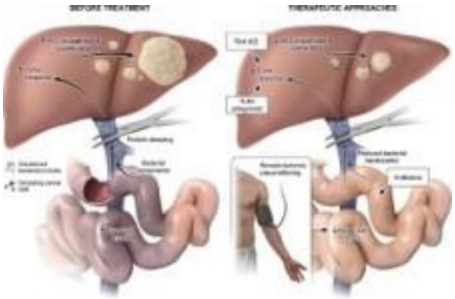
Background: There is growing evidence that liver graft ischemia-reperfusion (I/R) is a risk factor for hepatocellular carcinoma (HCC) recurrence, but the mechanisms involved are unclear. Herein, we tested the hypothesis that mesenteric congestion resulting from portal blood flow interruption induces endotoxin-mediated Toll-like receptor 4 (Tlr4) engagement, resulting in elevated liver cancer burden. We also assessed the role of remote ischemic preconditioning (RIPC) in this context.

Method: C57Bl/6j mice were exposed to standardized models of liver I/R injury and RIPC, induced by occluding the hepatic and femoral blood vessels. HCC was induced by injecting RIL-175 cells into the portal vein. We further evaluated the impact of the gut-liver axis (lipopolysaccharide (LPS)-Tlr4 pathway) in this context by studying mice with defective (global Tlr4-/-knockout mice, gut sterilization, and Tlr4 antagonist) or enhanced (lipopolysaccharide infusion) Tlr4 responses.
Results: Portal triad clamping provoked upstream mesenteric venous engorgement and increased bacterial translocation, resulting in aggravated tumor burden. RIPC prevented this mechanism by preserving intestinal integrity and reducing bacterial translocation, thereby mitigating HCC recurrence. These observations were linked to the LPS-Tlr4 pathway, as supported by the low and high tumor burden displayed by mice with defective or enhanced Tlr4 responses, respectively.
Conclusion: Modulation of the gut-liver axis and the LPS-Tlr4 response by RIPC, gut sterilization, and Tlr4 antagonism represents a potential therapeutic target to prevent I/R lesions, and to alleviate HCC recurrence after liver transplantation and resection.



[Graphical summary of the explored mechanisms]

P-380

FK506 aggravates cobalt chloride induced HepG2 cytotoxicity

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Background: The effects of FK506 on the endoplasmic reticulum (ER) mediated stress pathway accelerates cobalt chloride induced cytotoxicity in human hepatoma HepG2 cell line were investigated.
Methods: We examined the effects of FK506 on cobalt chloride induced cytotoxicity by western blots of poly ADP-ribose polymerase (PARP), CHOP, GRP78, Nrf2, ATF4, ATF6, XBP-1, Bak, Bax, and Bcl-2. And the catalytic activity of caspase-3 and -12 caspase in HepG2 cells was also measured.
Results: FK506 and cobalt chloride significantly induces the synergistic effect of HepG2 cytotoxicity in dose dependent manner. Increased active-PARP expression occurred at 24 hours after FK506 treatment on cobalt chloride induced HepG2 cytotoxicity and peak activation of cleaved caspasec-3 was also observed at 24 hours. FK506 aggravates cobalt chloride induced HepG2 cytotoxicity. GRP78 expression was increased 24 hours after FK506 treatment on cobalt chloride induced HepG2 cytotoxicity. CHOP and caspase-12 expressions were increased 24 hours after FK506 treatment on cobalt chloride induced HepG2 cytotoxicity. Expressions of ATF4 and ATF6 were same manners. Expression of XBP-1 was decreased beginning at 6 hours. FK506 exasperate endoplasmic reticulum stress by cobalt chloride induced cytotoxicity. Bcl-2 protein expression decreased, but FK506 induces expression of Bak and Bax by cobalt chloride induced cytotoxicity. Nrf2 expression was also noted.
Conclusions: FK506 and cobalt chloride significantly induces the synergistic effect of cytotoxicity in dose dependent manner. FK506 aggravates cobalt chloride induced cytotoxicity. FK506 accelerates expression of ER-stress related nuclear transcriptional factor.

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Generation of induced secretome from adipose-derived stem cells specialized for disease-specific treatment: an experimental mouse model

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Recently, the exclusive use of mesenchymal stem cell (MSC)-secreted molecules, named as the secretome, rather than cells has been evaluated for overcoming the limitations of cell-based therapy while maintaining its advantages. The goal of this study was to improve cell-free therapy by adding disease-specificity through stimulation of MSCs using disease-causing materials. We collected the secretory materials (named as inducers) released from AML12 hepatocytes that had been pretreated with thioacetamide (TAA) and generated the TAA-induced secretome (TAA-isecretome) after stimulating adipose-derived stem cells (ASCs) with the inducers. The TAA-isecretome was intravenously administered to mice with TAA-induced hepatic failure and those with partial hepatectomy. TAA-isecretome infusion showed higher therapeutic potential in terms of
(a) restoring disorganized hepatic tissue to normal tissue,

(b) inhibiting proinflammatory cytokines (interleukin-6 and tumor necrosis factor-α), and
(c) reducing abnormally elevated liver enzymes (aspartate aminotransferase and alanine aminotransferase) compared to the naïve secretome infusion in mice with TAA-induced hepatic failure. However, the TAA-isecretome showed inferior therapeutic potential for restoring hepatic function in partially hepatectomized mice. Our results suggest that appropriate stimulation of MSCs with disease-causing agents leads to the production of a secretome specialized for treating a specific disease. Additionally, isecretome therapy is expected to open a new way of developing various specific therapeutics based on the high plasticity and responsiveness of MSCs.

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Chloride intracellular channel 1 regulates angiogenesis in hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is one of the most fatal cancers around the world with high vascularity. Our previous study has proved that Chloride intracellular channel 1 (CLIC1) promotes the invasiveness of HCC cell lines. However, the role of CLIC1 in angiogenesis of HCC remains to be elucidated.
Method: The expression of CLIC1 is detected in 72 HCC specimens and corresponding normal tissues. HCC cell lines are transfected with lentivirus to construct CLIC1 overexpression and CLIC1 knockdown cell lines which are validated by western blot. Vascular endothelial cells (EA.hy926 cell line) are treated by supernatant collected from HCC cell lines with different expression of CLIC1 and the ability of angiogenesis is examined by tube formation assay. Different HCC cell lines are engrafted subcutaneously in immunodeficient mice to explore the relationship between CLIC1 and angiogenesis in vivo.
Results: CLIC1 expression is significantly higher in tumor compared to corresponding normal tissue and tumor with high CLIC1 level has a higher expression of CD34, which indicates microvascular invasion (MVI). EA.hy926 cells treated by supernatant collected from CLIC1 knockdown HCC cell lines formed less tube in tube formation assay and ELISA assay indicates that supernatant from CLIC1 knockdown HCC cell lines has a lower concentration of VEGF. In vivo experiment shows that tumors with higher CLIC1 expression grow faster and have more MVI.
Conclusion: Our study suggests that CLIC1 can promote angiogenesis in HCC.

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Systematic analysis of immune changes following liver transplantation for hepatocellular carcinoma

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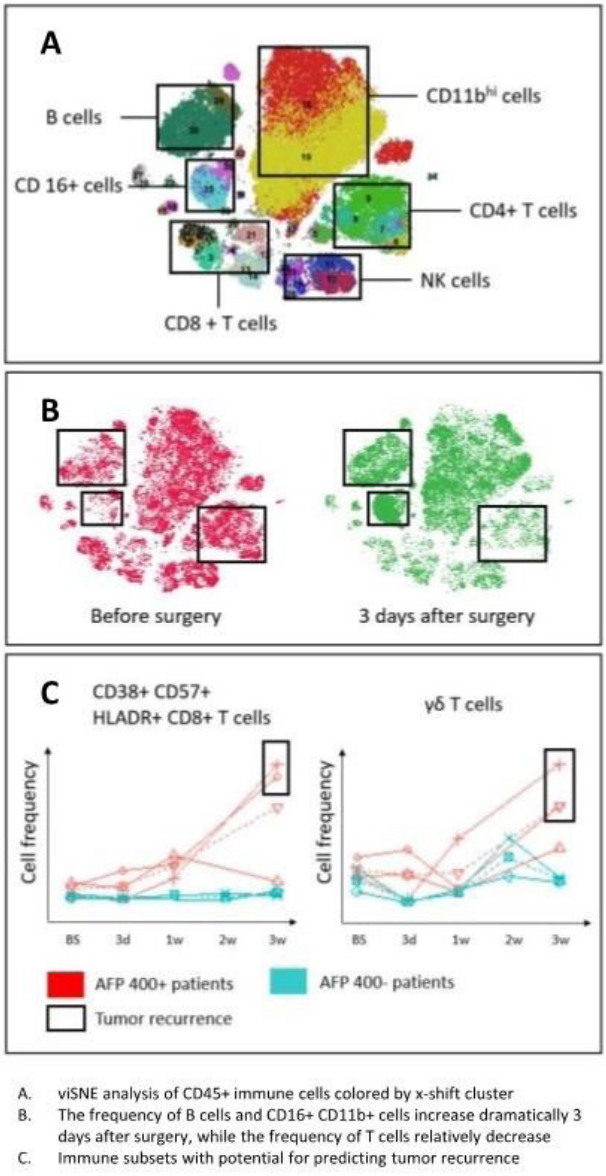
Background: Liver transplantation (LT) induces complex peripheral immune changes that have profound impact on prognosis especially in patient with hepatocellular carcinoma (HCC). Here we apply single-cell mass cytometry (CyTOF) to phenotype immune changes following LT for HCC to search for cytologic predictors for tumor recurrence and other complications of LT.
Methods: Peripheral blood samples were collected from LT patients with HCC before surgery, and at 3 days, 1 week, 2 weeks, 3 weeks after surgery. Corresponding clinical data was also recorded. Peripheral blood mononuclear cell (PBMC) from each sample were extracted and analyzed by CyTOF. Bioinformatic analysis was applied to identify unique immune subsets related to HCC recurrence and other complications of LT.
Result: Peripheral blood immune composition changes in a distinct way after LT for HCC. The frequency of B cells and CD16+ CD11b+ cells increase dramatically 3 days after transplantation, while the frequency of T cells and NK cells relatively decrease. The immune change pattern varies between AFP 400+ and AFP 400- patients. Clustering algorithm discovered 36 immune subsets. 9 of them are related to HCC recurrence, including γδT cells, plasmacytoid dendritic cells（pDC） and CD38+ CD57+ HLADR+ CD8+ T cells. Moreover, 3 immune subsets including CD45RA+ CD27+ CD8+ T cells are found to be related with early allograft dysfunction (EAD) and FOXP3+ macrophages may be related to acute graft rejection. These unique immune subsets have potential for predicting HCC recurrence and other complications as soon as 3 days after transplantation.
Conclusion: Systematic analysis of immune composition ravels a distinct changing pattern after LT for HCC. Immune subsets like γδT cells are potential predictors for tumor recurrence and CD45RA+ CD27+ CD8+ T cells have predictive potential for EAD.



A. viSNE analysis of CD45+ immune cells colored by x-shift cluster
B. The frequency of B cells and CD16+ CD11b+ cells increase dramatically 3 days after surgery, while the frequency of T cells relatively decrease
C. Immune subsets with potential for predicting tumor recurrence

[Graph ABC]

P-384

Regulation of CD36 by pigment epithelium-derived factor in non-alcoholic steatohepatitis

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Non-alcoholic fatty liver disease (NAFLD) has become a worldwide prevalence as it is the most common liver disease in developed countries. NAFLD is linked to increased incidence of obesity and many other metabolic disorders. Studies also support the idea of NAFLD as a hepatic manifestation of metabolic syndrome, a multisystem disease rather than a liver confined pathology. As the disease progresses, NAFLD is often accompanied by hepatocyte injury and inflammation, a condition referred to as non-alcoholic steatohepatitis (NASH). As severe NAFLD can lead to life-threatening conditions such as cirrhosis and hepatocellular carcinoma, understanding the molecular mechanisms is crucial for discovering new targets for prevention and treatment. Pigment epithelium-derived factor (PEDF) is a secreted glycoprotein first described as a neurotrophic factor. The role of PEDF in lipid metabolism was established when adipose triglyceride lipase (ATGL), a major triglyceride hydrolase, was characterized as its binding partner. Our data revealed that PEDF expression was decreased in a rat NASH model. We further showed that decreased PEDF levels in hepatocytes resulted in lipid accumulation due to up-regulation of fatty acid translocase (CD36), a major enzyme that facilitates fatty acid uptake. The increase in lipid uptake was dependent upon decreased ATGL activity. Moreover, we also found an up-regulation of CD36 in activated inflammatory macrophages, which showed decreased ATGL levels. Blocking ATGL activity further exacerbated the inflammatory phenotype in terms of TNF-α release and NLRP3 inflammasome activation. Taken together, our results suggest that the PEDF-ATGL-CD36 pathway can be a potential target of interest in NASH research.

P-385

Wip-1 deficiency in murine liver allografts aggravates ischemia reperfusion injury in liver transplantation

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Background: Ischemia reperfusion injury (IRI) is a major complication of liver transplantation and is closely related to graft function recovery. Neutrophils and peripheral macrophages (iM0) are

considered the main mediators of liver ischemia reperfusion injury through multiple ways. Liver resident macrophages (Kupffer cells), which represent the largest population of macrophages in the body, have been assumed to be the major responding cells against IRI. The wild-type p53-induced phosphatase 1 (Wip-1), a Ser/Thr protein phosphatase, has been shown to regulate the development and function of neutrophils and macrophages. The role of Wip-1 in liver IRI and underlying mechanisms remain to be elucidated.
Method: In this study, we used an established mouse model of liver transplantation. Livers from C57BL/6 (B6) wild-type (WT) or Wip-1$^{-/-}$ mice were transplanted into B6 wild-type mice. Fresh liver samples and serum were taken 24 hours after transplantation. Liver non-parenchymal cells were isolated for flow study.
Results: Compared with the wild-type controls, Wip-1-deficient liver allografts showed more liver damage, as evidenced by higher sALT/AST levels and increased histological hepatocellular necrosis. Immunofluorescence results showed that Wip-1 deficiency aggravated neutrophil and iM0 infiltration but reduced Kupffer cell infiltration. Flow results showed higher percentage of neutrophils (Ly-6G$^+$CD11b$^+$) and iM0 (F4/80$^+$CD11b$^+$) and lower percentage of Kupffer cells (F4/80$^+$CD11b$^-$) among CD45$^+$ cells in wip-1 deficiency livers compared with the control livers. The ratios of iM0/Kupffer cells was significantly higher in Wip-1 deficiency mice. In addition, the ratio of M1 macrophages (F4/80$^+$CD11c$^+$) to M2 macrophages (F4/80$^+$CD206$^+$) was higher in Wip-1 deficiency liver allografts.
Conclusion: Our results demonstrate that Wip-1 deficiency aggravates liver ischemia reperfusion injury after liver transplantation, which is associated with increased neutrophil/iM0 infiltration and a shift from M2 to M1 macrophage polarization.

P-386

Defining immunological differences between donation after brain death (DBD) and donation after cardiovascular death (DCD) liver grafts

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Background: The majority of UK donors are either DBD or DCD, with DCD carrying a higher risk of graft loss post-transplant. There is a great shortage of liver donations to meet the demand, with close to one third of livers are rejected based on broad and subjective criteria. The liver's immune system is known to play important roles in regulating inflammation and maintaining a tolerant environment. However, different modes of donation and conditions after retrieval (e.g. cold ischemia) may compromise normal hepatic immunity, which may affect organ quality and outcome post-transplant. Immune biomarkers may provide an objective way to assess organ quality. In this project we aimed to determine the main immunological differences between DBD and DCD and assess their association with adverse outcomes post-transplant.
Methods: Liver mononuclear cells (LMCs) were isolated from liver perfusates. Using flow cytometry LMCs were assessed to the expression of CD1d, CD3, CD4, CD8, CD14, CD19, CD24, CD27, CD38, CD40, CD69, CD95, CD161, IgD, IgM, HLA-DP-DQ-DR, PD1, Vα7.2, Vα24-Jα18, and γδTCR. 30 DBD, 20 DCD and 10 LRD livers were assessed. Peak levels of peripheral blood aspartate aminotransferase (AST) within 10 days post-transplant, a surrogate marker for organ rejection, histological signed of acute rejection (ACR) within 3 months post-transplant, and hospital stay were correlated with the above immunological parameters.
Results: DBD and DCD significantly differ in their expression B cells, antigen presentation molecules (CD1d and MHC class-II), innate-like T cell subsets, and activation molecules (PD1 and CD69). Immune cell parameters (CD1d, CD40, MHC class-II, iNKT cells, and γδT cells) are differentially implicated in ACR and raised AST post Tx in DBD and DCD.
Conclusions: Immune cell profiles in DBD and DCD are significantly different, and their association with ACR and peak ASC, in particular the expression of MHC class-II are opposing in DBD and DCD.

P-387

Detecting graft-derived cell-free DNA via Y-chromosome-specific-PCR andamplification-refractory-mutation-system-PCRin living-donor liver transplantation

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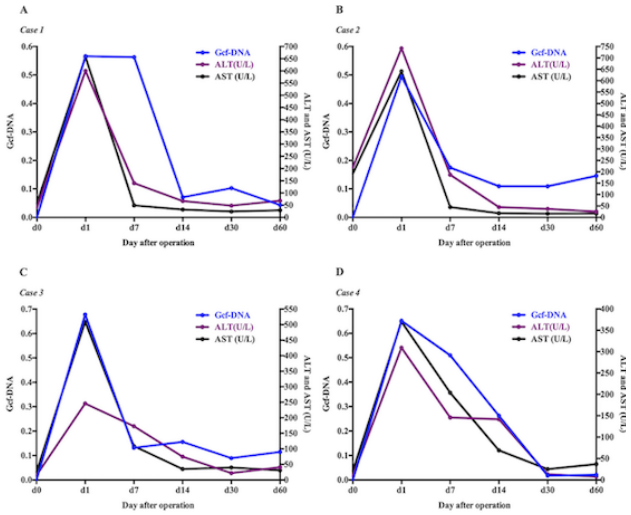
Introduction: Graft-derived cell-free DNA (Gcf-DNA) were known as a promising non-invasive biomarker in post-liver-transplantation patient. In consider of the pair of sex-mismatch and sex-match between the donor and the recipient, we applied two different methods to detect Gcf-DNA in living-donor liver transplantation (LDLT).
Methods: Totally 4 patients, age from 11-24 months, diagnosed with Ornithine Transcarbamylase Deficiency and Propionic Acidemia

were enrolled, and LDLT were performed with one of their parents as donors. 5ml whole-blood specimen were collected in d0, d1, d7, d14, d30 and d60 after operation, and the specimens were centrifuged to plasma and the cell-free DNA were extracted. Then, Y-chromosome-specific-PCR were used in two sex-mismatch pairs and Amplification-Refractory-Mutation-System-PCR were used in two sex-match pairs, which to identify the Gcf-DNA from the total cell-free DNA.
Results: All operations were performed uneventfully. As the figures showed, Gcf-DNA climbed up the highest in day 1, and gradually dropped down to lower than 0.1 as times goes. More, we compared the same-day transaminase to Gcf-DNA, which showed the similar "Λ" variation-curve.



[Figure 1]

Conclusion: This is the first report about detecting Gcf-DNA according to the different donor-recipient-sex-match-pair in LDLT. According to the result, Gcf-DNA can be a potential non-invasive biomarker to monitor graft-injury, because it reflected the graft-function elevated level because of ischemia and reperfusion injury while gradually declined lower than 0.1 as the graft function recovered. Especially applicable to the auxiliary-liver-transplantation, the liver functions often remained the normal level when the graft started to develop rejection or even full-blown rejection, because the native liver might cover the abnormal transaminase change from the graft. For the cross-auxiliary double domino donor liver transplantation and the auxiliary liver transplantation recipient, Gcf-DNA might provide a novel way to monitor the graft function.

P-388

The mechanism of miRNA-135a-induced epithelial to mesenchymal transition through suppression of autophagy and activation of AMP-activated protein kinase in Hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is one of the most common and aggressive malignancies worldwide. Treatment outcomes remain poor mainly due to lack of good diagnostic/prognostic markers and limited therapeutic strategies. The metastasis of cancer cells plays pivotal role in the mortality of hepatocellular carcinoma, in which epithelial-to-mesenchymal transition (EMT) is the key characterization of malignant transformation and is also the important feature for circulating tumor cells. We previously found that miR-135a targets ATG14, a key orchestrator of autophagy, and its expression was significantly associated with microvascular invasion (MVI) in the liver tissues of HCC. Our aim was to investigate whether the potential anti-autophagic miR-135a plays a crucial role in malignant progression in HCC and the mechanisms underlying.
Method: In this study, we performed *in vitro* functional analyses and investigate the relationship between miR-135a levels and expression of EMT genes using hepatoma cells. Then the experiment was conducted to characterize the downstream molecular events of miR-135a via RT-PCR and Western blotting.
Results: We found that transfection of miR-135a promotes phosphorylation of AMP-activated protein kinase a1 (AMPKa1) and the expression of EMT marker Vimentin (VIM), epithelial cell adhesion molecule (EpCAM), Yes-associated protein 1 (YAP1) and zinc finger E-box binding homeobox 1 (ZEB1), while inhibiting the expression of E-cadherin (CDH1) in both Hep3B and HepG2 cells. We also found that AMPKa1 siRNA significantly inhibited expression of miR-135a-induced EMT markers; on the contrary, antagomir of miR-135a significantly reduced the expression of EMT markeres, whereas chloroquine reverted expression of EMT markers.
Conclusion: Our results indicate miR-135a might achieve the progression of EMT mainly through AMPK activation and autophagy inhibition. This study provides a new clue to develop potential targets for prognostic and therapeutic uses in HCC.

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miRNA expression profiles of FFPE liver biopsies from transplanted HCV mono-infected and HCV/HIV co-infected patients

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After liver transplantation HCV/HIV co-infected patients showed higher mortality than HCV mono-infected. Nothing is known regarding possible miRNA alterations occurring in the grafts after transplantation into HCV or HCV/HIV-infected recipients. The aim of this study was to analyze post-transplant liver biopsies to detect, by nextgeneration sequencing (NGS), differentially expressed miRNAs involved in viral infection, inflammation and fibrosis. miRNAs sequencing was performed by analyzing 3 healthy livers, 3 HCV-infected and 3 HCV/HIV co-infected liver biopsies using the illumina HiSeq2500 platform. The DIANA-miRPath web-server was used to characterize the functions of differentially expressed human miRNAs based on the predicted miRNA targets provided by the DIANA algorithm. Up- and down-regulated miRNAs were analyzed separately, using the KEGG and Gene Ontology-Biological Process databases. Gene expression analysis highlighted 36 miRNAs differentially expressed between healthy and HCV liver biopsies (*padj< 0.05*) as well as 8 deregulated miRNAs between healthy and HCV/HIV-infected liver biopsies (*padj< 0.05*). Comparing HCV and HCV/HIV-infected liver expression profiles 15 miRNAs emerged as deregulated (*p< 0,005*). Gene-ontology analyses showed that, 6 months after transplantation, transplanted livers were already characterized by up-regulation of miRNAs strictly related to viral infection and immune system signaling such as miR-18a, miR-382-3p, miR-65 and by the down-regulation of miR-423-3p, miR-193a with a pathogenic role of DNA damage in HCV-induced carcinogenesis. Moreover, the comparison of HCV and HCV/HIV co-infected samples showed that double-infected patients differed from mono-infected ones for the expression of miR125a, miR675-3p involved in immunological and apoptotic processes and for the down-regulation of miRNAs such as miR29-3p, miR374a-3p, miR660, miR190a and miR409 implicated in extra cellular matrix remodeling that could be responsible for the earlier fibrosis onset in double-infected transplanted livers.miRNA expression can be reliably analyzed by NGS in stored FFPE tissues. Further studies should be conducted to establish whether they can become novel prognostic markers and therapeutic targets.

P-390

Induction of selective liver hypothermia prevents significant ischemia/reperfusion injuries after 24 hours

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Background: Induction of liver hypothermia is a surgical tool capable of preventing warm ischemic injuries. The protective mechanisms involved are not completely understood, but liver microcirculation regulation and reduction of inflammation are potential candidates to explain the attenuation of reperfusion injuries. The aim of this study was to investigate the effects of induction of selective liver hypothermia, the role of endothelial and inducible nitric oxide synthases (eNOS and iNOS), inflammatory cytokines (TNF-α, IL-1β, IL-6 and IL-10) and histopathological injuries in a rodent model.
Material and methods: Nineteen male Wistar rats were subjected to 90 minutes of partial 70% liver ischemia either in selective 26°C hypothermia (H group) or normothermia (N group). After 24-hour reperfusion, livers were sampled and sent for analyses. Anatomopathological sections were scored for sinusoidal congestion, ballooning, hepatocelllular necrosis and neutrophilic infiltrates.
Results: At the end of the experiment, liver tissue expressions of TNF-α, IL-1β, iNOS and TNF-α/IL-10 ratio were significantly reduced in the H group compared to N group, whereas IL-10 and eNOS were significantly increased. IL-6 expression was similar between the groups. Histopathological injury scores revealed a significant decrease in ischemia/reperfusion (I/R) injuries in H group.
Conclusions: Selective liver hypothermia prevents I/R injury, balancing the release of inflammatory and anti-inflammatory cytokines, preserving microcirculation, and preventing hepatocellular necrosis and leukocyte infiltration. Overall, selective liver hypothermia allows maintenance of the liver architecture.
Keywords: hypothermia, liver, ischemia/reperfusion, eNOS, iNOS.

P-391

Effects of CD38 activation/inhibition on hepatocellular ischemia reperfusion injury

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Background: Ischemia/reperfusion injury (IRI) during transplantation can lead to early graft failure and primary graft non-function and remains is a major challenge to liver transplantation. CD38, an ectoenzyme whose activities drive intracellular calcium metabolism and oxidative stress, has been shown to be directly implicated in IRI with inhibition of CD38 being shown as protective in some organs. The aim of this study was to investigate the protective effects of CD38 inhibition in a rat model of hepatic IRI.
Methods: The protective effects of CD38 inhibition were tested in vitro and in vivo. In vitro, primary liver cells were subjected to oxidative stress injury (H_2O_2) with and without CD38 inhibitor treatment (apigenin), and measures of cell health and viability were assessed. In vivo, liver IRI was induced in Sprague Dawley rats using a segmental (70% ischemia) hilar clamp model. Rats were subjected to 60 minutes of ischemia followed by varying durations of reperfusion with and without treatment with apigenin. Markers of liver injury including plasma ALT and AST, tissue MDA, ATP, and GSH, and histology were assessed.
Results: In vitro, apigenin treatment resulted in improved cellular health in response to oxidative stress injury. In vivo, hepatic IRI resulted in increased CD38 activity, which correlated with significant liver injury. Treatment of IRI livers with apigenin resulted in significantly reduced ALT and AST and an improvement in tissue MDA, ATP and GSH. Histology revealed improved maintenance of tissue architecture in apigenin-treated IRI livers.
Conclusion: CD38 plays a critical role in modulating hepatic IRI, and inhibition of CD38 provides significant protection. CD38 inhibition prevents CD38 activation, thus, blocking the downstream signaling necessary for harmful effects of NAD depletion and ROS production during reperfusion. Overall, CD38 inhibition may have potential as a therapeutic agent to be used during transplantation.

P-392

Safety of intra-operative blood salvage in hepatocellular carcinoma liver transplantation: tumor cell detection via spiral microfluidics technology

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Introduction: The application of intra-operative blood salvage auto-transfusion (IBSA) in hepatocellular carcinoma (HCC) liver transplantations (LT) remain controversial due to risk of tumour cell (TC) reintroduction. Current reports analyzing blood samples for TC remain limited due to suboptimal detection techniques. The aim of this study is to evaluate HCC TC presence in autologous blood recovered intra-operatively using highly sensitive spiral microfluidics. Secondarily, we sought to ascertain the effectiveness of the Cellsaver Machine (IOCS) and Leukocyte Depletion Filter (LDF) in removing TC.
Methods: A prospective study of all HCC patients who underwent LT at the National University Health System, Singapore from November 2017 - July 2018 was conducted. Autologous blood samples were collected intra-operatively using the IOCS and washed before filtration through the LDF. The samples were then processed using microfluidics technology and stained with antibody cocktails for TC detection.
Results: The eight patients recruited had pre-operative tumor characteristics within the University of California, San Francisco (UCSF) criteria. Median pre-operative alphafetoprotein level was 17µg/dL (1.6µg/dL-193µg/dL). Histopathologically, 3 patients (37.5%) had T1 tumors while others were determined as T2. Median tumor diameter was 51mm (22mm-105mm), while majority of patients (62.5%) had moderately differentiated tumors. One patient (12.5%) had presence of vascular invasion, but none had evidence of perineural invasion or tumor rupture. Median estimated blood loss was 2000mls (600mls-4000mls). All patients had presence of TC in their pre-operative venous and intra-operative blood loss samples. While three patient samples (from intra-operative blood loss) were found with TC after IOCS washing, all samples were negative for TC after LDF filtration.
Conclusion: The use of IOCS and LDF is effective in removing TC from autologous blood samples in HCC LT patients. The application of IBSA in HCC LT should be considered, as it appears to be safe with minimal risk of TC reintroduction after filtration.

P-393

Pathological interpretation and genetic polymorphisms of acute rejection associated with low serum 25-hydroxyvitamin D after living donor liver transplantation

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Background: Most cases of advanced liver diseases complicated with severe infection are associated with low serum 25-hydroxyvitamin D [25(OH)D] and vitamin D deficiency. This phenomenon may occur during liver transplantation.
Aim: To explore the histological interpretation of rejection and non-rejection graft pathological affected by the cytochrome P450 genetic modification in recipients of living donor liver transplantation (LDLT).
Methods: In total, 60 patients received liver graft biopsy after LDLT and were separated (1:1) into two groups: graft rejection group and non-rejection graft pathology group. We extracted both of the recipients' and donors' serum DNA to investigate the vitamin D receptor (VDR) rs2228530 and CYP2R1 rs10741657 single nucleotide polymorphisms (SNPs) using real-time polymerase chain reaction. We also extracted DNA from liver graft tissues to explore the genetic alleles of VDR rs2228530 and CYP2R1 rs10741657 after LDLT. Serum 25(OH)D concentrations were measured before and 30-day after LDLT.
Results: There were no significant differences in serum VDR rs2228530 and CYP2R1 rs10741657 genetic alleles between recipients and donors. The percentage of genetic modification was 33.4% (10/30) for the rejection and non-rejection groups in VDR rs2228530, and 66.7% (20/30) for both groups in CYP2R1 rs10741657. Serum 25(OH)D concentrations were significantly lower between before and 30-day after LDLT, compared with before LDLT, in the rejection (P=0.0001) and non-rejection graft pathology (P=0.0017) groups.
Conclusions: Genetic modification of VDR rs2228530 and CYP2R1 rs10741657 is associated with a low serum 25(OH)D in rejection after LDLT, but also graft pathology with non-rejection seems to be favorable for low serum 25(OH)D after LDLT.

P-394

Combined ischemic and rapamycin preconditioning alleviated liver ischemia and reperfusion injury by restoring autophagy in old mice

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Background: Old livers are more damaged by hepatic ischemia and reperfusion (IR) injury than young livers. The aim of this study was to investigate the effects of ischemic and rapamycin preconditioning on IR injury in old livers.
Methods: Young (8-week-old) and old (60-week-old) mice were subjected to IR or a sham control procedure. The old mice were randomly divided into six groups: IR (CON), IR with ischemic preconditioning (IPC), IR with rapamycin preconditioning (RAPA), IR with combined ischemic and rapamycin preconditioning (IPC+RAPA), IR with 3-methyladenine (CON+3-MA), IR with combined ischemic and rapamycin preconditioning with 3-MA pretreatment (IPC+RAPA+3-MA). Liver injury was evaluated 6 hours after reperfusion. Hepatocellular autophagy induction was also analyzed by western blotting.
Results: Compared to young mice, old mice showed aggravated liver IR injury. In old mice following IR, IPC+RAPA but not IPC or RAPA alleviated liver injury, as evidenced by lower levels of serum ALT, improved preservation of liver architecture with lower Suzuki scores, and decreased caspase-3 activity compared with CON. In addition, western blot analysis revealed increased LC3B II but decreased p62 protein expression levels in the IPC+RAPA group, indicating that autophagic flux was restored by combined ischemic and rapamycin preconditioning. Furthermore, autophagy inhibition by the inhibitor 3-MA abrogated the protective role in the IPC+RAPA group, while no significant effects were observed in the CON group.
Conclusions: Our results demonstrated that combined ischemic and rapamycin preconditioning protected old livers against IR injury, which was likely attributed to restored autophagy activation.

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NOD1 activates autophagy to aggravate hepatic ischemia-reperfusion injury in mice

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Hepatic ischemia/reperfusion injury (IRI) is tissue damage resulting from return of the blood supply to tissue after a period of ischemia or lack of oxygen. Much of the morbidity associated with liver transplantation and major hepatic resections is, in part, due to IRI. Both innate immunity and autophagy play important roles in hepatic IRI. With regard to innate immunity, one factor that plays a key role is NOD1, an intracellular pattern recognition receptor. NOD1 has recently been shown to be associated with autophagy, but the mechanisms involved with this process remain obscure. This relationship between NOD1 and autophagy prompted us to examine the role and potential mechanisms of NOD1 in regulating autophagy as related to hepatic IRI. We found that NOD1 was up-regulated during hepatic IRI and was associated with an activation of the autophagic signaling pathway. Moreover, levels of Atg5, a critical protein associated with autophagy, were decreased when NOD1 was inhibited by NOD1 siRNA. We conclude that NOD1 appears to exert a pivotal role in hepatic IRI by activating autophagy to aggravate hepatic IRI, and Atg5 was required for this process. The identification of this novel pathway, that links expression levels of NOD1 with Atg5-mediated autophagy, may provide new insights for the generation of novel protective therapies directed against hepatic IRI.

P-396

Wip-1 deficiency aggravates liver warm ischemia/reperfusion injury by mediating macrophage function

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Background: The wild-type p53-induced phosphatase 1 (Wip-1) is an important gene that takes part in mediating macrophage function and phagocytosis and migration. While its role in liver ischemia/reperfusion has not been interpreted.
Method: In this study, we studied the function of Wip-1$^{-/-}$ macrophage. Besides that, we used mouse liver 70% warm ischemia/reperfusion model to identify the role of Wip-1 in macrophage during liver injury. Wip-1 deficiency mice and wild type mice were applied for ischemia of 1 hour and reperfusion for 6 hours before further study. Since p53 is the main downstream gene of Wip-1. We further evaluated the ischemia/reperfusion injury in Wip-1$^{-/-}$p53$^{+/-}$livers.
Results: Wip-1$^{-/-}$ macrophage showed no difference of surface markers compared with wild type control except for CD36. Coculture results showed reduction of phagocytosis of apoptotic cells in Wip-1$^{-/-}$ macrophage. Wip1-deficient liver showed severer liver injury and increased macrophage/neutrophil infiltration compared with controls. Macrophage from Wip-1$^{-/-}$ livers after ischemia/reperfusion injury showed decreased CD36 expression. The depletion of macrophage cells by clodronate liposomes abrogated the induced neutrophil infiltration and alleviated the injury. Knocking down of p53 reversed the exacerbated liver injury, as shown by reduced neutrophil/macrophage infiltration and alleviated liver enzymes elevation.
Conclusion: Our results show that Wip-1$^{-/-}$ macrophage showed reduction of phagocytosis of apoptotic cells. Wip-1 knockout aggravates liver injury in a mouse warm ischemia/reperfusion model, and Wip-1$^{-/-}$ macrophage takes an important part in mediating the injury.

P-397

Potentiality of cryopreserved pig hepatocyte spheroids for BAL system development using serum-free solutions

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Primary hepatocytes are widely used for basic research, pharmaceutical testing, and they are clinically used for transplantation or in bioartificial liver (BAL) devices for the treatment of patients with liver failure. To realize this procedure, a hepatocyte bank system capable of supplying large numbers of hepatocytes must be established. However, hepatocytes are very susceptible to cryopreservation injury. On thawing, cryopreserved hepatocytes often have reduced viability and metabolic function in comparison with fresh cells.
Most cryopreservation protocols for hepatocytes use fetal bovine

serum at concentrations ranging from 5% to 90% (v/v). However, these solutions have been associated with clinically significant side effects. Moreover, serum can transfer pathogens. Thus, in this study, we sought to evaluate the viability and function of cryopreserved hepatocyte spheroids using serum free cryopreservation solutions with the intent to elucidate their efficiency for the BAL system.
Hepatocytes were harvested from 3~5 weeks old male pigs weighing 10 to 15 kg. Hepatocyte preparation was conducted using a modification of the two-step collagenase perfusion technique originally described by Seglen. Pig hepatocyte spheroids transferred to various cryopreservation solutions. After thawing, hepatocyte spheroids were immobilized using a 100mM calcium with 1.5% alginate solution.
The BAL system consists of a medium reservoir, a pump, and a cylindrical-type calcium-alginate packed-bed bioreactor bioreactor containing the immobilized hepatocytes.
In the present study, we determined the viability and liver functions of primary pig hepatocyte spheroids versus cryopreserved pig hepatocyte spheroids during exposure to ammonia medium seeking to determine the optimum condition for BAL system development using Serum-free solutions.
Cryopreserved hepatocyte spheroids in the serum free solutions maintained high levels of liver-specific functions. The most important application of this solution would be the ability to establish a cell bank of Immobilized hepatocyte spheroids for "off-the shelf" BAL system without serum.

P-398

Salinomycin-loaded LA-SN38 nanoprodrugs incorporated into DSPE-PEG2000 micelles enhanced anticancer activity by inhibiting cancer stem cell in liver cancer

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Background and aims: Hepatocellular carcinoma (HCC) is a highly lethal malignancy with a high rate of recurrence and limited treatment options. Systemic chemotherapeutic provides curative option for patients with advanced HCC, However, none of these regimens has shown significant survival benefit. Cancer stem cell (CSC) are believed to contribute to chemotherapy resistance. This study was aim to develop salinomycin-loaded supramolecular nanoprodrug codelivering salinomycin and SN38 to improve the therapeutic efficacy of HCC.
Methods: In the president study, we construct a SAL loaded LA- SN38 prodrug nanoparticle coated with DSPE-PEG, and the characterization and antitumor activity of the self-assembly nanoprodrug were evaluated both in vitro and in vivo.
Results: SAL effectively decreased the proportion of CD133+ hepatic tumor initiating cells. The codelivery of SAL and SN38 promoted apoptosis and exerted stronger inhibition of tumor sphere formation and metastasis of HCC cells. In addition, the combined treatment with the two drugs effectively suppressed tumor growth in nude mouse Patient-Derived tumor Xenograft model.
Conclusions: These results indicated that the using of supramolecular nanoprodrug codelivery stem cells kill drugs and chemotherapeutics is a potentially effective treatment to HCC, which might contribute to the improvement of survival outcomes of HCC patients.

P-399

Cytotoxicity of FK506 through TRAIL pathways in human Jurkat T cells

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Purpose: To elucidate the mechanism of cytotoxicity in FK506-treated Jurkat T cells, signal transduction pathway of TNF-related events was studied.
Methods: Viability of Jurkat T cells was measure by MTT assay. The catalytic activation of caspase-3 and caspase-9 proteases was determined by digestion of fluorogenic biosubstrates and Western blot with anti-caspase-3 and anti-caspase-9 antibodies. The levels of mRNA and proteins for p53, Bax, PUMA, Proline oxidase, TRAIL(TNF related apoptosis inducing ligand), TRAIL-R1(DR4), TRAIL-R2(DR5), Fas, FasL, TNF-α , IL-6, and NFκB were measured by RT-PCR and Western blot with specific antibodies. Also we further examined the localization of TRAIL family proteins using by fluorescent microscope with specific TRAIL family antibodies.
Results: FK506 decreased the viability of Jurkat T cells concentration- and time-dependently along with catalytic activation of caspase-3 and caspase-9, p53 phosphorylation, and changes in expression levels of Bax, PUMA, and Proline oxidase protein. It caused an increase in expression of TRAIL, TRAIL-R1(DR4), TRAIL-R2(DR5), Fas, and FasL in the levels of mRNA and proteins of Jurkat T cells. Furthermore, FK506 increased extracellular release of TNF-α and IL-6 cytokines in Jurkat T cells. It also induced the transactivation of NFκB through the dephosphrylation of Ser486 residues in Jurkat t cells.
Conclusion: These results suggest that FK506 induces apoptotic death of Jurkat cells through activation of caspase family protease, Bcl2 family protein-related mitochondrial dysfunction, activation of TNF-related death-receptor.

P-400

Messenger R N A and micro R N A profiles in fatty liver donors: Molecular networks during ischemia reperfusion injury

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Purpose: Liver steatosis (S) is a known risk factor for exacerbated ischemia-reperfusion injury (IRI) and poor outcomes post liver transplantation (LT). RNA profiling was performed to gain hepatic expression profiles of mRNAs and miRNAs in fatty (F) and non-fatty (NF) liver donors in paired pre-implantation (PI) and post-Reperfusion (PR) biopsies to identify those pathways associated with worse injury during IRI.
Methods: 88 samples from 44 LT patients were evaluated (Liver steatosis=macro steatosis >20-30%). Gene and miRNA expression were tested using microarrays and Ingenuity Pathway Analyses - Cytoscape were used for data analyses, integration and network identification.
Results: 237 mRNAs and 17 miRNAs were identified as differentially expressed when comparing PI biopsies between F vs. NF liver donors. When comparing PI vs. PR samples, 53 and 24 miRNAs and 2,730 and 1,338 probe sets were significant between F vs non-F livers, respectively. Using IPA filters, 18 miRNAs targeting 331 mRNAs with appropriated directionality in expression were identified from integrative analyses for F livers. Cell-to cell signaling interaction, cell cycle, cell death and lipid metabolism were the top biological functions associated with the differentially expressed molecular features. Adipogenesis pathway was identified as the top canonical function. Then, 10 miRNA -mRNA regulatory pathways were obtained, and networks were constructed for the F livers. The top regulatory network included as disease and molecular functions accumulation of lipids, apoptosis cell lines, quantity of antigen presenting cells, and quantity of macrophages with high positive consistency score: 89.3 (a high consistency score associates with increased consistent). Representative miRNAs and mRNAs were validated by real-time qPCR.
Conclusions: Integrated analysis of mRNA and miRNA profiles in liver tissue represents a powerful tool to identify novel targets for assessing with accuracy organ injury associated with graft steatosis.

P-401

PLK1 inhibitor synergizes SN38 prodrug-based nanoparticles to treat hepatocellular carcinoma

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Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related death worldwide. And lacking in early evident symptoms, most HCCs are diagnosed as late-stage with poor prognosis. As for late-stage HCCs, chemotherapy and small molecule targeted drugs are the only treatment options. However, the therapeutic effect is still far from promising. So there is an urgent need to develop high efficient therapies. Polo-like kinase 1 (PLK1) is a well-known regulator in mitosis and also plays an important role in DNA damage repair. PLK1 is over-expressed in many malignant tumors including HCC. Our previous studies revealed that the inhibition of PLK1 might sensitize the anti-HCC effect of SN38 (an active metabolite of irinotecan). Meanwhile, in order to improve the anti-tumor effect of SN38 and reduce its toxicity, we synthesized polylactide-tethered SN38 prodrugs. These SN38 prodrugs assembled with DSPE-PEG to form systemically injectable nanomedicines (NP-PLA-SN38). We then testified the combination therapy of PLK1 inhibitor and NP-PLA-SN38 both *in vitro* and in clinically relevant patient-derived xenograft (PDX) mouse models. In a word, the combination of nanoparticle drug delivery systems, appropriate modification of classic anti-cancer agents and small molecule targeted drugs might be a potentially useful strategy for further clinical translation.

P-402

The protective effect of antioxidants against hepatic and renal ischemia reperfusion injury

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Purpose: Hepatic/renal ischemia is a destructive event that is associated with high morbidity and mortality rates after organ transplantation. Hesperidin and cassia tora significantly contributes to the intracellular antioxidant defense system and has been reported to act as a powerful agent against superoxide, singlet oxygen and hydroxyl radicals. We sought to examine whether the effect of hesperidin and cassia tora prevented hepatic and renal tissue injury induced by ischemia-reperfusion (I/R).
Methods: 40 male Sprague-Dawley rats were allocated into 5 experimental groups; Control (n=10): sham, hepatic I/R (n=5): rats underwent occlusion of common hepatic artery and portal vein for 30min, sham, renal I/R (n=5): rats underwent occlusion of bilateral renal pedicle for 30min, hesperidin (n=10): rats received 500 mg/kg/d hesperidin for five days, cassia tora (n=10): rats received 500 mg/kg/d cassia tora for five days.
Results: In hepatic I/R group, pretreatment with hesperidin and cassia tora led to lower levels of AST, ALT (225±2, 74±3 , 371±2, 98±1 and 522±6, 191±4 respectively for hesperidin, cassia tora and I/R groups). In renal I/R group, pretreatment with hesperidin and cassia tora led to lower levels of BUN, Cr (33±2, 0.7±0.1, 42±1, 0.6±0.1 and 95±3, 2.1±0.2 respectively for hesperidin, cassia tora and I/R groups). Pretreatment with hesperidin and cassia tora showed lower level of IL-1, IL-6 and TNF-α than I/R group. Immunohistochemistry for Bcl2 and Bax indicated that Bcl2 expression in the hesperidin and cassia tora group was significantly increased compared with the the I/R group.
Conclusions: Hesperidin and cassia tora improved acute hepatic/renal I/R through its antioxidant and anti-inflammatory effects. These findings suggest that hesperidin and cassia tora are the potential therapeutic agents for acute ischemia-induced organ damage.

P-403

Sirtuin 1 associated to different hepatic protection outcome regarding levels of steatosis

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Introduction: Sirtuin-1 (Sirt1) is a NAD-dependent histone deacetylase has been associated to many processes of cytoprotection through downregulation of apoptosis, upregulation of autophagy and ROS detoxifying mechanisms. In spite of the various reserches regard Sirt1, its role remains unclear during the cold ischemia and liver steatosis.

Material and methods: Livers from male Zücker Lean and Zücker Obese rats (11 weeks aged) were washed and stored in IGL-1 solution at 4ºC for 24 hours. After rinsing with Ringer solution, livers were stored at -80ºC for subsequent analyses.
Results: Data revealed that there is an upregulation in both steatotic and non-steatotic livers of Sirt1 during cold ischemia. Sirt1 is associated with AMPK increases, a critical regulator of autophagy, which is concomitant with increased levels of autophagy in all cases. However, there is a differential behaviour in oxidative stress, with moderate increases in non-steatotic livers compared to steatotic, which is associated to increased levels of apoptosis.
Conclusion: Sirt1 is widely reported as a major cytoprotective mechanism that operates during the ischemic insult in both steatotic and non-steatotic livers. However, its upregulation is more associated to decreased levels of damage expressed as apoptosis and oxidative stress in non-steatotic livers than in steatotic ones.

P-404

FAS siRNA donor administration has the potential to alleviate ischemia-reperfusion injury in an arterialized rat liver transplant model

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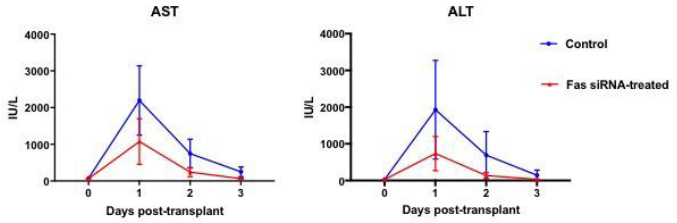
Background: Liver ischemia-reperfusion injury (IRI) is an inherent pathological process occurring in liver transplantation, which compromises graft, and patient outcomes. The degree of apoptosis is associated with IRI intensity. We hypothesized that silencing of apoptosis-associated genes can alleviate IRI leading to better graft and liver recipients survival rates.
Methods: Male Lewis rats were transplanted with a syngeneic liver graft employing an arterialized rat liver transplantation model. A prolonged cold ischemia time (CIT) of 22 hours was established in order to amplify the intensity of the IRI, reflected by the post-transplant transaminases levels. We administered 500ng of FAS siRNA diluted in 1 ml of PBS via the penile vein in donors rats (siRNA-treated group) two hours before the aorta cross clamping. Donors in the control group (Control) received an injection of PBS alone in the same conditions. Blood samples were collected daily until the

euthansia at day 3 post-transplant.
Results: We performed an initial experiment with 4 animals in each group. All animals survived until day 3 post-transplant. CIT (siRNA-treated: 1293±54min x 1330±60min Control, p=0.39) and anhepatic time (siRNA-treated: 17.00±0,5min x 16.25±1.18min Control, p=0.395) were comparable between the two groups. Recipients of siRNA-treated liver grafts showed lower levels of transaminases on the first day post transplantation with a trend to be statistically significant: AST (siRNA-treated x Control: 1074.00±621.23 IU/L x 2194.50±945 IU/L respectively, p=0.053) and ALT (siRNA-treated x Control: 734.00±464.15IU/L x 1929.50±1344 IU/L respectively, p=0.061). The histological analysis following the Suzuki criteria showed similar IRI damage in both groups.
Conclusion: Our preliminary results suggest that silencing of apoptosis-associated genes could be used to alleviate post liver transplantation IRI. Further experiments are necessary to corroborate this therapeutic strategy. Next, we are going to test FAS siRNA organ treatment during liver machine perfusion.



[Figure 1: AST and ALT outcome in the post-transplant period.]

P-405

Increases in ALDH2 protein content is associated to hepatoprotection through autophagy and UPS in fatty liver cold ischemia

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Introduction: ALDH2 has been widely reported to play a role in ethanol detoxification, and more recently it has been associated to cytoprotective mechanisms. However, its role in the specific frame of the cold ischemic insult has not been studied in depth in the liver.
Material and methods: Livers from male Zücker Obese rats (11 weeks aged) were washed and stored in IGL-1 and HTK solutions at 4ºC for 24 hours. After rinsing with Ringer solution, livers were stored at -80ºC for subsequent analyses.
Results: ALDH2 levels were concomitant with decreases in 4-HNE. Reported AMPK upregulation by ALDH2 correlates with decreased levels of p-mTOR and enhanced autophagy. Contained depletion of ATP as a consequence of enhanced autophagy is associated with reduced UPS activity. Critically low ATP levels are associated to increased UPS activity and more apoptosis. Increased levels of ALDH2 correlates with decreased levels of apoptosis and transaminases.
Conclusions: ALDH2 is associated to increased levels of cytoprotective autophagy. Enhanced levels of autophagy preserve the cells from ATP depletion and prevents UPS activity. Lessened UPS activity correlates with decreased levels of apoptosis and transaminases.

P-406

The potential role of Shp2 in suppressing hepatocellular carcinogenesis by bile acid metabolism

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Shp2 is an SH2-tyrosine phosphatase acting downstream of receptor tyrosine kinases (RTKs). Previous studies have shown that Shp2 deletion in hepatocytes suppresses hepatocarcinogenesis, means Shp2 is cancer-promoting genes. However, most recent data demonstrated contradictory conclusions, Shp2 acts as a tumor suppressor in hepatocellular carcinogenesis. In addition, Shp2 deletion multiplies bile in gall bladder, promotes the level of the serum bile acid and aggravates liver injury. Furthermore, bile acid biosynthesis is dramatically increased and both FGF15/19 and BA signals obviously activated in $Shp2^{hep-/-}$ liver. Our study is to determine the potential role of Shp2 in hepatocellular carcinogenesis regulated by bile acid metabolism.

P-407

MyD88 inhibitor acts as a suppressor In the oncogenesis and drug resistance of pancreatic carcinoma

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MyD88 was significantly different in cancer and adjacent tissues of pancreatic cancer. This paper confirms that MyD88-specific inhibitor ST2825 affects the development of tumor and increases the anti-tumor activity of Gemcitabine and explores its molecular mechanism.
The expression levels of MyD88, p-p65 and p-erk protein in pancreatic cancer and adjacent tissues were analyzed by immunohistochemistry. In this study, pancreatic cancer cell lines AsPC-1, BxPC-3, CFPAC-1 and PANC-1 cells were treated with MyD88-specific inhibitor ST2825 and pancreatic cancer first-line chemotherapeutic drug Gemcitabine. The cell cycle was detected by CCK-8, and the cell cycle was detected by flow cytometry. Cell cycle related protein cyclins, apoptosis-related protein Bax, activated PARP and caspase-3 MyD88, NF-kB pathway and ERK pathway were detected by Western blot. And to explore its molecular mechanism affecting cell function.
Immunohistochemical staining showed that MyD88, p-p65, p-erk protein was highly expressed in cancer tissues compared with adjacent tissues.
Pancreatic cancer cell line CFPAC-1 and PANC-1 were treated with MyD88-specific inhibitor ST2825, and the cell proliferation was decreased, the migration was decreased, the apoptosis increased, the G2 phase was blocked, the expression of cyclin B1 decreased, Protein Bax, activated PARP, activated caspase-3 expression increased, MyD88 no significant change, p-p65, p-erk expression decreased significantly. CFPAC-1 and PANC-1 were treated with ST2825 and Gemcitabine alone and ST2825 plus Gemcitabine .
The combined treatment group decreased cell clone formation, decreased migration, increased apoptosis, decreased p-p65, p-erk expression significantly compared with the control group and the monotherapy group, the expression of MyD88 had no significant change.
MyD88, p-p65, p-erk were highly expressed in pancreatic cancer tissues. Found that MyD88-specific inhibitor ST2825 may affect the development of tumor and increase the antitumor activity of Gemcitabine by regulating the activation of NF-kB pathway and ERK pathway.

P-408

Human marrow mesenchymal stem cells promote hepatocarcinogenesis by promoting the development of tumor stem cells

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Human marrow mesenchymal stem cells(BMSC) are reported to have a tendency to migrate to neoplasm. And the mechanism of the migration or cancer promotion have not been researched yet. In this study, we found human marrow mesenchymal stem cells could promote the formation of tumor spheres from hepatocarcinoma cells, and promote the migration and invasion of hepatocarcinoma cells by coculturing human marrow mesenchymal stem cells and hepatocarcinoma cells. Molecular markers associated with stem cells in the hepatocarcinoma cells, for example, CD90 and CD13 increased after coculturing with BMSC. In the tumor formation experiment in nude mice, the tumors from HCC-MSC co-inoculation group were significantly stronger than the HCC-alone inoculation group. Collectively, our findings establish that marrow mesenchymal stem cells facilitates hepatocarcinogenesis, with potential implications for therapeutic targeting.

P-409

Vismodegib promotes the delivery and efficacy of SN38 nanoparticles by suppressing desmoplastic response in pancreatic PDX model

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The dense extracellular matrix in pancreatic cancer limited the distribution and anti-tumor efficacy of nanoparticles. Diaruption of desmoplastic response by Hedgehog pathway blockage may promote the drug delivery and efficacy in pancreatic cancer. In this study, vismodegib, a special hedgehog inhibitor, was check out its anti-desmoplastic and pro-drug delivery activity. The results presented that vismodegib could inactivate hedgehog pathway at GLI1, decrease fibronectin expression in extracellular matrix, reopen blood vessels and promote blood perfusion in tumor. Furthermore, vismodegib improved anti-tumor activity of SN38 nanoparticles in bxpc-3 xenograft and PDX model. In conclusion, vismodegib may have potential to improve the prognosis of pancreatic cancer combined with SN38 nanoparticles.

Poster Round II, Session 1, 2, 3: Immunosuppression and Tolerance Induction

P-410

HEPHAISTOS study: Early use of everolimus plus reduced tacrolimus in de novo liver transplant recipients achieves high efficacy and safety compared to standard tacrolimus.

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Background: The HEPHAISTOS study (NCT01551212) compared the efficacy and safety of concentration-controlled everolimus [EVR] with reduced tacrolimus [rTAC] versus standard tacrolimus [TAC-C] in de novo liver transplant recipients [LTxR].
Methods: In this 12 months [M] prospective, open-label, multi-center study 333 patients [pts] were randomized 1:1 between day 7 to 21 after Tx to either EVR(3-8 ng/ml) + rTAC(< 5ng/ml), or TAC-C(6-10 ng/ml), all with steroids until M6. Here, we report M12 efficacy and safety results (n=169 EVR+rTAC, n=164 TAC-C).
Results: Randomization occurred on average 15 days after LTx. EVR+rTAC achieved comparable efficacy to TAC-C for all key parameters. At M12, incidence rates for Biopsy Proven Acute Rejection {BPAR] were 8.9% and 6.9% in pts treated with EVR+rTAC and TAC-C, respectively (Kaplan-Meier estimates). Most events were considered as “mild” (n=9 vs.n=7) and few events as “moderate” or “severe” (in total n=8 vs. n=7). Under treatment, no graft loss and 2 deaths occurred in the EVR arm, and 3 graft losses and 3 deaths in the TAC-C group. Safety profiles were similar, incidences of AEs leading to study drug discontinuation were 23.7% in EVR+rTAC, vs 23.2% in TAC-C group. Main reasons for discontinuation were renal and urinary disorders (1.2% EVR+rTAC, 7.3%TAC-C) and leucopenia (2.4%, 0.0%). Importantly, no new safety signals were identified during the study.
Conclusion: HEPHAISTOS confirmed early use of EVR in combination with reduced TAC in LTx recipients is feasible and safe with good efficacy outcomes.

P-411

Real-life experience with mTOR inhibitors treatment after liver transplantation

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Introduction: Immunosuppression with mammalian target of rapamycin inhibitors (mTORi) following liver transplantation (LT) is widely used to minimize calcineurin inhibitors (CNI) related nephrotoxicity. Less data are available about metabolic effects of mTOR inhibitors.
Aim: To determine the renal and metabolic effects of Everolimus (EVR) and Sirolimus (SIR) treatment in real-life LT patients.
Methods: A retrospective cohort study of patients treated with mTORi after LT. Demographic, clinical data, glomerular filtration rate (GFR), Body mass index (BMI), blood glucose, lipid profile and blood pressure (BP) measurements were collected over a period of 6 years. Initiation of BP, diabetes and lipid medications was recorded.
Results: In 52 patients that underwent LT between the years 1998-2017, treatment with mTORi was started. Treatment protocol was CNI minimization in 33(63.4%) patients and CNI withdrawal in 19(36.5%) patients. GFR improved significantly after initiation of mTORi (2.5mL/min/1.73 m^2 per year±1.2, p=0.037) without significant difference between two groups (62.9mL/min/1.73 m^2±22.6 vs. 61.9mL/min/1.73m^2±20.1 at the beginning [p=1.0]; 77.2mL/min/1.73 m^2±37.3 vs. 70.6mL/min/1.73 m^2±18.8 after 4 years [p=1.0] for CNI withdrawal vs. minimization, respectively). Most common side effects were aphthae (30.7%) and edema (15.3%). Treatment was discontinued due to side effects in 17(32.6%) of patients (16 on EVR and 1 on SIR, p=0.029). There was no significant difference in BP, weight, BMI, blood glucose, cholesterol and triglycerides values during follow up, however 23 patients (44.2%) were started on BP, diabetes or lipid lowering medications with no difference between two protocols; and SIR vs EVR. Patients on CNI minimization with SIR gained more weight compared to their counterparts (6.8kg ±3.3, p=0.042; 7.05kg ±3.4, p=0.041; respectively).
Conclusions: In this large single center cohort of LT recipients treated with mTORi we demonstrated improvement in GFR, reasonable side effects profile and metabolic changes. Following prospective data collection will help us to define a preferable treatment protocol.

P-412

MeltDose technology versus once-daily prolonged release tacrolimus in de novo liver transplant recipients

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Once-daily tacrolimus prolonged-released (TAC-PR) is associated with an increased adherence but still has low bioavailability. MeltDose technology has been used to create a new extended-release formulation of TAC once-daily (LCP-TAC) to enhance bioavailability. Aim of this study is to retrospectively compare de novo administration of LCP-TAC and TAC-PR in terms of therapeutic trough levels (ng/ml) and daily/dosage (mg/die) during the first 30 days after first liver transplantation. 35 liver transplanted patients were retrospectively enrolled in LCP- TAC (#16) or TAC-PR (#19) group as de novo primary immunosuppression. No significant differences were found between groups for patient's characteristics. The initial dose of tacrolimus did not differ between LCP-TAC and TAC-PR (5.19±1.72 vs 5.26±1.91, p=0.90). Tacrolimus daily dosage remained similar at day +3 and +5 (4.91±2.1 vs 5.17±1.92, p=0.70 and 4.97±2.21 vs 6.33±2.35, p=0.09) while at day +7, +15 and +30 the total daily dosage was inferior for LCP-TAC than TAC-PR being respectively 5.44±2.06 vs 7.68±2.91 (p=0.01), 5.33±2.23 vs 8.82±2.35 (p=0.0002) and 5.38±2.50 vs 9.81±3.78 (p=0.0008). The therapeutic trough levels were statistically significant higher for LCP-TAC at days +3 and +5 being respectively 5.05±3.58 vs 2.42±2.75 (p=0.032) and 7.35±5.12 vs 4.17±2.05 (p=0.037), while no differences were found for day +7, +15 and +30. A higher percentage of patients (40% vs 13%) achieved therapeutic trough levels within the first 5 days from transplant in the LCP-TAC. No episodes of acute rejection were recorded. LCP-TAC administration achieved therapeutic trough levels earlier than TAC-PR despite a 25% lower median dose of drug administered during the first month after liver transplantation. Tacrolimus given by MeltDose®technology might enhance bioavailability and reduce the amount of drug that should be administered to achieve similar therapeutic trough levels when compare to TAC-PR in de novo liver transplant recipients.

P-413

Preliminary study on screening novel effective mTOR inhibitors in suppressing T cell proliferation in vitro and rejection in vivo

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Aim: To study the application of novel mTOR small molecule inhibitors on the heart transplantation in mice.
Method: The lymphocytes in spleen of mice are extracted then further stained with CFSE. CD3/28 microbeads were utilized to act as lymphocyte stimulator in 96-well plates. After 5 days' co-culture, flow cytometry was performed in order to assess the inhibitory effect to lymphocytes of inhibitors. We utilized a pool of mTOR small molecule inhibitors, of which are mTORC1 inhibitor or mTORC1&mTORC2 dual inhibitors, then we chose rapamycin as positive control. A total of 21 small molecules has been screened in vitro up till now. Then we selected two inhibitors after BALB/c to B6 heterotopic heart transplants were administrated. Grafts survival time will be recorded once the heart palpation cannot be touched.
Result and conclusion: We found many inhibitors can suppress the proliferation of lymphocytes in vitro according to the CFSE staining result, of which PP242 and GSK2126458 can prolong the survival time of the grafts.

P-414

Ab initio mammalian target of rapamycin inhibitors in liver transplantation: mid-term results of observational cohort study

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Background: Ab initio mammalian target of rapamycin inhibitors (mTORi), without corticosteroids and induction therapy have been already reported by our group in liver transplantation (LT). The aim of present study is to assess mid-term safety and efficacy of mTORi ab initio after LT.
Methods: This is a retrospective cohort observational study of 140 patients who underwent LT from July 2009 to October 2018 [89%

male, median age 57 years (range 19-69)]; all recipients received mTORi-based immunosuppression associated with a low dose of calcineurin inhibitors (CNI) (n=131) or mycophenolate (n=9) from day 1 post-LT. Seventy-five patients (53%) were transplanted for hepatocellular carcinoma (HCC) within *up to 7 criteria*.
Results: One and three-years graft and patient's survival were 80%. The median follow-up was 25.4 (range: 1-111) months. All patients showed stable liver function over the follow-up except one patient who experienced biopsy proven acute rejection. Thirty-nine (27%) and six (4%) patients experienced new-onset dyslipidaemia and diabetes respectively; 16 (11.4%) patients required antihypertensive drugs. At the last follow-up, four (5%) patients had HCC recurrence and two (1.4%) de novo skin cancer. At last follow-up, thirty (21%) patients were on monotherapy (15% Everolimus, 6% Tacrolimus).
Conclusion: mTORi-based immunosuppression ab initio after LT seems to be safe and effective either after mid-term follow-up; although these findings required further investigation on well designed trial, Everolimus-based and low-CNI dose can be consider a valid option especially in recipients who require weak CNI-dose after LT.

P-415

Impact of maintaining tacrolimus trough level below 3 ng/mL after first year of liver transplantation

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Background: Most transplant centres target a tacrolimus trough level between 3-5 ng/mL for maintenance immunosuppression after liver transplantation. An alternative strategy is to reduce tacrolimus to the lowest possible dose and monitor liver function closely. We hypothesize that maintaining lower tacrolimus trough level below 3 ng/mL is not inferior to standard tacrolimus dose target.
Method: We conducted a retrospective study for all eligible adult patients who received liver transplantation from a single transplant centre in the past 5 years. The study was approved by local ethics committee. The subjects were monitored for tacrolimus levels, liver and renal function tests at least every 6 months. The low-tacrolimus group was defined as those who had tacrolimus levels < 3 ng/mL for >50% of the measurements between months 12 to 60 (n=31). The remaining subjects were analysed as control (n=52). The rejection rate, renal function, infection rate and overall survival were compared using Fisher's exact test, t-test, mood's median test and Kaplan-Meier analysis where appropriate. Statistical analyses were performed by R version 3.4.4.
Results: A total of 83 subjects were recruited. The baseline characteristics of both groups were similar, except low-tacrolimus group had lower eGFR at baseline. The rates of acute cellular rejection were not statistically different (low-tacrolimus 3.4% vs control 9.6%, Fisher's exact test p=0.41). A higher percentage subjects in the low-tacrolimus group had improved eGFR in the study period (p>0.05). The median change rate in low-tacrolimus group was higher than the control group (1.58% vs -1.54%, t-test p=0.22). The infection rates were similar in both groups (25.8% vs 23.1%, Fisher's exact test p=0.79). There was no difference in survival rates at year 5 (93.1%, p=0.83).
Conclusion: Targeting tacrolimus level < 3 ng/mL one year after liver transplantation does not result in inferior outcome, and may help preserve renal function.

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Endoscopic retrograde cholangiopancreatography: a possible powerful factor to increase tacrolimus trough levels in liver transplant patients

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Objective: Endoscopic retrograde cholangiopancreatography (ERCP) is commonly used to relieve problems on biliary ductal system for liver transplant patients. We found that the tacrolimus trough levels (C_0) fluctuated greatly after ERCP in several liver transplant patients. Therefore, the influence of ERCP on tacrolimus levels must be further investigated to optimize the treatments for liver transplant patients.
Methods: This study is a retrospective before-after study. From October 2017 to October 2018, 74 liver transplant patients that received ERCP were included. Dose-adjusted C_0(C_0/D) of tacrolimus before and after ERCP were analyzed.
Results: The C_0/D of tacrolimus increased in more than 80% patients after receiving ERCP during the first 3 days. On the first and third day after ERCP, the average C_0/D of tacrolimus increased by 45.79% (95% CI: 27.35-64.24,p< 0.001) and 31.39% (95% CI: 15.09%-47.69%,p= 0.001) compared with the baseline. This average value gradually returned to the basic level on the sixth day (p=0.354). The C_0/D of tacrolimus was elevated over 100% in 22% and 11.54% of the patients on the first and third day, respectively. In four patients, the C_0/D increased for over threefold.
Conclusion: ERCP can substantially increase the tacrolimus trough levels of partial liver transplant patients. Tacrolimus levels should be monitored for 1 week after ERCP was performed.

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Neutrophil-to-lymphocyte ration predicts acute cellular rejection in the living donor liver transplantation

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Background: The neutrophil to lymphocyte ration (NLR) have been shown to be strong predictors of inflammation and worse prognosis in variety of conditions that include transplantation. The aim of the study is to evaluate the effectiveness of NLR to predict the ACR after Living donor liver transplantation (LDLT).
Material and methods: This was a retrospective study that included all patients who underwent a liver biopsy after LDLT from 2009 to 2017. The NLR was calculated 4 weeks before transplantation, and on the time of transplantation and immediately prior to liver biopsy and the correlation between its values and the incidence of ACR were investigated.
Results: A total of 81 patients were reviewed (ABO compatible (ABOc)=66, ABO incompatible(ABOi)=15). ABOc and ABOi patients who had ACR findings, were 19 (28.8%) and 10 (66.7%), respectively. The patients who had ACR within one month after transplantation were 15(78.9%) and 7(70%).. In the ABOc group, there was no significant difference 4 weeks before transplantation (ACR : no ACR = 2.54±1.15 : 3.68±2.08, P=0.06) and transplantation (ACR : no ACR = 20.53±13.39 : 17.73±8.74, P=0.06). However, NLR at immediately prior to biopsy was significantly lower in ACR group (ACR : no ACR = 5.82±3.42 : 28.66±22.66, P=< 0.001- The liver function test (LFT) of the group of 'ACR' and 'no ACR' in ABOc LDLT were not significant different between two groups (Total bilirubin, P=0.48 ; ALP, P=0.31; ALT. P=0.22;, AST, P=0.31; g-GT, P=0.46). We evaluated the predictive value of NLR for ACR within one month in ABOc LDLT. The ROC showed AUC of 0.969. The NLR cutoff of 9.67 had a sensitivity 94.1% and specificity 86.7%.
Conclusion: This study showed that NLR could be thes non-invasive predictors of subclinical early ACR in the ABO compatible LDLT.

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Siomycin A decreased tryptophan degradation through downregulating IDO2 to suppress liver immune tolerance after transplantation

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Background: Forkhead box M1 (FOXM1) acts as a transcription factor plays an important role in multiple cellular processes, such as apoptosis, DNA damage repair and angiogenesis etc. Indoleamine 2,3-dioxygenase (IDO), IDO1 and IDO2, are the essential amino-acid tryptophan, which leads to immune tolerance in organ transplantation. However, the relationship between FOXM1 and IDO is still unknown.
Methods: We used FOXM1 inhibitor, Siomycin A, to suppress the expression of FOXM1. Through the RT-PCR and western-blotting to detect the expression of IDO2 under Siomycin A treatment in LO2 cells. Besides, we also measured the level of kynurenine (degradation of tryptophan) through Elisa assay. Moreover, we also take application of Siomycin A into mouse liver transplantation model to ensure the influence of FOXM1 to the survival rate of liver transplantation. Then we used Chromatin immunoprecipitation (CHIP) to understand the relationship between FOXM1 and IDO2.
Results: We observed that the expression of IDO2 was downregulated under the treatment of Siomycin A in LO2 cells. Furthermore, Siomycin A treated LO2 cells presented decreased ability of tryptophan degradation. CHIP assay indicated direct interaction of FOXM1 with IDO2 promoter in liver cells. Besides, through FACS, we found that Siomycin A-mediated increase in CD4+/CD25+/Foxop3+ Treg cells in mouse liver transplantation model. Totally, all these results indicated that FOXM1 may be a potential target in the therapy for liver transplantation immune tolerance.

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Very early immunosuppression predicts the first-year renal function post liver transplantation

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Background: A recent study has described a strong association between very-early immunosuppression (IS) post-Liver Transplantation (LT) and outcomes. We aimed to confirm these findings in a multicenter, retrospective long-term cohort.
Methods: Tac and CsA levels obtained during the first 15 days post LT were collected. High-IS was considered as a median Tac, CsA C0 or C2 higher than 10 ng/ml, 250 ng/ml or 1200 ng/ml, respectively or a peak of Tac > 20 ng/ml. Optimal-IS was defined as a median of Tac,

CsA C0 or C2 levels between 7-10 ng/ml, 150-250 ng/ml or 800-1200 ng/ml. Low-IS was defined as below the thresholds of optimal IS.
Results: The study included 432 patients. Tac was the main IS agent used compared with CsA-C0 and CsA-C2: 56.3%, 27.7% and 16%, respectively. Overall survival was 84.3%, 78.5% and 66.2% at 3, 5 and 10 years. The median eGFR at LT, 1, 3 and 5 year were 94.5, 79.4, 62.2 and 66.6, respectively. Decreasing in eGFR was significantly higher in patients exposed to optimal and high IS compared with low IS at 1- (coeff. -9.8 ml/min, p=0.009; coeff -13.8, p< 0.001, respectively), 3- (coeff. -13 ml/min, p< 0.001; coeff -10.6, p=0.004, respectively) and 12-months post-LT (coeff. -10.4 ml/min, p=0.002; coeff -11.2, p=0.001, respectively). However, this association was no longer significant at 3-, 5- and 7-years post-LT. There were no differences in terms of graft loss among low versus optimal and high-IS groups (HR 1.049, p= 0.812 and HR 0.851, p=0.451).
Conclusions: In our series, very-early immunosuppression has an important impact on first year renal function. However, no association was found between very-early post-operative over-IS and long-term outcome measures following LT.

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Could IL-2 receptor blocker be used for prolonged maintenance, calcineurin free, immunosuppression in post liver transplant recipients?

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Introduction: Basiliximab is a chimeric monoclonal antibody that blocks interleukin-2 receptor on activated T lymphocytes. It is used as an induction agent in the perioperative period. The first dose of the drug is given two hours before organ transplantation and second dose 4 days after transplant. The drug is used in conjunction with maintenance calcineurin inhibitor and steroids with or without Mycophenolate mofetil. Basiliximab is also used for steroids sparing or minimizing/ delaying use of calcineurin inhibitors (up to 5 days) and in cases of steroid resistant rejection successfully. However, utility of Basiliximab as a maintenance agent without calcineurin inhibitors has not been described.
Aim of the present study is to examine the utility of IL-2 blocker as a maintenance agent without calcineurin inhibitors (CNI) after liver transplantation (LTx).
Patients and methods: After IRB approval we found four patients where Basiliximab was used post LTx to avoid CNI for 7 days to 496 days post LTx for neuro toxicity(n=3) and nephrotoxicity (n=1). One of the patient (case#4) received Basiliximab pre operatively as an induction and subsequently as a maintenance agent, while the remaining three patients received Basiliximab post LTx as a maintenance agent. (Figure below).
Results: All patients had complete recovery from neuro and nephrotoxicity. None of them had any episode of acute rejection with stable liver function at 3 months to 7 years follow up.
Conclusion: Our observations suggest IL-2 receptor blocker can be successfully used as a maintenance immunosuppression agent without CNI for prolonged period after LTx without incurring acute rejection.

Case No	Age	Days CNI on hold	Reason to hold CNI	Basiliximab Total Doses	Follow up
1	27	496	Neuro toxicity	14	7.2 Years
2	68	58	Neuro toxicity	4	4.3 years
3	66	7	Nephrotoxicity	2	4 Months
4	62	15	Neuro toxicity	4	3 Months

[Figure]

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Tablet form or capsule form combined with tacrolimus after liver transplantation: a prospective randomized trial

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Background: The tablet and capsule form have advantage and disadvantage. Generally, the tablet form (500 mg) of mycophenolate mofetil (MMF) provides more convenience of taking drugs and cost-effectiveness than the capsule form (250 mg). We examined the efficacy and safety of MMF in its different forms combined with tacrolimus in liver transplant recipients.
Methods: Randomized controlled trial was performed to compare the efficacy and safety between the tablet form of MMF (Tablet group) versus the capsule form of MMF (Capsule group) in liver transplant patients. Study period was between 2014 and 2017 and 116 patients were enrolled. Primary endpoint was the incidence of biopsy-proven acute rejection (BPAR) rate for 24 weeks after liver transplantation. Secondary endpoints were patient survival, serum creatinine levels, and adverse events.
Results: Fifty-six patients were Capsule group and 60 patients were Tablet group. There were no statistically significant differences in MMF dose, MPA trough levels, and tacrolimus trough levels between the two groups. The incidence of BPAR at 24 weeks after randomization was 7.1% in Tablet group and 10.0% in the Capsule

group, respectively. (P=0.855). All patients with BPAR had good response of steroid pulse therapy and increased tacrolimus. Two patients in the Capsule group and one patient in the Tablet group was dead because of graft failure. Serum creatine levels and eGFR after liver transplantation were not different between the two groups. The incidence of serious adverse events was 7.2% in the Tablet group and 7.6% in the Capsule group, respectively. Serious events were not related with tablet or capsule.
Conclusion: Low-dose MMF in tablet form combined with tacrolimus regimen is safe and effective for preventing BPAR in the early period after liver transplantation.

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Dendritic cells transduced with autoimmune regulator exhibit immature properties and prolong heart allograft survival

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Objective: The expression of the Aire (Autoimmune regulator) gene was observed to inhibit the maturation and activation of dendritic cells (DCs) and induce transplantation tolerance.
Methods: The bone marrow-derived DCs were cultured in vitro, and the Aire gene was transferred into DCs by means of green fluorescent protein (GFP) fluorescent adenoviral vector. The Aire gene-modified immature (imDCs) was detected by flow cytometry and enzyme-linked immunosorbent assay (ELISA). The phenotypic and functional changes of DCsbefore and after lipopolysaccharide (LPS) stimulation were established. A mouse model of abdominal heterotopic heart transplantation was established. Three days after the operation, the receptors were administered to the dorsal vein of the penis for injection of phosphate buffered saline (PBS) and imDCs. DC-GFP and DC-Aire were used to observe the heart graft activity and survival time of each group of mice. At the same time, the grafts were taken for hematoxylin-eosin (HE) and immunofluorescence on the 11th and 100thday after operation. The graft rejection intensity of each group was compared.
Results: DCs overexpressing Aire remained stable in immature state after lipopolysaccharide stimulation: low expression of human major histocompatibility complex (MHC)-II, CD40, CD80, CD86, secretion of low-level interleukin (IL)-12 [(536.80±93.46) pg/ml, p=0.014] and high level IL-10 [(420.50±38.69) pg/ml, P=0.024], and the difference between the two groups was statistically significant. Postoperative graft survival time in the Aire group was significantly better than the other groups [(28.6 ± 4.8) d, P = 0.016]. Postoperative immunohistochemistry suggested that the heart graft activity in the Aire group was superior to other controls.
Conclusion: Aire gene effectively inhibited the maturation and activation of immature DCs under the action of exogenous stimulating factors such as lipopolysaccharide, inhibiting antigen presentation, prolonging graft survival to some extent, and inducing transplantation of immune tolerance.

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Study on feasibility of changing to cyclosporine from tacrolimus for better glycemic control in liver transplant recepients

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Background: Post liver transplant diabetes mellitus (PLTDM) is reported to occur in 12.2 to 33%of patients at 1 year follow-up. Tacrolimus and cyclosporine, both with similar mechanism of immunosuppession, have different action on glycemic control. More patients are reported to require antidiabetic therapy with tacrolimus regardless of diabetic status at baseline on long term follow-up. Only a few trials have assessed glycemic control after the change in treatment regimen from tacrolimus to cyclosporine. In the present series we intended to study the impact of changing to cyclosporine from tacrolimus on the glycemic status of the individuals with uncontrolled DM post liver transplantation.
Methods: Six patients who underwent living related liver transplantation between June 2017 to April 2018 with uncontrolled DM post transplantation were included in the study. All patients were receiving tacrolimus and were off steroids at the time of changing to cyclosporine. We noted random blood sugar levels, treatment modification of DM and graft function before and after changing to cyclosporine.
Results: All patients were males with age ranging from 29 to 56 years. Three were diabetic before transplantation, while the other 3 developed diabetes post transplantation. The aetiology of CLD was NASH in 3, ethanol in 2 and HBV in 1.None of the patients had any prior acute rejection episode. The random blood sugars before changing to cyclosporine was 350-450mg%.After a mean follow-up of 2 months, blood sugar levels improved to 150-200mg%. Five patients receiving insulin reported decrease in insulin requirement after changing to cyclosporine. One patient who was on Metformin continued taking it at the same dose. There was no episode of acute rejection after changing to cyclosporine.
Conclusion: Liver transplant patients receiving tacrolimus who develop uncontrolled d DM post transplant show better glycemic control after changing to cyclosporine.

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Machine-learning models to predict tacrolimus dosage in liver transplant recipients

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Introduction: Tacrolimus is the most widely used immunosuppressive agents to prevent rejection after solid organ transplantation. However, the use of tacrolimus should be cautious due to its narrow therapeutic index and variability of individual bio availabilities. Machine learning techniques could be good modality to decide optimal dosage of tacrolimus, compared with traditional statistical models, have many advantages including high power and accuracy, we have implemented a new approach to find the optimal dose of tacrolimus by machine learning technique.
Method: We retrospectively reviewed the postoperative tacrolimus levels of patients who underwent liver transplantation at the Seoul National University Hospital from March 2016 to March 2018. We implemented an artificial intelligence model predicting future tacrolimus level by tacrolimus concentrations in the previous two days, sex, height, and daily changing body weight. We investigated hyperparameters (the number of layers in the network and the number of nodes in each layer) using a grid search and found the model with the lowest validation error.
Results: A machine learning model was derived using data from the 187 patients. As a result of testing the model with 18 patients, the predicted value of the model had an error of 1.5 ug/L from the actual measured tacrolimus level. Simulating the model in random case with a calculated tacrolimus dose to ensure the next drug concentration to be within the therapeutic range, more than 95% of the final predicted tacrolimus level comes in the therapeutic window.

P-425

Squint: unique tacrolimus related toxicity

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A 33 year old patient underwent OLT for ethanol related decompensated cirrhosis. The patient received allograft from a 20 year old deceased donor. The early post transplant period was uneventful with good allograft function. The patient was discharged on CNI based immunosuppression .
2 months post OLT the patient presented with diplopia to out-patient clinic. There was no associated history of fever, cough, cold, seizures, tremors, etc. The examination revealed squint with normal uniocular vision but diplopia with binocular vision(complete neuro/oplthalmologic exam performed). There was no other motor or sensory deficit. The patient was admitted and underwent MRI brain, basic labs with tacrolimus level and CSF examination (complete viral profile).
The blood work was non contributing with normal liver function tests. The CSF exam did not reveal any evidence of bacterial or viral infection. MRI brain revealed small focus of hemorrhage in the anteroinferior aspect of left cerebellar hemisphere, pons and upper medulla. The tacrolimus level was 7.7 ng.
A final diagnosis of tacrolimus related neurotoxicity was finally achieved and patient was switched to cyclosporine. The patient did not experience any further deterioration of diplopia/squint after initiation of cyclosporine. Repeat MRI was performed after 1 month and 6 months of index event. The study revealed grossly unchanged foci of the hemorrhage as compared to index scan with no new lesions.
The patient showed slow improvement following withdrawal of tacrolimus. The squint resolved completely after 6 months of change of immunosuppression. No further neurotoxicity was observed with cyclosporine.

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Inhibition of autophagy prolongs recipient survival through accelerating CD8+ T cell apoptosis in a rat liver transplantation model

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In liver transplantation (LT), acute rejection (AR) remains a common complication that significantly shortens recipient survival although various immunosuppressors have been used in clinical practice. In recent years, manipulating immune tolerance has been regarded as one of the promising solutions. Autophagy, an evolutionarily conserved protein degrading system, has been reported to be involved in the immune rejection and may become a target to establish immune tolerance. However, its role in AR after LT has not been elucidated. Here, we showed that the autophagy of $CD8^+$ T cell was strongly enhanced in patients with AR and autophagy level was positively correlated with the severity of rejection severity. Similar findings were observed in the acute rejection rat model. Furthermore, administration of autophagy inhibitor 3-methyladenine (3-MA) significantly prolonged graft survival through inhibiting autophagy of $CD8^+$ T cell, which resulted in decreased viability and function of $CD8^+$ T cell. In addition, inhibition of autophagy of activated CD8+ T cells largely reduced the stabilization of intact mitochondria and subsequently increased the production of mitochondrial superoxide (MitoSOX) in vitro.
Conclusions: We firstly showed inhibiting autophagy significantly prolongs liver allograft survival by accelerating apoptosis of CD8+ T cells , which will provide a novel strategy for immune tolerance induction.

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Mixed chimerism following graft versus host disease in a recipient of a liver transplant

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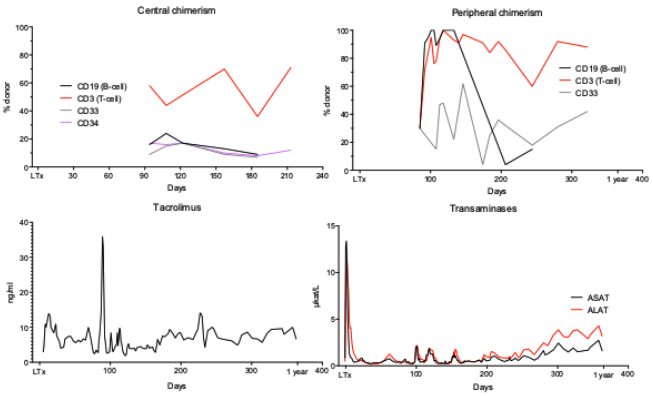
Background: Graft versus host disease (GVHD)-may present a rare but severe complication to transplantation. We present the case of a 69-year-old male patient who underwent liver transplantation and developed severe GVHD.
Case: Prior to liver transplantation two hepatocellular cancer lesions (within UCSF criteria) had been treated with chemoembolization. There was history of long-term pruritus and toxic dermatitis requiring cyclosporine A treatment.
The patient was ultimately transplanted with a split liver graft from a young male donor. Immunosuppression was based on basiliximab, followed by steroids and mycophenolate with delayed tacrolimus introduction. The patient was discharged 13 days post-transplantation following steroid-reduction due to steroid-induced psychosis.
The patient developed severe maculopapular rashes and neutropenia ten weeks post-transplantation. Skin biopsy showed GVHD. The condition deteriorated to GVHD grade IV with extensive gastrointestinal and cutaneous involvement followed by hemodynamic instability requiring ICU support.
The immediate challenge was a decision on either increased immunosuppression, or suspension of immunosuppression in favor of rejection of passenger leukocytes. Finally, anti-thymoglobulin regime was started and the patient recovered.
Immunological monitoring by peripheral blood and bone marrow tests for chimerism showed 88% peripheral and 71% central donor T-cell fraction at latest measurements. B-cell population peaked 100% peripheral and 24% central donor chimerism (15% and 9% in latest tests). Flow-cytometric Assay for Specific Cell-mediated Immune-response in Activated whole blood showed severe reduction in immunological response to mitogens.



[Figure 1. State of chimerism over time. Tacrolimus concentrations and transaminases.]

Conclusion: The patient recovered and was well at a one-year follow-up apart from persistent pseudomonas aeruginosa pneumonia. Liver function remains unaffected with tacrolimus 1mg q.a.d and concentrations < 2 ng/ml. Pretranspant cyclosporine A treatment might have created a preconditioning situation where passenger lymphocytes proliferate leading to GVHD with potential state of tolerance.

P-428

Once-daily tacrolimus is safe for pregnancy and childbirth after living donor liver transplantation (case)

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Background: The feasibility of once-daily tacrolimus is recently and widely accepted in the field of liver transplantation. However, there are very few reports about the risk and outcome of once-daily tacrolimus in pregnancy and livebirth after live donor liver transplantation.
We present a patient who did a full-term delivery after living donor liver transplantation with once-daily tacrolimus.
Method: The patient was born with biliary atresia and underwent Kasai operation 100 days after birth. She underwent live donor liver transplantation due to liver cirrhosis at the age of 28. Her brother was live donor and donor had experienced no complication. The patient suffered bile leakage at the anastomotic site 7 days after LT and PCDs were inserted. She was discharged 30 days after transplantation. However, biliary stricture at the anastomotic site was happened. She suffered intermittent biliary stricture and cholangitis for 3 years. We managed biliary complications by insertion of PTBD. There was no more biliary complication for 1 year. She was married and planned on being pregnant after liver transplantation. Therefore, we prepared the pregnancy with obstetrician. All kinds of medicine except tacrolimus were not prescribed before pregnancy. Tacrolimus once-daily medication was used during pregnancy and monthly follow up was done. We tried to use minimal dose of tacrolimus and the dose was from 2.5mg to 4.5mg and the range of trough level was between 1.9 and 6.2ng/mL.
Results: There were no complications including rejection during pregnancy. There was no additional biliary complication during pregnancy. Ten months later she did a full-term cesarean delivery without events. The child has no malformation and body weight was 3.4 kilogram at the time of delivery.
Conclusion: Planned pregnancy and childbirth with once-daily tacrolimus for patients who are stable surgically after liver transplantation can be done successfully.

Poster Round II, Session 1, 2, 3: Malignancies

P-429

EPS8L3 promotes hepatocellular carcinoma proliferation and metastasis by modulating the EGFR-ERK pathway

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Background: As a member of epidermal growth factor receptor kinase substrate 8(EPS8) family, the role of EPS8 like 3 protein (EPS8L3) has not been studied in malignancies. However, EPS8 has been reported to be associated with prognosis and functions in some kinds of cancers. In this study, we studied the role and prognostic value of EPS8L3 in hepatocellular carcinoma(HCC).
Methods: Sample data from TCGA and our hospital were used to assess the prognostic value of EPS8L3 in HCC. Human HCC cell lines LM3 and Huh7 with stable and transient expression of EPS8L3 were used in this study for the proliferation and migration analysis. The cell proliferation assay and colony formation assay were applied to evaluate proliferative ability, while transwell chamber models were used to evaluate migratory and invasive abilities. For *in vivo* experiments, subcutaneous xenografted tumors and pulmonary colonization assays were performed.
Results: EPS8L3 was overexpressed in HCC tissues compare with adjacent non-tumor tissues, and was associated with a poor clinical prognosis. Knockdown of EPS8L3 significantly inhibited cell proliferation by downregulating p21/p27 expression and inducing G1/S transition arrest, while the proliferative ability was restored in EPS8L3 overexpressed HCC cells. Both *in vitro* and *in vivo* experiments showed that EPS8L3 could promote the migration and invasion of HCC by promoting MMP2 expression. Furthermore, we demonstrated that EPS8L3 could affect the activation of the EGFR-ERK pathway by modulating EGFR dimerization and internalization, and ERK phosphorylation.
Conclusion: Expression of EPS8L3 was increased in human HCC samples and correlated with prognosis. It played a pivotal role in HCC cell proliferation and metastasis through regulating activation of the EGFR-ERK pathway. Hence, EPS8L3 maybe a potential therapeutic target for HCC.

P-430

The post liver transplant HCC recurrence calculator using machine learning: a proof of concept

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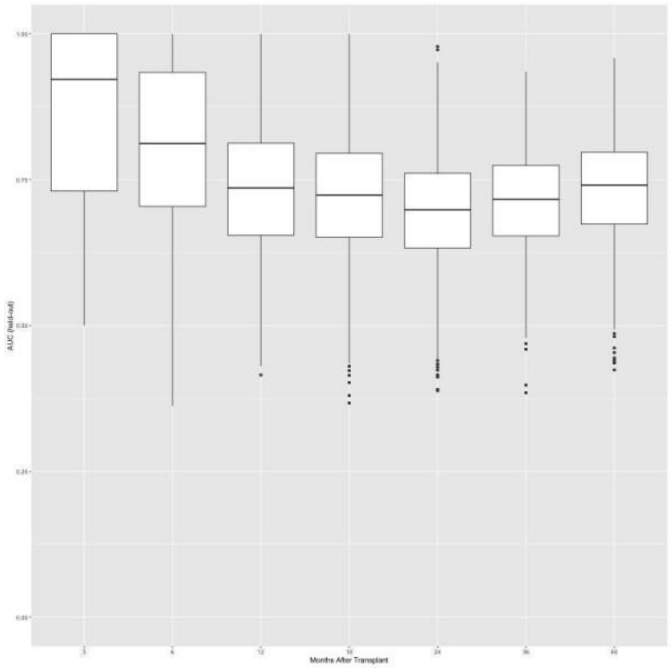
Background: The liver transplant listing criteria for hepatocellular carcinoma (HCC) is controversial. Policies aim to prevent recurrence but it is difficult to encompass the numerous contributive factors. This study takes advantage of machine-learning to incorporate all available features in a post-transplant recurrence prediction calculator.
Method: The calculator was developed using the Toronto General Hospital HCC database. This dataset includes all patients with HCC listed for liver transplantation between 2000-2016, and comprehensively includes serial imaging morphology, AFP, bridging therapy, treatment response, and post-transplant outcome.
A Cox proportional hazards model was used to model time to recurrence following liver transplant. Over-fitting was limited by encouraging coefficient sparsity using a least absolute shrinkage and selection operator (LASSO) penalized maximum likelihood procedure. The coefficients were calibrated on 90% of the data. Performance was evaluated over 1000 iterations by assessing the AUC and concordance on the held-out data. Variables selected by LASSO in over 50% of iterations were selected to run the analysis of the 5-year recurrence risk in the model. Alternative recurrence risk algorithms (AFP score and MORAL) were compared.
Results: The dataset included 694 patients who underwent liver transplant for HCC. The overall concordance of the model with disease-free survival was satisfactory (concordance 0.706, sd: 0.075). The AUC for prediction of recurrence at various time points demonstrates the predictive power of the model(Figure). Including all variables meeting the selection criteria, the AUC at 5 years post transplantation was 0.742 (95% CI 0.736-0.748).
By comparison, the AUC for AFP score at 5 years post-transplantation was 0.605 (95% CI 0.598-0.611) and that of MORAL was 0.589 (95% CI 0.583-0.595).
Conclusion: A comprehensive HCC recurrence risk calculator using machine learning is possible with higher accuracy than other available scores.



[Figure: AUC values of the HCC Recurrence Calculator at various times after liver transplantation]

P-431

TOX promotes the exhaustion of antitumor CD8+ T cells by preventing PD1 degradation in hepatocellular carcinoma

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Background: T cell exhaustion drives compromised anti-tumor immunity. We investigated the key regulator of T cell exhaustion in hepatocellular carcinoma (HCC), aiming to find potential therapeutic target to restore the anti-tumor function of exhausted CD8+ T cells.
Method: TIL-CD8+ T cells of various states, including fully functional ($PD1^{-}TIM3^{-}$), partial exhausted ($PD1^{int}TIM3^{+}$) and severe exhausted ($PD1^{hi}TIM3^{+}$), were sorted by flow cytometry and sent for transcriptome sequencing analysis. CD8+ cells partially or completely deficient in *Tox* were transferred in *Cd8*$^{-/-}$ mice bearing HCC. TIL-CD8+ T cells with TOX-knockdown or -overexpression were transferred into patient-derived xenograft (PDX) HCC mice in combination with anti-PD1 therapy. Furthermore, inhibitory receptors, transcription factors, cytokines, cell proliferation and apoptosis were assayed in TOX-knockdown or overexpressed TIL-CD8+ T cells. Transcriptome sequencing analysis was performed in TOX-overexpressed or control CD8+ T cells. Mechanism underlying the regulation of TOX in PD1 expression was studied in TIL-CD8+ T cells.
Results: We found that TOX was more abundant in exhausted CD8+ T cells compared to functional ones in HCC. Knockdown of TOX in CD8+ T cells inhibited tumor growth and increased the infiltration of CD8+ T cell in tumor. Knockdown of TOX alleviated CD8+ T cell exhaustion and improved the response of CD8+ T cells to anti-PD1 therapy in PDX HCC model. Mechanically, binding of TOX to PD1 in cytoplasm facilitated the endocytic recycling of PD1 in TIL-CD8+ T cells, thus maintaining abundant PD1 expression.
Conclusions: TOX promotes CD8+ T cell exhaustion in HCC by regulating endocytic recycling of PD1. Down-regulating TOX expression in CD8+ T cells shows synergetic effects with anti-PD1 therapy, thus highlighting a promising strategy in cancer immunotherapy.

P-432

Microfluidic chip combined with magnetic-activated cell sorting technology for tumor antigen-independent sorting of circulating hepatocellular carcinoma cells

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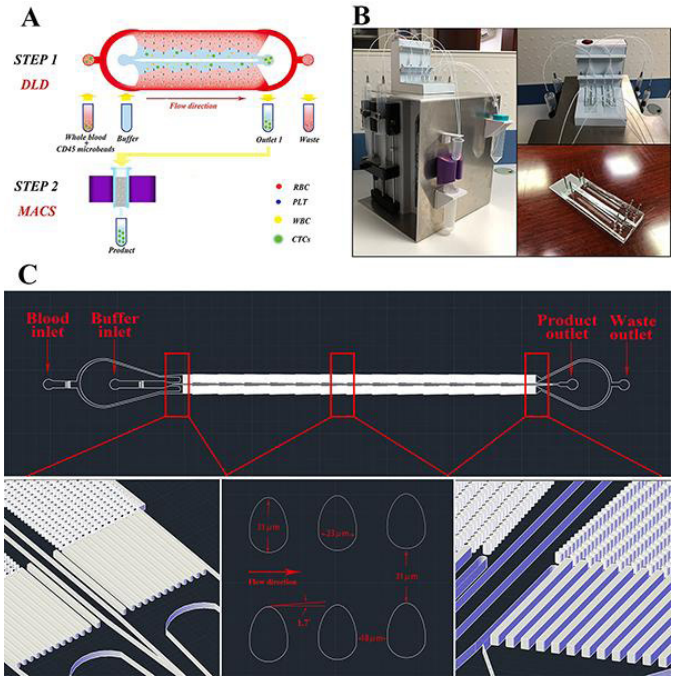
Purpose: We aimed to generate a capture platform integrates a deterministic lateral displacement (DLD) microfluidic structure with magnetic-activated cell sorting (MACS) technology for a miniaturized, low-cost, efficient, portable, high active and tumor antigen-independent circulating tumor cell (CTC) separation.
Methods: The microfluidic structure was based on the theory of DLD and designed to remove most of the red blood cells and platelets. Whole Blood CD45 microBeads and a magnetic-activated cell sorting separator were then used to remove bead-labeled white blood cells. We overexpressed green fluorescent protein in the human liver cancer cell line HEPG-2 by lentivirus for simulating CTCs in blood, which used to determine the CTC isolation efficiency and carry out stability testing of the device. To evaluate the performance and clinical value of our platform, Abnova CytoQuest™ CR was used for comparison for the processing of blood samples from 12 hepatocellular carcinoma patients undergoing liver transplantation

in a clinical follow-up experiment. The isolated cells were stained and analyzed with a laser scanning confocal microscopy.
Results: Using our integrated platform, at the best flow rate (specimen at 120 µl/min and buffer at 200 µl/min), we achieved depletion of white blood cells and an 86% yield of CTCs. In our follow-up of metastatic patients, CTCs that underwent epithelial mesenchymal transition were found. These CTCs were missed by the CytoQuest™ CR bulk processing approach, whereas our platform displayed increased sensitivity for CTCs with EpCAM^{low} expression.
Conclusions: Our platform, integrating the microfluidic structure with MACS technology, provides an attractive method for CTC isolation by enabling processing of large volumes of blood with high throughput and efficiency and can isolate CTCs regardless of tumor surface epitopes.



[(A) Platform schematic.(B) The overall system. (C) DLD device design.]

P-433

Living donor liver transplantation with two-stage hepatectomy for patients with isolated, irresectable colorectal liver metastases - the LIVER-T(W)O-HEAL STUDY

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Background: Colorectal cancer is the third most common malignancy worldwide. The occurrence of liver metastases worsens the prognosis of the patient significantly if the tumor burden is not resectable.
Liver transplantation might be an option for otherwise irresectable colorectal liver metastases. In this study, we evaluate the role of two-stage hepatectomy in combination with a left-lateral living donor liver transplantation.
Methods: Patients with irresectable liver metastases having a stable disease or tumor regression after at least eight weeks of systemic chemotherapy without an extrahepatic tumor burden (except resectable lung metastases) are suitable for study inclusion. A randomization is not planned since the control arm (systemic chemotherapy) is well established and the superiority of the transplantation procedure has to be expected.
The surgical treatment consists of two steps: in a first operation, a left hemihepatectomy in the recipient will be performed. At this place, the left-lateral liver lobe (segments II and III) of a living donor will be transplanted. To induce a growth of the graft, a (subtotal) portal vein ligation will be performed. Approximately after two weeks, the removal of the right hemiliver will conducted if the control imaging shows a sufficient growth of the graft.
Results: The patient recruitment is ongoing. There were already patients transplanted in both centers. In total, three patients have been already transplanted with this protocol. Up to now, they are tumor-free and in good clinical health.
Discussion: With the design of the LIVER-T(W)O-HEAL study, it might be possible to offer patients with otherwise irresectable colorectal liver metastases a curative treatment option. The key point of this study will be, most probably, the patient's selection.

P-434

Liver transplant outcomes for locally advanced intrahepatic cholangiocarcinoma are comparable to hilar cholangiocarcinoma within mayo criteria: a single center experience

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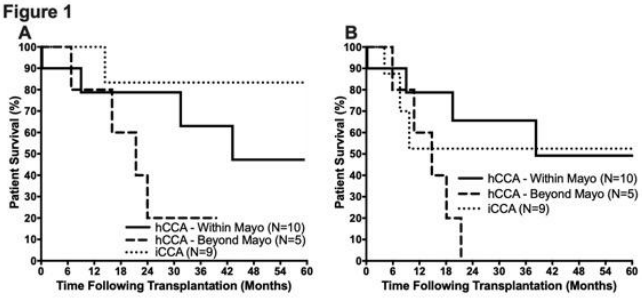
Introduction: In contrast to hilar cholangiocarcinoma (hCCA), Intrahepatic cholangiocarcinoma (iCCA) is considered a contraindication for liver transplantation (LT); however, we recently reported favorable outcomes for locally advanced iCCA with neoadjuvant therapy. This study compares LT outcomes for iCCA and hCCA based tumor size at transplant.
Methods: Pts without extrahepatic disease or vascular involvement underwent neoadjuvant chemotherapy and radiation (hCCA only). A minimum 6 mo of stability was required prior to LT.
Results: From 2010-2018, 24 pts (9 iCCA, 15 hCCA) underwent LT for CCA. Of hCCA, 5/15 (33%) were beyond Mayo; whereas, 100% iCCA were >3cm. Median iCCA cumulative diameter was 8.5cm and 5/9 (56%) were multifocal. For hCCA within Mayo, cumulative diameter was 11.7cm and 2/5 (40%) were multifocal, while cumulative diameter was 0.7cm and none were multifocal for hCCA beyond Mayo. Overall survival was 100%, 83%, and 83% at 1-, 3- and 5yrs for iCCA compared with 79%, 49%, and 49% for hCCA within Mayo (p=0.47), and 80%, 20%, and 20% for hCCA beyond Mayo (p=0.06)(**Figure 1A**). Recurrence free survival was 83%, 53%, and 53% for at 1-, 3- and 5yrs for iCCA compared with 79%, 49%, and 49% for hCCA within Mayo (p=0.81) and 60%, 0%, and 0% for hCCA beyond Mayo (p=0.29)(**Figure1B**). CCA reoccurred in 1/10 (10%) hCCA within Mayo compared with 4/5 (80%) hCCA beyond Mayo and 3/9 (33%) iCCA. Recurrence correlated with size and multifocality, for hCCA but not iCCA.

Figure 1



[Figure 1: Overall and recurrence free survival following LT for iCCA and hCCA beyond or within Mayo]

Conclusion: These data suggest comparable outcomes for LT locally advanced iCCA and hCAA within Mayo, while locally advanced hCCA beyond Mayo trend towards worse outcomes. Sustained response to neoadjuvant therapy rather than tumor size may represent reasonable selection criteria for LT for iCCA; whereas, LT should be avoided in patients with hCCA beyond Mayo.

P-435

Salvage versus primary living donor liver transplantation for hepatocellular carcinoma: good strategy for long-term survival but higher incidence of recurrence

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Background: Liver transplantation (LT) is able to completely remove malignant tumors and also cure underlying cirrhotic liver that renders a pathogenic environment for hepatocellular carcinoma (HCC) development. The study aimed to analyze the beneficial effect of liver transplantation for patients with HCC in an Asian country with a predominance of living donor liver transplantation (LDLT).
Methods: This is a retrospectively review of 289 patients who had been undergone LDLT for HCC between May 2005 and March 2017 in the transplantation institute of Chang Memorial Hospital at Linkou, Taiwan. The clinicopathological parameters of all patients were thoroughly assessed to determine beneficial factors for patients after LT.
Results: Overall, only 25 patients (8.7%) had HCC recurrence after LDLT in the institute. Univariate and multivariate analysis of clinical features showed that previous hepatectomy (Hazard ratio=3.810, *p*=0.008) is an independent risk factor for HCC recurrence after LT, indicating that salvage LT had an inferior outcome in terms of recurrence-free survival as compared with primary LT for HCC. However, the long-term outcome measured from the time of HCC diagnosed showed that patients with salvage LT had a better survival curve than that of patients with primary LT. Of that, the 5-year overall survival of patients were 89.1% for patients in the salvage LT group *versus* 73.5% for patients in primary LT group.
Conclusion: LDLT based on the expanded hepatocellular carcinoma criteria achieved a satisfactory result with very low incidence of HCC recurrence. Although salvage LT had a higher incidence of HCC recurrence after LT, it remains a promising strategy for improving patient's long-term outcome.

P-436

Correlation between classification of circulating tumor cells in peripheral blood and early recurrence in patients with hepatocellular carcinoma after liver transplantation

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Aims: To investigate the detection and subtype identification of circulating tumor cells (CTC) in peripheral blood of patients with hepatocellular carcinoma(HCC), and to analyze the correlation with early recurrence after liver transplantation.
Methods: A total of 25 recipients of liver transplantation for HCC were were enrolled in this study from January 2016 to January 2017. The CanPatrolTM CTC second generation capture technique combined with RNA in situ hybridization (RNA-ISH) was used to detect preoperative and postoperative peripheral blood CTC in patients undergoing liver transplantation.
Results: 22 patients were positive for peripheral blood CTC before transplantation. Univariate analysis showed that the total number of CTCs and the proportion of interstitial CTCs were closely related to the TNM stage of HCC and the degree of tumor differentiation. During follow-up, 8 of the 25 recipients relapsed (8 were positive for all CTCs, 7 of which were positive for interstitial CTC). The Cox risk ratio model showed that the number of interstitial CTCs could be used as an independent prognostic factor for predicting tumor recurrence after transplantation. The recurrence time of interstitial CTC≥1 was significantly earlier than that of interstitial CTCs (P< 0.05). The majority of CTC patients (19/25) had a decrease in the total number of CTCs after transplantation, but the proportion of peripheral blood CTC (6/8) in patients with postoperative tumor recurrence increased compared with the preoperative. Patients with an increased proportion of interstitial CTC after surgery had a shorter recurrence time than patients with decreased (or constant) proportion of interstitial CTC.
Conclusion: The preoperative high CTC or high interstitial CTC ratio and the increase of postoperative interstitial CTC ratio are prone to tumor recurrence and interstitial type. Interstitial CTC can be used as an independent indicator to determine the time of tumor recurrence after liver transplantation in patients with HCC.

P-437

Liver transplantation with treatments and primary liver transplantation for hepatocellular carcinoma: comparisons of long-term outcomes

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Background: This study aimed to evaluate long-term outcomes of liver transplantation (LT) with treatments and primary LT for hepatocellular carcinoma (HCC).
Method: This retrospective study included 920 patients who underwent LT for HCC between 2005 and 2015. Radiological response after treatment was evaluated with modified Response Evaluation Criteria In Solid Tumors measurements. Recurrence-free survival (RFS), overall survival (OS), and their associated factors were evaluated by using the Kaplan-Meier method, log-rank test, and Cox proportional hazard model.
Results: The RFS rates at 1-, 5-, and 10-years were 89.8%, 82.4% and 79.7% and the corresponding rates for OS were 93.6%, 83.1% and 80.2%, respectively. The RFS and OS rates of Organ Procurement and Transplantation Network (OPTN) T3 with successful downstaging were not significantly different from those with OPTN T2 without treatment (p=0.069 and p=0.295, respectively) and were significantly higher than those of OPTN T3 without treatment or with downstaging failure (all p≤0.029). In a multivariable analysis, independent predictors of HCC recurrence after LT were beyond the Milan criteria on imaging at LT (hazard ratio [HR], 7.03; 95% confidence interval [CI], 5.05-9.78; p< 0.001) and alpha-fetoprotein (AFP) ≥1000 ng/mL at LT (HR, 2.70; 95% CI, 1.79-4.06; p< 0.001). Beyond the Milan criteria on imaging at LT (HR, 3.60; 95% CI, 2.58-5.02; p< 0.001), AFP ≥1000 ng/mL at LT (HR, 2.59; 95% CI, 1.71-3.91; p< 0.001), and Model for End-Stage Liver Disease score (HR, 1.04; 95% CI, 1.02-1.06; p< 0.001) were independent predictors of OS after LT. OPTN T3 with downstaging failure had more aggressive tumor biology including worse tumor grades, microvascular invasion, and satellite nodule compared to those with successful downstaging (all p< 0.001).
Conclusion: OPTN T3 should undergo LT after successful downstaging. OPTN T3 with successful downstaging was associated with a low rate of HCC recurrence and excellent post-transplant survival.

P-438

Hepatitis C remains the main etiology of hepatocellular carcinoma among liver transplant recipients in the United States in the direct-acting antiviral era

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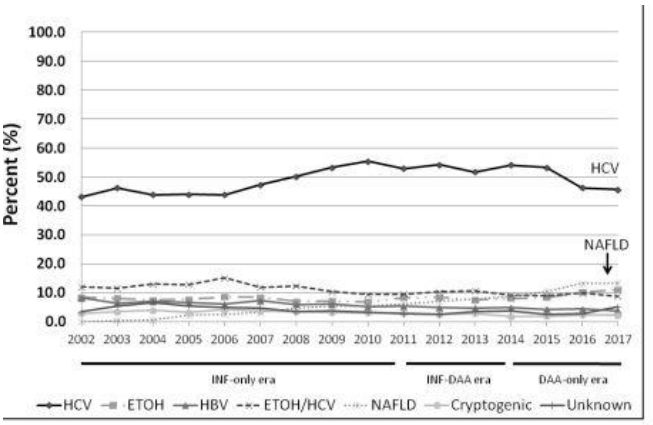
Background: Hepatocellular Carcinoma (HCC) remains one of the main indications for deceased donor liver transplant (DDLT) in the United States. Following the discovery of direct-acting antivirals (DDAs) we are now able to cure the majority of patients with Hepatitis C virus (HCV). We aimed to evaluate the etiologies of liver disease in DDLT recipients with HCC in recent years.
Methods: We evaluated the Scientific Registry of Transplant Recipients (SRTR) data from 1987 to September 2017 in adult DDLT recipients in the United States.
Results: Among 132,731 adult DDLT recipients, HCC was the indication for LT in 27,855 (21%) recipients. After implementation of MELD in 2002, the prevalence of HCC-related DDLT steadily increased from 5.3% in 2001 to 36.1% in 2015. In 2016, there was a slight decrease in the proportion of HCC-related LT to 30% that may be explained by the adjustment in MELD exception policy in 2015. There has been an overall 14.6% decrease in HCV cases (1.4% per/year), in the interferon-free DAA-era, from 2014 to 2016. However, HCV continues to be the most common etiology in 50% of the HCC cases in DAA-era (**Figure1**). There has been a steady increase in the proportion of NAFLD from 2014 (8.8%) to 2016 (13.2%), consistent with an overall 50% increase (16.7% increase per year). During the same time period, there has been a 26% increase in alcoholic liver disease (ALD) consistent with a 8.6% increase per year (**Figure1**).
Conclusion: HCC remains a major indication for DDLT in the US. Although there has been a slight decrease in HCV in HCC, HCV continues to be the most common etiology in half of HCC patients even in the DAA-era. There is a rising fraction of NAFLD and ALD in HCC-related LT recipients.



[Figure1. The trend of etiologies of liver disease in HCC-related liver transplant recipients.]

P-439

Clinical characteristics associated with HCC in African American patients

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Background: In United states, African-Americans (AA) have a higher incidence of hepatocellular carcinoma (HCC) and lower overall survival compared to Caucasians.Here we compared clinical characteristics of HCC in AA to those of Caucasians which may contribute to ethnicity dependent HCC outcomes over the last decade.
Method: Patients being treated for HCC at LSUHSC-Shreveport, an urban tertiary medical center from 2008 to 2018 were identified. Data was collected retrospectively and included demographics, comorbidities, liver disease characteristics and tumor parameters. Statistical comparisons were performed by Student's t-test.
Results: 240 cases of HCC were identified over 10 years: 188 (78%) male, with mean age at HCC diagnosis was 60.5 years. Compared to Caucasians (45.8%), AA patients (54.2%) were more likely to have diabetes (37 versus 18, $p< 0.05$), larger HCC size at diagnosis (5 versus 3.9 centimeters, $p< 0.05$) and higher AFP value (18723 versus

5744, p=0.05) at diagnosis. AA patients were marginally more likely to have HCV infection (113 versus 87, p=0.1). There was no statistically significant difference in both the groups regarding age, BMI, MELD scores, smoking status, single versus multiple liver lesions at diagnosis or rates of associated portal vein thrombosis. Etiology of cirrhosis for the whole group was HCV in 44.3% followed by combined HCV/alcohol use in 35.1% followed by other causes. **Conclusion:** We conclude that AA patients with HCC have significantly larger HCC lesion size, higher AFP values and increased incidence of modifiable metabolic risk factor like diabetes on diagnosis, than Caucasian patients even though they had similar BMI, MELD scores and rates of portal vein thrombosis. These factors represent important new indices which should be considered in screening HCC in AA.

P-440

Downstaging of hepatocellular carcinoma with Yttrium-90 radioembolization prior to Liver transplantation

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Background: Liver transplantation (LT) is a well-established procedure for hepatocellular carcinoma (HCC) within the Milan criteria. Yttrium-90 microspheres radioembolization (Y90-RE) has shown to be an effective and safe treatment of primary liver tumors. We retrospectively evaluate the efficacy of the Y90-RE as downstaging tool in patients with HCC beyond Milan criteria. **Methods:** From January 2002 to August 2018, 450 patients were transplanted at the San Camillo Hospital Center. One-hundred-ninety-eight patients were transplanted for HCC, and in 31 cases the patients were treated with Y90-RE before LT. **Results:** Ten patients were treated with Y90-RE within the Milan criteria, and 21 patients were out of criteria before Y90-RE. Eight patients had macrovascular invasion. Sixteen patients had an increasing MELD score between Y90-RE and LT. On the other hand, alpha-fetoprotein decreases after Y90-RE treatment in all cases. No patient death was observed in Y90-RE procedure or at LT. Among the patients in the downstaging group (DG), 12 patients (57%) had a complete response (CR) and 9 (43%) a partial (PR) according the RECIST criteria. No patients had progression. All patients with macrovascular invasion had regression of tumoral vascular extension. Nine patients in the DG underwent to a combined approach with a surgical resection (6 open hepatic resection and 3 laparoscopic). In the bridging group (BG), bridging was achieved in 100 % of cases. From LT, overall mean survival was 46,4 months (40 for the DG and 58,8 for the BG). After LT, 7 patients (all in the DG) developed a recurrence with a median free survival of 29.6 months: 3 patients are dead and 4 are alive with treated recurrence. **Conclusions:** We successfully performed LT after downstaging with Y90-RE.Y90-RE has specific roles in inducing contralateral lobe hypertrophy and in downstaging to liver transplantation also for infiltrative HCC with macrovascular invasion.

P-441

Directly acting antivirals causing increased incidence of HCC: Is it a myth or are we equipped with a double edged sword?

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Background: Directly acting antivirals (DAA) have brought about a paradigm shift in the management of Hepatitis C (HCV) infections. However, some studies have raised concerns about DAA use being associated with increased incidence of hepatocellular carcinoma (HCC). We did a retrospective analysis and timeline review of patients who underwent Liver transplantation (LT) for hepatitis C related chronic liver disease (CLD) and compared their trend with those of hepatitis B (HBV) and NASH related CLD patients. **Method:** Study was conducted on 1646 patients who underwent LT for HCV(n=859), HBV(n=337) and NASH(n=450) related cirrhosis from February 2007 to October 2018. We divided the timeline in two eras (eraA and eraB, before and after 2015) based on the availability of DAA in South Asian countries. Observations were recorded as, number of patients undergoing LT, the MELD score and incidence of HCC reported on histopathlogical examination (HPE) of explanted liver. Observations were further compared using Fisher's exact test. **Results:** Patients undergoing LT for HCV related cirrhosis reduced from 590 in eraA to 269 in eraB (p=0.0008). However incidence of HCC showed a significant rise in HPE of patients included in eraB (p=0.02). Mean MELD scores (excluding exception criteria) also showed difference in patients with HCV related CLD between eraA and eraB 18.03 v/s16.59 (p=0.06). No such differences were observed in patients undergoing LT for HBV and NASH related CLD. **Conclusion:** Patients undergoing LT for HCV related CLD has reduced after 2015. DAAs may have also reduced the episodes of decompensation in HCV related CLD patients as reflected by lower MELD scores. However more patients with HCV related CLD showed HCC on their histopathological examination in recent years, whether this can be attributed to DAA use requires further prospective trials.

P-442

Sequential delivery of multi-prodrugs for synchronous intracellular anti-tumor effect in HCC

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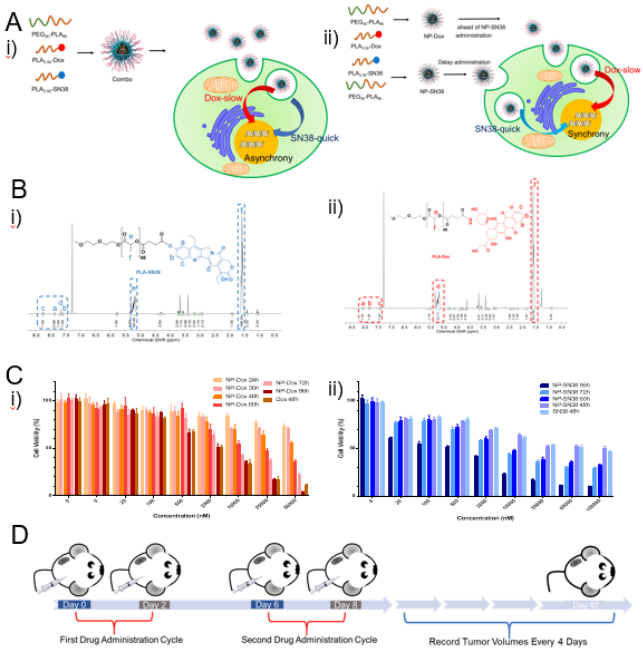
Hepatocellular carcinoma (HCC) liver transplantation accounts for 30%-45% of the total annual liver transplantation worldwide. However, recurrence of HCC after liver transplantation has always been a disturbing problem. Recurrent HCCs are often difficult to resect, and drug resistance is widespread. More imopotantly,recurrence of tumors may involve other important organs, such as lung and brain. Multidrug combination is a trendy strategy to inhibit tumor recurrence, growth and metastasis. 7-Ethyl-10-hydroxycamptothecin (SN38) and Doxorubicin (Dox) achieve in vivo long circulation and tumor targeting through the strategy of prodrug modification. Furthermore, SN38 prodrug and Dox prodrug are administrated at different time due to their different release efficience. we find the sequential prodrug delivery strategy is efficient in vitro and in vivo. The tumor inhibit rate is enhanced to 70% compared with CPT-11 and dox free drug combination, only 25%. Patient-Derived tumor Xenograft (PDX) is also used for testing the effectiveness of our drug deliver strategy and achieves good results.



[Illustration for Sequential Delivery of Multi-prodrugs.]

P-443

Metroticket 2.0 validation in an Australian liver transplant cohort

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Background: Predicting the prognosis of patients with hepatocellular carcinoma (HCC) who undergo liver transplant (LT) is complex. The Metroticket 2.0 model (1) was derived to predict HCC-specific survival using radiological tumour characteristics and alfa-fetoprotein (AFP). We aimed to evaluate this model in an Australian context.
Methods: All adult patients diagnosed with HCC between 1st January 1998 and 3rd June 2013 who later underwent cadaveric LT at a quaternary referral centre were included. The outcome was HCC-specific survival at 5-years. Prognostic scoring systems including Milan, UCSF and Milan "up-to-7" criteria were compared with the Metroticket model for predicting five-year HCC-specific survival.
Results: 197 patients were included. Hepatitis C was the most common cause of underlying liver disease (59%). Locoregional therapy before LT was undertaken in 124 (63%) patients. Prior to LT, 188/197 (95%) were within Milan criteria, 191/197 (97%) within Metroticket criteria, 190/197 within UCSF criteria (96%) and 195/197 (99%) were within Milan "up-to-7" criteria. Sixty-eight (33%) patients died during a median post LT follow-up of 7 (IQR 4.2- 11.2) years, with 13 (6%) due to HCC recurrence. 5-year overall survival was 75% and 5-year HCC specific survival was 94%.The calculated Metroticket median predicted 5-year HCC-specific survival was 95% (IQR 92-98%) (Figure 1). The sensitivity and specificity for predicting survival were respectively: Metroticket criteria; 98% and 17%, Milan criteria; 96% and 17%, UCSF criteria; 97% and 17%. The positive and negative predictive values were respectively: Metroticket criteria; 95% and 33%, Milan criteria 95% 22%, UCSF criteria 95% and 28%.
Conclusions: In a single-centre Australian LT cohort where most patients were within Milan criteria at transplant, the Metroticket 2.0 predicted HCC-specific survival is similar to observed data. The Metroticket model has better sensitivity and negative predictive values for HCC-specific survival compared with conventional scoring systems.

P-444

Improved survival in patients with hepatocellular carcinoma with a combined treatment strategy in bridge to liver transplantation: an intention-to-treat-study

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Introduction: Liver transplantation (LT) is the best curative treatment for liver-only hepatocellular carcinoma (HCC). Patients with a compensated liver disease can wait as long as 18-24 months on the waiting list. A treatment in bridge to transplantation is necessary to control the evolution of HCC.
Method: Patients inscribed on the LT waiting list between january 2011 and december 2014, and having an HCC were reviewed. Analysis were conducted in intention-to-treat. All HCC treatments before LT were studied. 3 groups were defined : untreated patients, unique treatment, and combined treatments(more than one neoadjuvant therapy). The primary study endpoint was overall survival (OS) after treatment. Recurrence-free survival (RFS) and OS after LT were studied. Risk factors for waiting list drop-out and RFS after LT were studied in univariate and multivariate analysis.
Results: 168 patients were included in this study, of which 120 were transplanted. Treated patients had a significantly better liver function than untreated patients according to MELD and Child-Pugh scores (p< 0.001). Patients with a combined treatment had an improved OS after initial treatment when compared to either the unique treatment group (p=0.047) or to the other two groups together (p=0.037). RFS and OS after LT were not significantly different between the groups. Tumor dowstaging on pre-LT imaging was the only independent predictor for not being dropped out of the list in multivariate analysis. A high alpha-fetoprotein score at the time of transplantation was the only independent prognostic factor for worse RFS after LT (p=0.034).
Conclusion: This retrospective intention-to-treat study shows that combined treatment improves OS after initial treatment. Downstaging before LT is a predictive factor for recurrence. A high alpha-fetoprotein score is a risk factor for recurrence after transplantation.

P-445

Living donor liver transplantation for advanced hepatocellular carcinoma with portal vein tumor thrombosis after concurrent chemoradiation therapy

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Locally advanced hepatocellular carcinoma (HCC) with portal vein thrombosis carries a 1-year survival rate < 10%. Localized concurrent chemoradiotherapy (CCRT), followed by hepatic arterial infusion chemotherapy (HAIC), was recently introduced in this setting. Here, we report our early experience with living donor liver transplantation (LDLT) in such patients after successful down-staging of HCC through CCRT and HAIC. Between December 2011 and December 2017, nineteen patients with locally advanced HCC with portal vein tumor thrombosis (PVTT) at initial diagnosis were given CCRT, followed by HAIC, and underwent LDLT at the Severance Hospital, Seoul, Korea. CCRT [45 Gy over 5 weeks with 5-fluorouracil (5-FU) as HAIC] was followed by HAIC (5-FU/cisplatin combination every 4 weeks for 3-12 months), adjusted for tumor response. . The 1-year overall survival and disease-free survival rate were 90.9% and 87.5%, respectively. The 3-year overall survival and disease-free survival rate were 72.7% and 49.0 %, respectively. There were eight instances of post-transplantation tumor recurrence during follow-up monitoring (median, 46 months; range, 1-72 months) Median survival time from initial diagnosis was 33 months (range 11-110 months). Using an intensive tumor down-staging protocol of CCRT followed by HAIC, LDLT may be a therapeutic option for selected patients with locally advanced HCC and portal vein tumor thrombosis.

P-446

MicroRNA200a enhanced antitumor effects in combination with doxorubicin in hepatocellular carcinoma

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Background: The inflammatory reaction in hepatocellular carcinoma (HCC) tumor microenvironment correlates with recurrence and poor prognosis after liver resection surgery. MicroRNA-200a (miR-200a) negatively regulates epithelial-mesenchymal transition and promotes immunomodulatory function in tumors. However, the effects of miR-200a in response to HCC tumors undergoing chemotherapy are unknown. Here, we investigated the effects of miR-200a on tumor cell growth, autophagy, mitochondria metabolism and promoting polarization of macrophages in HCC tumor cells treated with doxorubicin.
Method: qPCR for miR-200a were performed in tumor and liver tissues from patients with HCC. Proliferation assay (CCK8) and half-inhibitory concentration were employed in Huh-7 and HepG2 cells with doxorubicin or not. We stably upregulated miR-200a in Huh-7 and HepG2 cells using lentivirus transduction, and down-regulated miR200a using shRNA targeting endogenous miR200a. Effect of miR-200a on cells growth, autophagy, mitochondria metabolism with or without doxorubicin treatment was differentiated. Culture medium from tumor cells was collected to treat macrophages derived from THP-1. The effects of superanant from induced macrophage on HCC cells was defined with doxorubicin or not.
Results: MiR-200a level in HCC tissues was lower than the adjacent non-tumor tissues (P < 0.01). Human liver tumor cells were successfully transfected with Lv-miR-200a, and shRNA targeting miR-200a (Lv-anti-miR-200a) silenced miR-200a expression. MiR-200a expression was negatively associated with tumor differentiation and liver fibrosis (P =0.030; P =0.032). Lentiviral miR-200a over-expression significantly inhibited HCC cell proliferation and reduced the IC50 value of doxorubicin, while inhibition of endogenous miR200a had the opposite effect. Over-expression of miR-200a increased autophagy, decreased glycolysis, induced anti-tumor differentiation of macrophages and synchronized with doxorubicin, this was reverted with silencing endogenic miR-200a .
Conclusion: MiR-200a strengthened the anti-tumor effects of doxorubicin in HCC cell, which might through up-regulating autophagy levels, inhibiting mitochondria function and induced macrophages anti-tumor function.

P-447

Risk factors for waitlist drop-out among patients with exception points due to unresectable HCC in a large volume liver transplantation unit in Brazil

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Background: Even though exception points may facilitate the access to liver transplantation (LTx) among candidates with unresectable hepatocellular carcinoma (HCC), waitlist drop-out is still prevalent in this subgroup. We sought to identify independent predictors of this outcome in this subgroup.
Methods: Single-center retrospective study with a prospectively collected database between 2006 and 2015. Patients with preoperative diagnosis of HCC listed for deceased-donor LTx with exception points within the Milan-BR criteria were selected. Risk factors for watilist drop-out were identified through univariate and multivariate analysis.
Results: 414 LTx candidates were included. The drop-out rates in 3, 6 and 12 months were 8.9%, 15.7% and 24.1%. On the univariate analysis, patients who were removed from the waitlist were older (*p* 0.015), with a higher frequency of cryptogenic cirrhosis (*p* 0.001), with higher levels of serum alpha-fetoprotein (*p* 0.001), and presented with more frequent progressive disease according to the mRECIST after bridge therapy wtih transarterial chemoembolization (*p* 0.000), whereas blood type B seemed to protected against this adverse outcome (*p* 0.008). Among the selected variables, only progressive disase after bridge therapy with transarterial chemoembolization was identified as an independent predictor of waitlist drop-out [HR 7.9 (CI95% 4.77-13.09), *p* 0.000].
Conclusions: Waitlist drop-out is frequent among LTx candidates with unresectable HCC, affecting up to 24.1% of our patients one year after inclusion on the waiting list. Among the studied variables, poor response to bridge therapy after transarterial chemoembolization was identified as an independent risk factor for this outcome. This may be considered as a surrogate marker of aggressiveness. Possibly, individuals who responde poorly to this form of bridge therapy should be considered for multimodal treatment.

P-448

Expression profile analysis of circular RNAs in early recurrence of hepatocellular carcinoma

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Background: Hepatocellular carcinoma (HCC) is one of the most common cancers all over the world with high recurrence rate. Circular RNAs (CircRNAs) have been shown to play an important role in tumor biology. However, the contributions of circRNAs to early recurrence of HCC remain largely unknown.
Methods: We detected the differential expression of circRNAs in 3 early recurrence HCC tissues and 3 non-early recurrence HCC tissues utilizing RNA sequencing. Gene Genomes (GO) analysis was further

performed on circRNA host genes.
Results: A total of 43 circRNAs were identified differentially expressed between early recurrence HCC tissues and non-early recurrence HCC tissues. GO analysis demonstrated that most of the circRNA host genes were associated with cell migration, cytoskeleton and actin binding.
Conclusion: Differential expression of circRNAs were observed in early/non-early recurrence of HCC. Our study may provide the potential diagnostic biomarkers and therapeutic targets for early recurrence of HCC.

P-449

Narrow margin and even R1 resection for hepatocellular carcinoma do not impact on the salvage liver transplantation strategy on an intent-to-treat basis

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Background and aims: Hepatectomy for hepatocellular carcinoma (HCC) should be planned in patients with tumor that is potentially amenable to a R0 resection. In clinical practice, intraoperative decision for so-called narrow margin by necessity may be required in case of proximity with major vasculo-biliary structures. The objective of this study was to assess on an intent-to-treat (ITT) basis whether by necessity primary hepatectomy with narrow margin affects the short- and long-term outcomes in patients enrolled in the salvage liver transplantation (LT) strategy.
Method: From 2007 to 2016, patients enrolled in the salvage LT strategy were divided into 2 groups: narrow (< 10 mm) vs. wide (≥ 10 mm) resection margin groups. R1 resection was defined as positive histologic margin involvement.
Short-term outcomes, recurrence rate, transplantability rate of recurrence and ITT overall survival (ITT-OS) were evaluated.
Results: A total of 81 patients were studied: 43 patients with narrow margin and 38 with wide margin. The mortality and morbidity, recurrence rates, pattern and delay of recurrence, transplantability following recurrence, and ITT-OS were similar between the two groups. These results were maintained when comparing patients with R1 resection to those with R0 resection.
Conclusion: On an ITT basis, hepatectomy with narrow margin or R1 resection did not impair short-term outcomes and, more importantly, the transplantability of recurrence and survival of patients enrolled in the salvage LT strategy. Narrow margin and even R1 resection by necessity following hepatectomy in the setting of salvage LT strategy should not be the basis for altering the strategy.

P-450

While tumour FDG-18 PET avidity is a good prognostic marker for recurrence post-LDLT in NAFLD/NASH patients with HCC, alpha fetoprotein is not

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Introduction: With the obesity epidemic spreading worldwide, non alcoholic fatty liver disease (NAFLD) and non alcoholic steatohepatitis (NASH),have emerged as prime etiologies for cirrhosis in hepatocellular carcinoma (HCC) patients.
Methods: We analysed epidemiology, pathology, outcomes of HCC patients with NAFLD/NASH undergoing living donor liver transplantation (LDLT) at our center. Recipients were labeled as NAFLD/NASH based on presence of steatosis/steatohepatitis on histopathology, or presence of ≥3 of: serum triglycerides>150 mg/dl or high density lipoprotein < 40 in males/< 50 mg/dl in females; diabetes mellitus (DM) or FBSL>100 mg/dl;hypertension (HT);BMI >25 kg/m^2. We accept all patients with HCC irrespective of tumour size or number for LDLT, provided there is no extrahepatic disease or macrovascular invasion.
Results: Of 446 HCC patients (pathology proven) undergoing LDLT (2004-2017), 43(9.6%) had NAFLD/NASH. Forty were males, mean age was 58±8 years, 26 had DM,15 had HT. 60% had tumours beyond Milan, 49% beyond UCSF criteria. Mean pre-LT AFP level was 161±614 ng/ml (only 20 [46.5%] had raised AFP levels).The 5-yr OS/RFS post LDLT were 75%/73%. After a 43 month median follow (range 1-129 months), 10(23%) developed HCC recurrence (similar to our overall series recurrence rate of 19%,p=0.53), 7 of them died. In our overall series, the 4 prognostic factors for OS/RFS were beyond UCSF criteria, tumour FDG-18 PET avidity, microvascular invasion, AFP ≥200 ng/ml. Of 10 NAFLD/NASH HCC patients who recurred, 6 had tumours beyond UCSF, 9 had FDG avid tumours, 9 showed microvascular invasion (MVI), all had AFP levels < 200 ng/ml. The most common site of recurrence was the liver (contrary to lungs, in our overall series). Tumour FDG-18 PET avidity was the only prognostic factor for both, OS (p=0.01) and RFS (p=0.007).
Conclusion: Tumour FDG-18 PET avidity is a good prognostic marker in HCC patients with NAFLD/NASH cirrhosis. Contrary to other etiologies, pre-LT AFP level is not.

P-451

Outcomes of liver transplantation for hepatocellular carcinoma in septuagenarians

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Background: The impact of advanced age on liver transplantation (LT) for hepatocellular carcinoma (HCC) has not been well studied. We sought to compare post-OLT survival and tumor recurrence outcomes of patients older than 70 to younger patients.
Methods: This is a single-center retrospective cohort study of all consecutive patients with HCC treated with LT between 1998 and 2018. Patient and tumor characteristics as well as post-LT survival and oncologic outcomes were compared among patients older and younger than 70 years.
Results: A total of 45 patients >70 years were identified and their outcomes compared to 588 patients < 70 years. The median follow-up duration for the cohort was 54 months (IQR 23-103). Baseline, preoperative and tumor characteristics were comparable among the two age groups. Post-LT outcomes were not significantly different between age groups. Patients >70 and < 70 had comparable 5-year survival rates of 67 and 71% (p=0.349) respectively and 5-year recurrence-free survival rates of 78 and 86% (p=0.581). Finally, the time to recurrence was not significantly different in the two groups with a median of 13 (IQR 7 - 31) for patients < 70 and 25 months (IQR 16 - 42) for those >70 (p=0.151).
Conclusion: Advanced age is not associated with worse survival or tumor recurrence outcomes. Selected patients older than 70 should have a fair evaluation for LT for HCC without age being a deciding exclusion factor.

Table 1: Comparison of baseline and tumor characteristics in patients >70 and <70 years.

	Age >70 (n=45)	Age <70 (n=588)	*P* value
Baseline characteristics			
Age, years	71.6 (70.7 – 72.6)	59.6 (53.8 – 63.9)	<0.001
Gender, male	73%	79%	0.453
BMI, kg/m²	27 (25 – 30)	27 (25 – 31)	0.666
ESLD etiology			0.065
HCV	53%	64%	
HBV	9%	12%	
NASH	20%	7%	
Alcohol	11%	9%	
Other	7%	8%	
Lab MELD at Tx	11 (9 – 15)	13 (9 -18)	0.288
Match MELD at Tx	25 (22 – 28)	25 (22 – 29)	0.706
AFP at Tx	8 (4 – 18)	12 (6 – 34)	0.060
Max preTx AFP	18 (6 – 60)	24 (9 – 107)	0.181
Radiological tumor characteristics			
Number of tumors			0.074
0	0%	9%	
1	51%	49%	
2	20%	22%	
3	16%	8%	
≥4	13%	12%	
Largest tumor size, cm	2.8 (2 – 4)	2.5 (1.5 – 3.8)	0.079
Total tumor size, cm	3.7 (2.4 – 6.5)	3.1 (1.9 – 5.3)	0.094
Bilobar tumor	7%	13%	0.334
Within Milan Criteria	86%	79%	0.323
Pathologic tumor characteristics			
Grade			0.119
Unknown	3%	14%	
1	8%	8%	
2	47%	32%	
3	32%	27%	
4	11%	19%	
Macrovascular invasion	4%	3%	0.648
Microvascular invasion	19%	28%	0.268
Lymphatic invasion	3%	7%	0.483
Bilobar	18%	20%	0.844

Data reported as % or Median (IQR)

Figure 1: Kaplan-Meier Survival Analysis of OS in patients >70 and <70 years

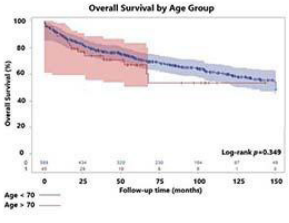
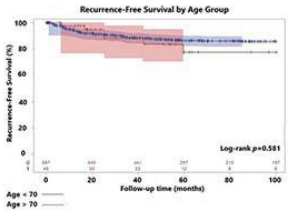


Figure 2: Kaplan-Meier Survival Analysis of RFS in patients >70 and <70 years.



[Images]

P-452

Does meeting the Milan Criteria at the time of recurrence of hepatocellular carcinoma after curative resection have an impact on pprognosis?

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Background: The survival outcomes of recurrent hepatocellular carcinoma (HCC) after curative resection remains unclear due to lack of clear basis for the selection of treatment option.We investigated overall survival (OS) after intrahepatic recurrence and re-recurrence free survival (rRFS) of the patients with recurrent HCC, and whether Milan Criteria (MC) status at resection and recurrence impacts on OS and rRFS.
Method: We enrolled 959 patients who experienced recurrence after primary hepatic resection for HCC. We divided the cohort into four groups according to MC at two periods: IN-rIN MC (within MC at resection-recurrence within MC), IN-rOUT MC (within MC at resection-recurrence out of MC), OUT-rIN MC, and OUT-rOUT MC.
Results: In the entire cohort, 1-, 3-, 5-year OSafter recurrence was 81.0%, 55.7%, and 45.8%, respectively, while rRFS was 63.7%, 46.1%, and 42.0%, respectively. The IN-rIN MC group had the best outcomes (5-year OS and rRFS, 54.5% and 45.7%, respectively). The IN-rOUT and OUT-rIN MC groups had better 5-year OS outcomes than the OUT-rOUT MC group (46.5%, 38.6%, and 24.8%, respectively [P< 0.05]). However, 5-year rRFS did not differ among the three groups (37.5%, 36.6%, and 31.9%, respectively [P>0.05]).
Conclusion: Survival after first recurrence following curative primary resection for HCC was affected by MC at the both time of resection and recurrence. Both the IN-rOUT and OUT-rIN MC groups with similar survival outcomes, can be saved via curative treatment.

P-453

The receptor tyrosine kinase-like orphan receptor 1 inhibits human cholangiocarcinoma progression by promoting nuclear localization of β-catenin

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Background: The receptor tyrosine kinase-like orphan receptor 1 (ROR1) is a transmembrane receptor tyrosine kinase (RTK) of vital importance during normal embryonic and fetal development, but is not expressed in most mature tissues.
Methods: The expression of ROR1 was detected by qRT-PCR and western blot analysis in human intrahepatic cholangiocarcinoma cells (ICC) and tissues. The ICC cells were transfected with ROR1 lentiviral expression vector for silence (9810, HuCCT1) and overexpression (CCLP1, RBE). The abilities of cells invasion and migration were detected by transwell assay. The expression of ROR1 and EMT-associated markers were analyzed by western blot. The nude model of subcutaneous xenograft and pulmonary colonization were established to observe its effect on tumor proliferation and metastasis. We used mass spectrometry analysis and coimmunoprecipitation to screen and identify the proteins which interact with ROR1.
Results: ROR1 was highly expressed in human ICC cells and tissues. It was negatively correlated with the prognosis of patients and closely related to tumor proliferation and metastasis. Knockdown of ROR1 strongly inhibited proliferation, invasion and migration characteristics of ICC cells, whereas the result was contrary when ROR1 was overexpressed. Western blot demonstrated that the expression of epithelial marker E-cadherin was increased but the mesenchymal makers N-cadherin and Vimentin were decreased when ROR1 was silenced. Meanwhile, knockdown of ROR1 significantly increased the nuclear entry of β-catenin. In vivo experiments, knockdown of ROR1 significantly weakened the ability of subcutaneous tumor-forming and reduced the lung colonization. Mass spectrometry and coimmunoprecipitation confirmed that ROR1 was closely related to receptor-mediated endocytosis and cytoskeleton.
Conclusion: These results establish ROR1 as a key biomarker that regulates cholangiocarcinogenesis and metastasis. It provides a new theoretical basis and therapeutic target for the diagnosis and treatment of human intrahepatic cholangiocarcinoma.

P-454

Retrospective comparison of the safety and efficacy of selective internal radiation therapy (with yttrium-90 microspheres) versus transarterial chemoembolization as first-line treatment for intermediate stage HCC

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Background: There is little data comparing treatments for intermediate stage hepatocellular carcinoma (HCC). This study compares transarterial chemoembolization (TACE) vs. yttrium-90 microspheres (Y-90) as first-line therapy in patients with intermediate stage HCC
Methods: The electronic medical records of patients from two liver transplant centers undergoing either TACE or SIRT for initial treatment of HCC were retrospectively reviewed. Inclusion criteria were age greater than 21 years, HCC meeting criteria for LI-RADS 5 and/or OPTN 5, at least one lesion>2.5 cm, Child Pugh A-B, total bilirubin< 3.5 and ECOG status 0-2. All included subjects met one or more of the following endpoints: 3 months follow up, transplant, and/or death. Exclusion criteria were prior treatment of HCC, vascular invasion, metastatic disease, and/or active alcohol use.
Results: Between 2013 to 2017, 68 underwent TACE and 31 underwent Y-90 as initial treatment. Median follow-up from first treatment to most recent follow-up was 73.47 vs. 41.20 months respectively. There was no difference at baseline between age, sex, MELD, Childs-Pugh score, and ECOG status. HCV was the predominant etiology in both cohorts. The distribution of lesions (38.2% vs. 40.7% multifocal disease) and median size of the largest lesion were also similar (3.2 vs. 4.3 cm).
Outcomes comparing Y-90 vs TACE: Overall survival was comparable in both initial treatment groups (Figure 1). Presence of vascular invasion (17.6% vs. 9.7.8%) and metastasis (8.8% vs. 3.2%) were similar. 43.4 percent of TACE patients were successfully transplanted vs. 12.9 percent in the Y-90 group; however, a significantly higher proportion of the TACE group was listed for OLT (55.9% vs. 9.7%).
Conclusion: TACE and Y-90 are both efficacious and safe therapies for treatment of HCC. Preliminary data suggests that outcomes may be similar and further study is ongoing to characterize initial treatment modalities of intermediate HCC.

P-455

Living donor liver transplantation for hepatocellular carcinoma: Shifting paradigm from poor to favorable prognostic factors

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Background: Various extended criteria (EC) have been proposed to expand the pool of transplantable HCC patients beyond Milan criteria (MC). Comparable outcomes in EC HCC patients have been shown after controlling for various poor prognostic factors. We hypothesized that presence of certain unequivocal favorable prognostic factor (FPF) can assist generous selection of HCC

patients for transplantation without compromising outcomes.
Methods: We included 117 patients transplanted for HCC between April 2012 and May 2017. Four pre-transplant FPFs with 5 year recurrence free survival (RFS) ≥ 90% were identified; 1) Tumor size ≤ 4 cm (RFS= 93%), 2) Well/Moderate differentiated HCC (RFS= 95%), 3) AFP ≤ 40 ng/ml (RFS= 97%) and 4) >50% response to TACE (RFS= 100%). Cox regression was performed to identify independent predictors of RFS. Patients were then grouped based on number of FPFs.
Results: Multivariate analysis identified tumor size ≤ 4 cm, well/moderately differentiated tumors and AFP ≤ 40 ng/ml as FPFs. In patients with one FPF (N=17), 10/17(58.8%) were EC patients, 12(70.5%) had poor differentiation, 7(41.1%) had MVI and 3 (17.6%)had AFP >40 ng/ml (max=1906 ng/ml). Patients with one (N=17), two(N=47) and three(N=46)FPFs had 5 year RFS of 86%, 92% and 98% (P < 0.0001). Patients without any FPFs had a 3 year RFS of 14%. With the current model, more patients were transplanted when compared with MC(32.1%), UCSF criteria (21.9%), Metro Ticket 1 (MT 1)(15.6%), Metro ticket 2 (MT 2)(33.7%), Toronto criteria (TC) (5.7%) and Hangzhou criteria (7.7%); without any significant difference in RFS i.e. MC (93% vs 92%) (P=0.7), UCSF criteria (92% vs 95%)(P=0.7), MT 1 (93% vs 93%) (P=0.9), MT 2(94% vs 89%) (P=0.2), TC (92% vs 100%)(P=0.5) and Hangzhou criteria (93% vs 88%) (P=0.5).
Conclusion: With the current model, the transplantable HCC pool can be substantially increased without compromising recurrence free survival.

P-456

Preoperative risk stratification for recurrence of negative-AFP hepatocellular carcinoma after liver transplanation

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Aim: To assess the outcomes of patients with negative-AFP hepatocellular carcinoma (HCC)after liver transplantation (LT) and to identify risk factors for early and late recurrence.
Methods: Retrospective analysis of 739 adult patients with HCC who had undergone LT between 2008 to 2018 at our institute, were divided into negative-AFP group(n=310) and positive-AFP group(n=429) depending on preoperative serum level of AFP (cut off 20 ng/mL). Preoperative radiological selection criteria were assessed. Pre-LT risk factors and post-LT outcomes were compared between groups. Predictors of early and late recurrence were evaluated.
Results: Negative-AFP HCCs patients had lower recurrence rates at 1-year (26% vs 42%, HR:1.70 ; 95%CI:1.24-2.34, p< 0.001), at 2- year (37% vs 62%, HR:1.73 ; 95%CI:1.30-2.30, p< 0.001) and at 5-year (61% vs 75 %, HR:1.67; 95%CI:1.27-2.19, p< 0.001).The recurrence probabilities were lower significantly (p< 0.001) in patients with negative-AFP and within Milan than patients with positive-AFP beyond Milan at 1- year (8%vs 60%), 2-year (13%vs 81%) and 5-year(29%vs99%). Predictors of early recurrence(within 2 years) for negative-AFP-HCCs patients were age >40 (HR: 0.44;95%CI:0.25- 0.79,P=0.012); MELD >25 (HR:1.99; 95%CI:1.11-3.58,p= 0.032); macrovascular invasion (HR:3.92; 95%CI:2.4-6.35; p< 0.001); largest nodule diameter (HR:1.12; 95%CI:1.07-1.17,p< 0.001);total tumor diameter (HR:1.13; 95%CI:1.08-1.17,p< 0.001),nodule number >3 (HR:1.60; 95%CI:1.08-2.37; P =0.024). Characteristics of both groups were similar but older age, smaller largest nodule diameters, lesser macrovascular invasion were found in the negative-AFP HCCs group.
Conclusion: Based on preoperative assessment, 42% of total HCCs patients were negative-AFP HCC with lower probabilities for early and late recurrence at 1, 2, 5-year compared with patients with positive-AFP-HCCs. Early recurrence predictors of negative-AFP-HCCs were age >40; MELD >25; macrovascular invasion; largest nodule diameter; total tumor diameter, nodule number >3. Preoperative risk stratification based on AFP cut off 20ng/mL with inclusion other predictors to selection criteria may improve the allocation of patients for liver transplanation.

P-457

WTAP promotes tumor progression through repressing ETS1 in a m6A-mediated modification in hepatocellular carcinoma

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Background: Epigenetic modification frequently participated in human carcinogenesis. N6-methyladenosine (m6A), the most abundant chemical modification of eukaryotic mRNA, was involved in plenty of tumors. The classical “writers” of N6-Methyladenosine comprised of METTL3, METTL14 and WTAP. It has been reported that METTL3 and METTL14 play significant roles in human hepatocellular carcinoma (HCC), while the effect of WTAP, without methyltransferase activity, has not been systematically identified. The study aims to demonstrate the involvement of WTAP in the progress of HCC.
Methods: qRT-PCR, Western bolt and immunohistochemistry (IHC) assay were utilized to examine the expression of WTAP in HCC cell lines. siRNA and shRNA targeted to WTAP were transfected

into several HCC cells to find out the influence of WTAP towards biological behaviors of WTAP; Meanwhile, RNA-seq、MeRIP-seq、RIP、RNA pull-down and luciferase reporter assay were applied to explore the downstream targets and passways of WTAP.
Results: WTAP was significantly up-regulated in HCC, with the parallel clinical outcomes that overexpression of WTAP was associated with poor prognosis of HCC patients. We verified that knockdown of WTAP substantially reduced HCC cell proliferation, migration, and colony formation in vitro and remarkably suppressed HCC tumorigenicity in vivo, and overexpression of WTAP led to the opposite events. Through transcriptome sequencing and m6A sequencing, we dug out a target of WTAP, ETS1, which was further confirmed to be a suppressor in HCC. MeRIP-qPCR and RIP-qPCR were employed to prove that ETS1 was regulated in WTAP-mediated m6A modification with the participation of RNA-binding proteins. Knockdown of WTAP remarkably repressed ETS1 mRNA m6A modification and promoted the expression of ETS1.
Conclusion: Up-regulation of WTAP contributes to the progression of HCC. WTAP abolishes the expression of ETS1 in HCC via an m6A-dependent mechanism. Our findings extend the understanding of m6A methyltransferase and epigenetic alterations in liver carcinogenesis.

P-458

Dynamic prediction formulae for HCC recurrence after living donor liver transplantation

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Purpose: Liver transplantation **(LT)** is an established curative therapy for select cases of hepatocellular carcinoma **(HCC)**. However, the selection criteria vary and are highly associated with recurrence rate. At present, several models for prediction of HCC recurrence are one-step formula. We set up multi-stepwise of selection criteria including morphology, AFP, PET scan and pathology according to multi-step approach to select HCC patients for living donor LT(LDLT). The study aimed to formulate the dynamic recurrence rate at the time points of initial visit, just before transplant and after availability of pathology.
Methods: Institutional database was reviewed to identify the patients listed for LDLT with HCC from January 2000 to December 2017. Patient and tumour characteristics were recorded with a median follow-up period of 6.5 years. Logistic regression modelis used to predicate the recurrence rate.
Results: Out of 492 pathology-proven HCC listed patients, 56 patients were HCC recurrence. At first evaluation, only the tumour morphology and AFP are available. The first formula was f = -2.378 + 0.705 * I(peak AFP > 130) + 0.898 * I(UCSF beyond) and the accuracy was 69.3%.
Before transplantation, the PET scan result, response of AFP, and image after treatment were added. The second formula was f = -2.354 + 2.009 * I(PET +ve) and its the accuracy was 82.7%.
After transplantation, the definite pathological report was added. The third formula was obtain: f = - 3.423 + 1.154 * I(Total size > 7.8 cm) + 1.436 * I(PET +v)+ 1.542 * I(mVI=I) + 1.634 * I(Unfavorable). The accuracy was 82.7%.
Conclusion: The accuracy of predictive recurrence rate of HCC increase with the accumulation of clinical data. The dynamic formulas . provide to adjust recurrence rate at different time points and facilitate the decision-making of selection and treatment for LDLT dependent on recurrence rate.

P-459

Expanded living-donor liver transplantation criteria for patients with hepatocellular carcinoma based on the Japanese nationwide survey: the 5-5-500 rule

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Expansion of the liver transplantation indication criteria for patients with hepatocellular carcinoma (HCC) has long been debated. Here we propose new, expanded living-donor liver transplantation (LDLT) criteria for HCC patients based on a retrospective data analysis of the Japanese nationwide survey. A total of 965 HCC patients undergoing LDLT were included, 301 (31%) of whom were beyond the Milan criteria. Here, we applied the Greenwood formula to investigate new criteria enabling the maximal enrollment of candidates while securing a 5-year recurrence rate (95% upper

confidence limit) below 10% by examining various combinations of tumor numbers and serum alpha-fetoprotein/des-gamma-carboxy prothrombin values, and maintaining the maximal nodule diameter at 5 cm. Finally, new expanded criteria for LDLT candidates with HCC, the 5-5-500 rule (nodule size ≤ 5 cm in diameter, nodule number ≤ 5, and alfa-fetoprotein value ≤ 500 ng/ml), were established as a new regulation with a 95% confidence interval of a 5-year recurrence rate of 7.3% (5.2-9.3) and a 19% increase in the number of eligible patients. In addition, the 5-5-500 rule could identify patients at high risk of recurrence, among those within and beyond the Milan criteria. In conclusion, the new criteria - the 5-5-500 rule - might provide rational expansion for LDLT candidates with HCC.

P-460

Mixed HCC-cholangiocarcinoma - a single institution experience

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Background: Combined hepatocellular carcinoma - cholangiocarcinoma (cHCC-CCA) is a rare primary liver tumour that contains both hepatocytic and cholangiocytic differentiation with a reported incidence of 1%. Preoperative diagnosis is difficult and thus only identified on post-operative histopathology. We sought to evaluate our centre's experience with cHCC-CCA in patients who underwent resection and liver transplantation (LT) for presumed HCC.
Methods: A retrospective review of all patients with HCC who underwent either resection or LT since 2012 was performed.
Results: One hundred and nineteen patients underwent resection and 73 underwent LT, of which 5 patients in each group (4.2% and 6.8% respectively) were found to have cHCC-CCA on histopathology. All patients who underwent LT were within UCSF criteria. The median tumour size in the resection group was 2.5 (2.2 - 20) cm and 4.8 (2.6 - 8.1) cm in the LT group (p = 0.690). AFP levels between both groups were also comparable. The median MELD was higher in the LT group (17 (7 - 26)) compared to the resection group (7 (7 - 8)) (p = 0.056). All resections were R0 resections.
Three patients (60%) in the resection group and 4 patients (80%) in the LT group had recurrence. In the resection group, 2 had intrahepatic recurrence, while another had distant recurrence. All patients in the LT group had distant recurrence. The median time to recurrence was 4 months
(1 - 9) in the resection group and 4.5 (2 - 9) in the LT group (p = 1.00).
Conclusion: Outcomes for patients with cHCC-CCA are poor and recurrence rates are high. Compared to traditional HCC, recurrence after LT is common. More is needed to identify these patients preoperatively in order to avoid aggressive surgical therapy until effective multimodality treatment is identified in the future.

P-461

The long noncoding RNA *HULC* promotes secretion of exosomes from hepatocellular carcinoma cells by sponging *miR-372-3p*, which targets *Rab11a*

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Background: Highly upregulated in liver cancer (HULC) is a long noncoding RNA (lncRNA) which has recently been identified as a key regulator in hepatocellular carcinoma (HCC) progression. However, its role in the secretion of exosomes from HCC cells remains unknown.
In this study, we explored the mechanism trough wich HULC promotes the secretion of exosomes from HCC cells.
Methods: The expression of HULC in serum-derived exosomes and liver tissues of HCC was detected by quantitative PCR (qPCR). HULC up-regulation plasmid or down-regulation small interfering RNA (siRNA) plasmid was transfected into HCC cells. The phenotypes of HCC cells were detected by TUNEL, CCK8 and transwell assays. The expression of microRNA-372-3p (miR-372-3p), Rab11a mRNA and protein were detected by qPCR and Western blot, respectively. The binding of miR-372-3p with HULC and Rab11a was detected by dual-luciferase reporter assay.
Results: We found that the expression of HULC in serum exosomes of patients with HCC was higher than that in serum exosomes from healthy controls, and HULC levels were higher in liver cancer tissues than in adjacent normal tissues. The expression of HULC in serum exosomes and liver cancer tissues correlated with the TNM Classification of Malignant Tumours (TNM). In addition, the expression of HULC in tissues correlated with that in HCC serum exosomes. Upregulation of HULC promoted HCC cell growth and invasion, while it repressed apoptosis; notably, it also facilitated the secretion of exosomes from HCC cells. Moreover, qPCR assays

showed that HULC repressed microRNA-372-3p (miR-372-3p) expression. We also identified Rab11a as a downstream target of miR-372-3p. Dual-luciferase reporter assays suggested that miR-372-3p could directly bind both HULC and Rab11a.
Conclusion: Our findings indicate the importance of the HULC/miR-372-3p/Rab11a axis in HCC and provide new insights into the molecular mechanism regulating the secretion of exosomes from HCC cells.

P-462

Liver transplantation for malignant liver tumors of non HCC: a single center case study

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Objective: To study the value of liver transplantation for the malignant liver tumors of non HCC.
Method: The data of 40 adult patients with non HCC who underwent liver transplantation were retrospectively analyzed. Among them, 23 cases were intrahepatic cholangiocarcinoma and 2 cases were hepatblastoma. There were 1 cases of fibrous lamellar hepatocellular carcinoma. 1 cases of malignant hemangioma. 2 cases of hepatic epithelioid hemangioendothelioma. 1 cases of hepatic angiosarcoma. Multiple low differentiated soft tissue angiosarcoma of the liver was seen in 1 cases. Metastatic adenocarcinoma in 4 cases, colorectal cancer metastasis in 3 cases, bladder cancer metastasis in 1 cases. Neuroendocrine tumors metastases in 2 cases. There were 2 cases of liver metastases from gastrointestinal stromal tumors. Small cell lymphoma liver involvement in 1 cases.
Result: Of the 23 patients with cholangiocarcinoma, 1 died of severe intrahepatic infection. Recurrence occurred in 12 patients. 2 cases of hepatblastoma and 1 cases died of recurrence. The other 1 cases survived without tumor. 1 cases of fibrous lamellar hepatocellular carcinoma died of tumor recurrence. 1 cases of malignant hemangioperangioma died after operation. There were 2 cases of epithelioid hemangioendothelioma, 1 cases died during perioperative period, and 1 cases survived without tumor. 2 cases of hepatic sarcoma recurred and died. 3 cases were liver metastases from colorectal cancer and 1 cases survived without tumor. 1 cases of liver metastases from bladder cancer recurred and died. 2 cases of liver metastases from neuroendocrine tumors survived. There were 2 cases of liver metastases from gastrointestinal stromal tumors, 1 cases died during perioperative period, and 1 cases survived.
Conclusion: Some patients with cholangiocarcinoma, hepatoblastoma, epithelioid hemangioendothelioma, neuroendocrine tumor, liver metastasis and gastrointestinal stromal tumors have good results after liver transplantation. However, some cholangiocarcinoma, partial hepatoma and sarcoma of liver have poor prognosis.

P-463

HJURP promotes hepatocellular carcinoma proliferation by destabilizing p21 via the MAPK/ERK1/2 and AKT/GSK3β signaling pathways

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Background: Holliday junction recognition protein (HJURP) has been implicated in many cancers including hepatocellular carcinoma (HCC). However, the underlying mechanism by which HJURP promotes HCC cell proliferation remains unclear.
Methods: RT-qPCR and immunohistochemistry were used to detect HJURP expression in HCC and adjacent tumor tissues and HCC cell lines. The localization of p21 were determined by immunofluorescence and western blot. Co-immunoprecipitation and western blot were used to validate the p21 stability and signaling pathways affected by HJURP. The effects of HJURP on HCC cell proliferation were assessed both in vivo and in vitro. The ERK1/2 pathway inhibitor U0126 and AKT pathway agonist SC-79 were used to treat HCC cell lines for further mechanistic investigations.
Results: HJURP expression was higher in HCC tissues than in para-tumor tissues. Moreover, ectopic HJURP expression facilitated the proliferation of HCC cells, whereas the depletion of HJURP resulted in decreased cell growth in vitro and in vivo. Furthermore, the effects of HJURP silencing were reversed by p21 knockdown. Likewise, p21 overexpression inhibited cell growth ability mediated by HJURP elevation. Mechanistically, HJURP destabilized p21 via the MAPK/ERK1/2 and AKT/GSK3β pathways, which regulated the nucleus-cytoplasm translocation and ubiquitin-mediated degradation of p21. Clinically, high HJURP expression was correlated with unfavorable prognoses in HCC individuals.
Conclusions: Our data revealed that HJURP is an oncogene that drives cell cycle progression upstream of p21 in HCC. These findings may provide a potential therapeutic and prognostic target for HCC.

P-464

Hemochromatosis gene overexpression promotes tumor growth in hepatocellular carcinoma recurrence after curative treatment

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Background: Our previous study identified that hemochromatosis (HFE) involved in acute phase liver graft injury after liver transplantation. Here, we aimed to explore the role of HFE in hepatocellular carcinoma (HCC) recurrence and tumor growth after curative treatment.
Methods: One hundred and sixteen HCC patients who underwent hepatectomy were recruited to explore the clinical relevance of HFE expression and tumor recurrence as well as overall survival. The tumorigenic role of HFE in HCC cells was investigated *in vitro* MTT assay, colony formation assay and *in vivo* subcutaneous tumor model. The underlying mechanism was further explored.
Results: HFE expression was frequently increased in HCC tissues compared with non-tumor tissues (**Fig. 1A**). Higher HFE expression was significantly correlated with poor overall survival (Log Rank = 5.387; p = 0.02) and higher recurrence (Log Rank = 9.853; p = 0.002) after hepatectomy (**Fig. 1B**). HFE expression in normal liver cell (MIHA) and low metastasis HCC cell line (PLC/PRF/5) was relatively lower than in high metastasis one (MHCC97L). The proliferation and migration abilities of HFE knockdown cells were significantly decreased when compared to controls *in vitro* (**Fig. 1C**). Similarly, the tumorigenic ability decreased significantly in SCID mice (**Fig. 1D**). Furthermore, the mitochondrial membrane potential indicated by TMRM signal in HFE knockdown cells was much more dim than control group (**Fig. 1E**). Consistently, the higher cleaved-PARP expression was increased in HFE knockdown cells when compared to controls, which indicated targeting HFE could inhibit tumor cell growth by inducing apoptosis (**Fig. 1F**).
Conclusions: HFE may promote HCC recurrence and growth after curative resection by inhibiting the mitochondria-mediated apoptosis. Inhibiting HFE expression could be a new therapeutic target for HCC recurrence after liver surgery.

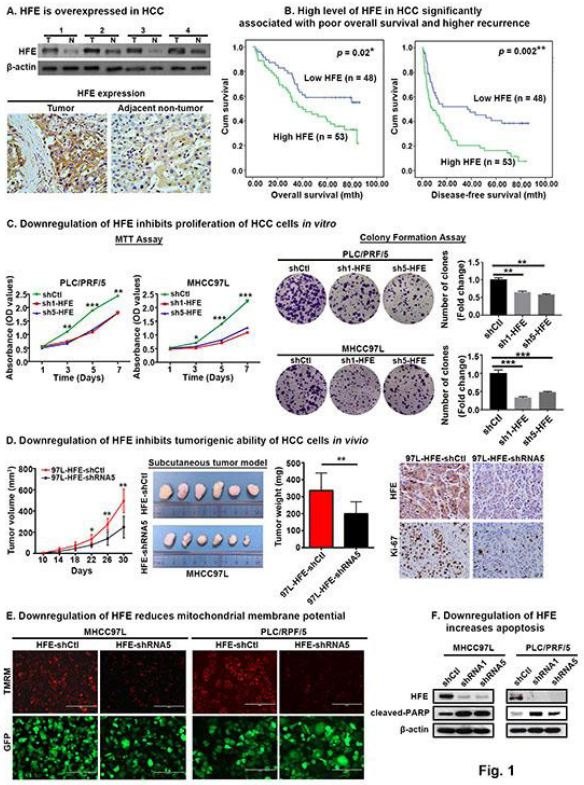

Fig. 1

[Fig. 1]

P-465

Expanding transplant criteria for HCC beyond Milan is associated with high risk of early systemic tumor recurrence: Proceed with caution!

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Background: There is intense enthusiasm to extend liver transplantation for hepatocellular carcinoma (HCC) beyond Milan/ UCSF criteria in light of encouraging reports of equivalent outcomes for advanced HCC. We aimed to evaluate the frequency and nature of HCC recurrence in patients transplanted beyond standard criteria.
Methods: We analyzed HCC recurrence in patients transplanted for HCC between August 2009 and March 2018. We offer LT to patients with tumors within UCSF criteria. Patients presenting with HCC beyond UCSF are considered for LT only after successful downstaging by loco-regional therapies. All patients beyond Milan underwent Whole body PET and bone scan to rule out metastases prior to LT.
Results: 748 adult LT were performed during the study period. HCC was the primary indication for LT in 147 patients. On initial imaging, 131 patients were within Milan (Milan), 7 were outside Milan but within UCSF (UCSF) and 9 patients beyond UCSF (bUCSF). 77 patients had undergone atleast one loco-regional treatment for bridging or down-staging prior to LT. All patients were within or downstaged to UCSF with no major vascular invasion or systemic metastases at LT. After median follow-up of 16 months (6-65 months), 12 patients developed HCC recurrence. Recurrent HCC was diagnosed in 5 patients (3.8%) in Milan group, 3 patients (43%) in UCSF group and 4 patients (44%) in bUCSF group. 10 patients (83%) developed recurrence within the first year. 11 patients (92%) had recurrence in extra-hepatic locations alone.
Conclusions: Transplantation outside Milan criteria is associated with significant risk of systemic tumor recurrence even after successful loco-regional down-staging. Expansion of criteria should be done cautiously until effective systemic therapies is available to deal with post-transplant recurrence

P-466

Favorable outcome of pathologic downstaging by locoregional treatment for hepatocellular carcinoma in liver transplantation

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Purpose: There was no distinct guideline how to take into account the effect of pretransplant locoregional treatment (LRT) in hepatocellular carcinoma (HCC) staging system. The aim of this study was to investigate the prognosis of pathologic downstaging (PDS) by the elimination of total necrosis after liver transplantation.
Methods: We conducted a study of 326 HCC patients underwent liver transplantation between September 2005 and December 2016.
Results: Five-year HCC recurrent free survival (RFS) of PDS group (85.1%) was similar with no LRT group (88.8%) but higher than non-PDS group (68.9%; $P< 0.001$). When compared according to the adjusted T stage and PDS status, PDS T1 (82.4%) showed similar 5 year RFS with non-PDS T1(86.5%). Non-PDS T2 cancers had worse outcome regardless of MC ($P=0.982$) or UCSF criteria (0.466). When preoperative examination, less than 1 viable tumor, less than 1cm of tumor size and less than 20 ng/mL of serum alpha fetoprotein were associated with PDS.
Conclusions: Current study showed that PDS by LRT was associated with favorable outcome in HCC patients after liver transplantation.

P-467

Validation of the simplified AFP model for the prediction of recurrence of HCC for patients with hepatocellular carcinoma within the Milan-BR criteria

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Background: The simplified AFP model improves the prediction of recurrence of HCC in liver transplant recipients (LTxR), both for patients within and beyond the Milan criteria. However, in Brazil we apply the Milan-BR criteria, which disregards lesions with less than 2 cm, for the purpose of Tx candidacy. We sought to validate the AFP model in a cohort of LTxR selected for transplantation with the Milan-BR criteria.
Methods: Single-center retrospective study with a prospectively collected database. Patients with preoperative diagnosis of HCC listed for deceased-donor LTx with exception points within the Milan-BR criteria were selected. Assessment and internal validation of the AFP model was done by means of receiver operating characteristic (ROC) analysis.
Results: 288 LTxR within the Milan-BR criteria were included, out of which 30 (10.4%) required preoperative downstaging. They were mostly male [243 (84.8%)], HCV-infected [187 (64.9%)], with average age of 58.0±7.9 years and with average MELD of 13.4±5.1. The median waiting list time with exception points was 155.0 (IQR 109) days. 2 year overall (66.8% vs. 83.5%, p 0.04) and disease-free survival (75.1% vs. 92.9%, p 0.003) were lower among patients with AFP model > 2. The simplified AFP model presented with AUC 0.712 (95% CI 0.656-0.764, p 0.0001) for predicting recurrence.
Conclusions: The simplified AFP model provides important prognostic information for LTxR with HCC and may improve follow-up of those with a higher risk of post-operative recurrence. This has been previously validated for patients within the Milan criteria, and is also applicable for patients within the Milan-BR criteria.

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Effect of Child Pugh grade on long-term prognosis after liver transplantation for hepatocellular carcinoma

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Background and aims: Whether HCC patients with Child-Pugh C grade of liver function were suitable for liver transplantation remained controversial. The aim of the current study was to identify the possible effect of Child-Pugh grade on long-term prognosis after liver transplantation for HCC.
Methods: A total of 352 patients receiving liver transplantation for HCC were enrolled in this study to identify the risk factors of mortality and recurrence and explore the possible effect of Child-Pugh grade on long-term prognosis after liver transplantation. Univariate and multivariate COX analysis were used to identify risks factors and Kaplan-Meier analysis was used to compare the overall and recurrence-free survival.
Results: Analysis of the patients enrolled revealed an association of HCC recurrence with exceeding Milan criteria (P=0.026), macrovascular invasion (P< 0.001) and AFP ≥ 400ng/ml (P=0.001). Milan criteria (P=0.04), macrovascular invasion (P=0.001) and AFP ≥ 400ng/ml (P=0.001) were also independent risk factor of post-operative mortality. The effect of Child-Pugh grade was not statistically significant neither on recurrence nor mortality. Further analysis revealed that patients with liver function level of Child-Pugh grade A and B had similar 5-year overall survival as patients with liver function level of Child-Pugh grade C (55.0% vs. 61.4%, P=0.752), the 5-year recurrence-free survival of patients with different liver function level was also comparable (49.6% vs. 57.9%, P= 0.733).
Conclusions: Exceeding Milan criteria, macrovascular invasion and AFP ≥ 400ng/ml were independent risk factors of mortality and recurrence after liver transplantation of HCC patients. Patients with liver function of Child-Pugh grade C had similar long-term prognosis with patients with liver function of Child-Pugh grade A and B.

P-469

Evaluation of the deMELD model for the prediction waitlist drop-out among patients with HCC in a large volume liver transplantation center in Brazil

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Background: The controversy regarding the competitive advantage provided by exception points to patients with hepatocellular carcinoma (HCC) waitlisted for liver transplantation (LTx) is yet to be resolved. Models providing insights into how these patients behave while on the waitlist, as well as drop-out and mortality are desirable for allocation purposes. The deMELD was proposed as an attempt to advance this discussion. It considers variables such as MELD score, number an size of HCC nodules and serum alpha-fetoprotein levels. We sought to validate the deMELD model in a cohort of patients with HCC in a large volume liver transplantation center in Brazil.
Methods: Single-center retrospective study with a prospectively collected database. Patients with preoperative diagnosis of HCC listed for deceased-donor LTx with exception points. Assessment and internal validation of the deMELD was done by means of receiver operating characteristic (ROC) analysis.
Results: 414 LTx candidates were evaluation, and which 47 (11.4%) were downstaged before inclusion. At the moment of this analysis, 292 (70.5%) had undergone LTx, 93 (22.5%) had dropped-out of the waitlist, and 29 (7.0%) were currently waitlisted. The median waitlist time was 154 days (IQR 124 days). The drop-out rates 3, 6 and 12 months were 8.9%, 15.7% and 24.1%. The average deMELD scores for successful LTx recipients or for those currently waitlisted and for those who dropped-out were 11.3±11.1 and 10.1±9.1 (p 0.613). The deMELD presented with AUC 0.535 (95% CI 0.485-0.583, p 0.549) for predicting waitlist drop-out.
Conclusions: In a cohort of patients with HCC, the deMELD presented a poor performance to identify those with a higher risk of waitlist removal. Further refinements of this score, particularly on the number and size of the HCC nodules, may increase its predictive capacity and improve its usability in clinical practice for allocation purposes.

P-470

Anti-GPC3 CAR-T therapy suppresses hepatocarcinoma and IL7 and CCL19 expression enhances the infiltration of CAR-T cells in tumor

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Immunotherapy represents one of the major breakthroughs in the treatment of cancer patients, among which the CAR-T therapy is one of the most promising hotspots. For the treatment of hepatocarcinoma (HCC), we developed the CAR-T cells which targeted GPC3 in HCC cells and expressed IL-7 and CCL19 proteins at the same time. Results of *in vitro* cytotoxicity assay illustrated that anti-GPC3 CAR-T cells showed markedly enhanced cell function. Meanwhile, the tumor xenograft model in immunodeficient mice suggested that anti-GPC3 CAR-T cells significantly restrained the growth of tumor, while the expression of IL-7 and CCL19 in CAR-T cells enhanced the cell infiltration in tumor compared to control group. Our results demonstrated that GPC3 can be the specific target of CAR-T therapy in HCC and with co-expression of IL-7 and CCL19, anti-GPC3 CAR-T therapy showed great prospect in HCC treatment.

P-471

Tumor necrosis as a result to pre-transplant bridging treatment for hepatocellular carcinoma and its effect on post-transplant outcome

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Background: As a bridge to liver transplantation, locoregional treatments are commonly employed in hepatocellular carcinoma (HCC) patients to prevent tumor progression during waiting time. Objective of our study was to evaluate the rate of complete pathologic response in patients undergoing locoregional bridging treatment, analyze its effect on post-transplant recurrence, and identify factors predicting the ability to achieve complete pathologic response.

Methods: We performed a retrospective review of all adult patients who underwent liver transplantation for HCC between January 2007 and December 2017 in our transplant center. Locoregional bridging therapies included radiofrequency ablation, TACE, radioembolization or a combination of the above. The type and number of treatment as well as the time from last treatment to liver transplantation was recorded.

Results: On explant specimen, complete pathologic tumor necrosis was achieved in 35.4% of patients. There were no differences regarding age, gender, underlying liver disease, MELD score and Milan criteria in patients with complete tumor necrosis compared to patients without. Patients with treatment response had significantly smaller (28 [12-175] vs. 36 [12-225] mm, p 0.0023) and less tumor nodules (>3 nodules in 20.7% vs. 37.4%, p 0.0278). Pre-treatment AFP was lower in the complete response group, but without statistical significance (14.1 [1.1-43611.0] vs. 28.0 [1.1-538184.0] IU/ml, p 0.0760). On explant specimen, poor differentiation (1.6% vs. 21.7%, p 0.0003) and microvascular invasion (0.0% vs. 20.0%, p 0.0001) were significantly less frequent in the complete response group. Patients with complete treatment response developed significantly less frequently recurrent HCC (3.2% vs. 23.5%, p 0.0005). Multivariate analysis detected tumor size / numbers and poor differentiation being individually associated with decreased odds of treatment response.

Conclusion: Successful bridging treatment leading to complete necrosis may facilitate successful liver transplantation in HCC patients. Treatment response is less likely achieved in tumors of large numbers or size and poor differentiation.

P-472

Glutamine synthetase promotes hepatocellular carcinoma invasiveness through epithelial-mesenchymal transition

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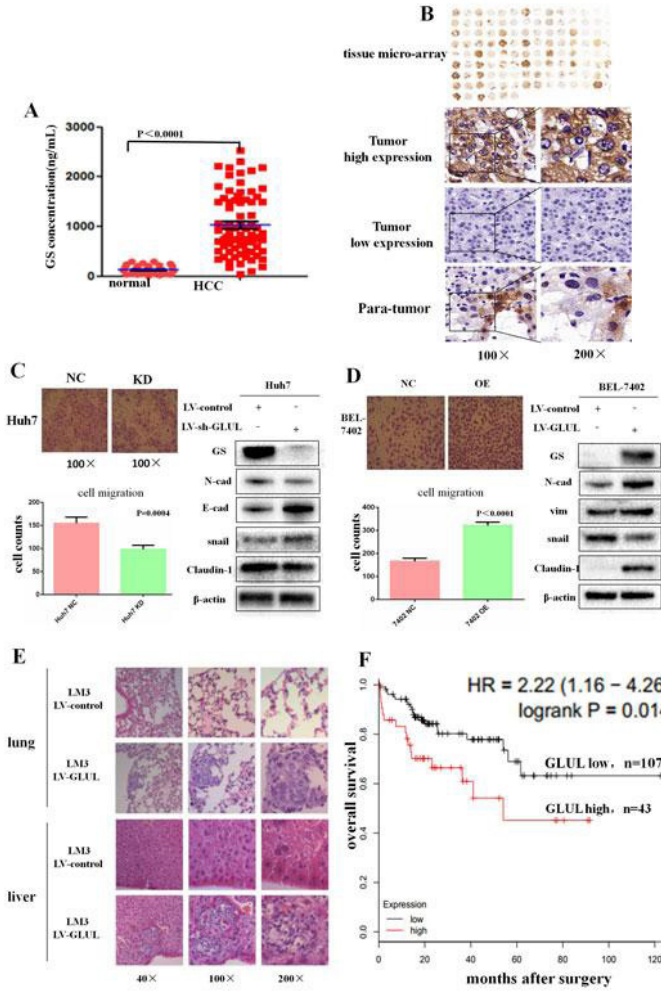
Background: Glutamine synthetase(GS) is over-expressed in some human malignancies including hepatocellular carcinoma(HCC). However, its underlying biological mechanisms by which GS promotes HCC progression has not been broadly explored.

Methods: ELISA was used to test the concentration of GS in plasm of HCC patients (n=200) and normal individuals (n=60). The expression level of GS in the HCC tissue and the counterpart para-tumor tissue were determined by tissue microarray (n=119) and immunohistochemistry. The effects of GS on HCC cell invasiveness were assessed in vitro and in vivo. Western blot(WB) was applied to detect the expression of EMT relative markers.

Results: The concentration of GS in plasm of HCC patients were higher than in that of normal counterparts (Fig A) and the expression of GS in HCC tissues were higher than in para-tumor tissues (Fig B) in majority of HCC patients. In vitro, the invasive ability of Huh7 cell, whose expression level of GS is high in wild type, was suppressed and the expression level of biomarkers contributing to EMT was reduced after knocking down the expression of GLUL with LV-shGLUL (Fig C), while the invasive ability of Bel-7402 cell, whose expression level of GS is low in wide type, was promoted and the expression level of biomarkers facilitating to EMT was elevated after overexpressing GLUL with LV-GLUL (Fig D). At the same time, over-expression of GLUL could improve the invasiveness of LM3 cell in vivo, via tail intravenous injection LM3 cells infected with LV-GLUL (Fig E).Clinically, high expression of GLUL-mRNA was associated with poor survival of HCC patients (Fig F).
Conclusions: Our research demonstrated that high expression GS promotes HCC progression through facilitating EMT. And these findings may provide a potential prognostic and therapeutic target for HCC.



[Glutamine Synthetase Promotes Hepatocellular Carcinoma Invasiveness through Epithelial-mesenchymal T]

P-473

Recurrence of hepatocellular carcinoma (HCC) after liver transplantation: patterns and prognostic factors in a single center experience, King Faisal Specialty Hospital and Research Center (KFSH&RC)

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Background: Predicting HCC recurrence after liver transplant (LT) is a crucial topic that relies predominantly on pre-LT tumor morphology and explant histopathology. Our study aim is to identify HCC recurrence predictive factors by analyzing a cohort of LT cases at KFSH&RC.
Method: The study is a retrospective review on post-LT adult patients reported hepatocellular carcinoma on explanted liver between 1st January 2011 and 30th November 2016. The minimal follow-up period was 23 months. We excluded early death less than two months and cases outside the pre-LT workup protocol. Using SPSS program, binary regression analysis was conducted at a P value of 0.25 for clinically plausible predictive factors such as pre-LT tumor morphology, AFP level, pre-LT logo-regional treatments, type of liver transplant, the timing of LT and post-LT histopathology findings. The statistically significant variables were subjected to Categorical Principal Components Analysis (CATPCA). Then, multivariant Cox regression analysis was conducted reporting hazard ratio (HR).
Results: 112 cases were included (median follow-up period was 52.5 months). The recurrence rate was 8.9%. Half of these cases had multi-organ recurrence. The liver was 50% of the time one of the recurrence sites. 60% of the recurrences were within two years of follow-up. The recurrence rate for Beyond Millan within UCSF cases was 25% after pre-transplant loco-regional downstaging. Five years survival rate was 89% (+/- 15.2). The initial AFP at diagnosis (Mean 385.47 ng/ml) was the most statistically significant predictive variable with an equivalent hazard ratio (HR1.001, Sig 0.001). The biggest tumor diameter at diagnosis variable (Mean 3.72 cm) had a 30% increase in the risk of recurrence (HR 1305, Sig 0.052).
Conclusion: Although Milan criteria is considered too conservative LT selection criteria in HCC cases, our study confirms that HCC morphological characteristic is the most clinically and statistically significant predictor of HCC recurrence post-LT.

P-474

Upfront Living Donor Liver Transplant(LDLT) versus loco-regional therapy(LRT) preceding LDLT for Hepatocellular Carcinoma(HCC): a single centre experience of 12 years

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Introduction: Liver transplant for Hepatocellular Carcinoma(HCC) requires LRT first in most centres depending on the criteria being followed. This helps to observe the biology of the tumor and to buy some time till the availability of the organ. With LDLT, this waiting may not be required.
Materials and methods: 419 patients underwent LDLT for HCC in our institute between 2006-2018. 100 patients received LRT, 319 underwent upfront transplant. The method of LRT included multiple sessions of TACE(114), RFA+MWA(26), TARE(5), EBRT(10), CT(4) and resection(7).
Results: 26 recurrences were noted in the LRT group (26%) and 48 in the upfront transplant group (15%) (p=0.014). The follow up ranges from 3-130 months. In the LRT group 20 recurrences were noted in the subgroup which showed some response to LRT(20/86) and 6 in those who did not show any response to LRT(6/14)(p=0.174). Amongst the upfront transplant, recurrence was 5/44 in the incidentally detected HCC group vs 42/275 in the previously diagnosed cases(p=0.648). The mean time to recurrence(TTR) was 15 months in the LRT group vs 16 months in the upfront transplant group.
Conclusion: Our data shows that the incidence of recurrence of HCC was lower in the upfront transplant group as compared to the LRT group. There was no difference in the recurrence of HCC amongst the subgroup which either responded or not responded to LRT therapy. There was also no difference in recurrence in the incidentally found HCC vs known HCC prior to transplant groups. In those with recurrence, the mean TTR was also similar between the groups. Hence, upfront liver transplant may be a better option than LRT, especially in the setting of living related liver transplant.

P-475

Spindle and kinetochore associated complex subunit 3 promotes tumor growth by regulating Cdk2/p53 phosphorylation in hepatocellular carcinoma

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Spindle and kinetochore-related complex subunit 3 (SKA3) is a part of the spindle and kinetochore-related complexes, which are crucial for the proper timing of late mitosis. However, the correlation between SKA3 and hepatocellular carcinoma (HCC) is not clear. Here, we demonstrated that bioinformatics analysis revealed that the high expression of SKA3 correlated with poor prognosis for hepatocellular carcinoma patients. Consistently, immunohistochemical staining of 114 pairs of tumors also showed higher SKA3 expression than adjacent normal liver tissues. Furthermore, small interfering RNA transfection was used to down-regulate SKA3 in LM3 and Huh7 cell lines. Cell count KIT-8 (CCK8) assay was used to analyze cell proliferation ability. Cell migration and invasion were measured by scratch wound healing test and transwell assay. The subcutaneous xenotransplantation model was used to investigate the role of SKA3 in vivo. As a result, down-regulation of SKA3 significantly inhibited tumor proliferation and invasion in vivo and in vitro. Mechanistically, gene enrichment analysis (GSEA) showed that SKA3 might affect tumor progression through cell cycle and P53 signaling pathway. In addition, SKA3 knockout resulted in G2/M phase arrest and severe apoptosis, as demonstrated by inhibition of CDK2/p53 phosphorylation together with down-regulation of p21 and BAX/Bcl-2 expression level in HCC cells. Overall, these findings uncover a role for SKA3 in regulating the proliferation and apoptosis of hepatocellular carcinoma cells. Our present study provides novel insights into the mechanism of tumorigenesis in hepatocellular carcinoma.

P-476

The tumor mutational burden of Chinese advanced cancer patients estimated by a 381-cancer-gene panel

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Purpose: Tumor mutational burden (TMB) calculated by whole-exome sequencing (WES) is proved to be effective to predict the clinical benefit of immune checkpoint blockades. We aimed to determine if a 381-caner-gene panel (CGP) could be used to estimate TMB, delineate the landscape of TMB of Chinese patients including those received liver transplantation and identify mutated genes and pathways related to higher TMB.
Methods: We first evaluated the correlation between TMB estimated by a 381-cancer-gene panel MasterView and WES using the data from the melanoma sample cohort. 3023 formalin fixed, paraffin-embedded tumor specimens from 2932 Chinese patients with advanced solid tumor were profiled for 381 gene sequencing, the baits of which covered 4,557 exons of 365 cancer-related genes and 47 introns of 25 genes frequently rearranged in cancer (All performed in a lab who achieved full marks five times in the external quality assessment by College of American Pathologists [CAP]). Using the sequencing data, we estimatedTMB of Chinese advanced solid tumor and identified mutated genes and pathways related to higher TMB level.
Results: 381-CGP-mutational burden was strongly associated with those calculated by WES (R^2 = 0.978). The median TMB for each tumor type was 5.65 (colorectal cancer), 4.84 (lung cancer), 4.03 (hepatobiliary cancer), 4.03 (gastric carcinoma), 4.03 (breast cancer) mutations/mb respectively. No correlation was observed between TMB level and age (P = 0.577) or gender (P = 0.307). The TMB of patients with mismatch repair (MMR) or DNA repair response (DDR) pathway deficiency was significantly higher than that without MMR or DDR pathway deficiency (P < 0.001).
Conclusion: The 381-cancer gene panel is a clinical practicable method to assess tumor mutational burden compared with whole exome sequencing. DNA damage response (DDR) and mismatch repair (MMR) deficiency are correlated with higher tumor mutational burden of Chinese patients with advanced solid tumors.

P-477

MiR-206 suppresses progression of intrahepatic cholangiocarcinoma via acting on hepatic stellate cells

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Intrahepatic cholangiocarcinoma (iCCA) is a highly malignant neoplasm for which fibrosis is the major risk factor. This study aims to clarify roles of miR-206 in iCCA. We analyzed miR-206's expression and clinical correlation in 42 pairs of iCCA samples, showing that miR-206 was downregulated in iCCA compared with adjacent normal parenchymal tissues. Decreased miR-206 expression was associated with increased size and presence of metastases. Alpha-SMA expression, a marker of hepatic stellate cell (HSC) activation, in tumor-associated HSCs was negatively correlated with miR-206 expression implying that these cells may promote tumor growth. Experiments *in vitro* and *in vivo* showed that pathological behaviors of HUCCT1 and RBE cells (two CCA cell lines) were directly and indirectly enhanced by co-culturing with LX2 cells (a HSC line) compared with monoculture, and this effect was blunted by miR-206 expression. Further studies indicated that in LX2 cells, up-regulation of miR-206 inhibited proliferation and activation of HSC. Overexpression of miR-206 suppressed LX2 activation via the Anxa2/GSK-3β/β-catenin axis. Taken together, our data identify HSC as an important driver of iCCA malignancy. MiR-206 suppresses the promoting effect of HSC. This research characterizes miR-206's role in iCCA and provides a new target for iCCA therapy.

P-478

Pediatric liver transplantation for hepatoblastoma: a single-center 10-year experience

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Background: Liver transplantation (LT) remains the only surgical treatment for patients with unresectable hepatoblastoma (HB). The aim of this study was to evaluate the outcomes of LT for unresectable hepatoblastoma and identify risk factors for tumor recurrence at our center.
Methods: We performed a retrospective analysis of 18 children who underwent LT for unresectable HB between February 2007 and June 2017.
Result: Median age at diagnosis was 24 months (IQR: 19-30). Median alpha-fetoprotein (AFP) level at diagnosis was 638,438 ng/mL (IQR: 407,048-1,119,038). The staging at diagnosis was PRETEXT III in 6 patients and IV in 12 patients, while the preoperative staging after neoadjuvant chemotherapy was POST-TEXT II/III/IV in 2/9/7 patients. Eight patients presented pulmonary metastases at diagnosis and 4 of them received lung resection before LT. Median age at LT was 30 months (IQR: 25-36). Two patients underwent salvage transplants due to tumor recurrence after liver resection. Adjuvant chemotherapy was administered in all patients. Complications included T-cell mediated rejection in 3 patients and biliary stricture in 1 patient. Ten-year overall survival was 94.4%. Tumor recurrence was observed in 5 patients and one of them died at 1.6 years after LT. In 4 of the 5 patients, recurrence was detected in lung and complete resection was performed. Of 5 patients with tumor

recurrence, 4 patients had extrahepatic lesions at diagnosis and 2 patients still remained metastatic lesion before LT, which was surgically removed. Extrahepatic disease at diagnosis was a significant predictor of tumor recurrence ($P < 0.05$).
Conclusion: Excellent survival could be obtained in patients with unresectable HB, although the patients with extrahepatic lesions before LT revealed a high rate of tumor recurrence after LT. Further investigation of an appropriate management for extrahepatic lesions before LT should be needed.

P-479

Comparison of post-embolization syndrome after hepatic artery embolization in liver cirrhotic patients versus non-cirrhotic patients

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Aim: Post-embolization syndrome (PES) is commonly seen following trans-arterial embolization (TAE) of liver tumors and consists of abdominal pain, nausea, vomiting and fever. It has been our observation that patients with liver cirrhosis have less PES compared to patients without cirrhosis, independent of tumor type. Our aim in this study was to support this observation by performing a retrospective comparison between patients with cirrhosis and patients without cirrhosis.
Methods: This is a retrospective cohort study which includes 181 patients with either normal or cirrhotic liver who underwent 274 TAE procedures for liver tumor at Mayo clinic between January 2015 and December 2017. The extracted parameters using medical records were: tumor type, etiology of liver cirrhosis, length of postprocedural hospitalization, grading of severity of PES symptoms using Southwest Oncology Group Toxicity Coding scale.
Results: Of 274 procedures, 152 were performed in 98 patients with liver cirrhosis and 122 were performed in 83 patients with non-cirrhotic liver. 102 procedures (67.1%) in the liver cirrhotic group and 29 procedures (23.8%) in non-cirrhotic group were not complicated by PES (p-value of Chi-square < 0.0001) whereas 50 procedures (32.9%) in liver cirrhotic group and 93 procedures (76.2%) in noncirrhotic group were complicated by PES (p-value of Chi-square < 0.0001). In patients with PES, mild/moderate symptoms controlled by oral therapy occurred in 34 (22.4%) in cirrhotic group and 43 (35.2%) in non-cirrhotic group (p value =0.01546) whereas severe symptoms that required parenteral therapy occurred in 16 (10.5%) in cirrhotic group and 50 (41%) in non-cirrhotic group (p value =0.01546).
Conclusion: In this cohort of patients, patients without cirrhosis were more likely to develop significant PES than those with underlying cirrhosis. This data may be used to decide which patients require inpatient observation following hepatic artery embolization.

P-480

Effect of down-staging therapy on outcomes of liver transplantation for hepatocellular carcinoma: Based on Hangzhou criteria

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Background: To explore the effect of down-staging therapy on the outcomes of patients beyond Hangzhou criteria.
Methods: A retrospective review of 62 patients who received down-staging therapy based on TACE before liver transplantation（LT）between January 2014 to December 2017 in our center was undertaken, Kaplan-Meier estimator was used to analyze the outcomes.
Results: Patients were divided into three groups：met the Hangzhou criteria on initial hepatocellular carcinoma diagnosis and remained within Hangzhou criteria after down-staging (Group A, n=33); beyond the Hangzhou criteria on initial but met Hangzhou criteria after down-staging (Group B, n=12, 9 patients remained beyond Milan criteria before LT) and those remained beyond Hangzhou criteria after down-staging (Group C, n=17). Kaplan-Meier´s 3-year post-LT survival probabilities in the Group A,B and C were 70.1%, 66.7% and 31.8% (Group A versus B p=0.801;Group B vs C p=0.013), recurrence-free probabilities were 77.8%, 83.8% and 22.1% (Group A vs B p=0.957; Group B vs C p=0.003).
Conclusion: The post-LT overall survival and recurrence-free survival of those patients beyond Hangzhou criteria on initial diagnosis but within Hangzhou criteria after down-staging were similar to those met Hangzhou criteria on initial. Patients beyond Hangzhou criteria may get better outcomes after successful down-staging therapy, even though they do not met Milan criteria after therapy.

P-481

CCT3 promotes the degradation of p53 by ubiquitination pathway in hepatocellular carcinoma

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CCT3 is member of the chaperonin containing TCP1 complex (CCT), assists the folding of proteins upon ATP hydrolysis as molecular chaperone. We illustrated that expressions of CCT3mRNA and protein are highly up-regulated in hepatocellular carcinoma (HCC) tissues, and high level of CCT3 is correlated with poor survival in HCC patients. knock down CCT3 suppress the growth of HCC by inducing cell cycle arrest at G1 stage in vitro and in vivo. We also identified the interaction between CCT3 and p53 by co-ip assay, and We further confirmed that CCT3 can reduce the level of p53 by promoting ubiquitination of p53. Collectively, our study suggests that CCT3 promotes the ubiquitination of p53 and reduces the level of p53, further to inhibit tumor growth, and provides a potential drug target for treatment of HCC.

P-482

The potassium channel Eag1 enhances hepatocellular carcinoma proliferation by modulating the SKP2-p27/p21 pathway and metastasis through pseudopod formation

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Background: As one of the potassium channels, Eag1 is involved in various physiological processes and plays an important role in the tumorigenesis of many kinds of human cancers. However, the role of Eag1 in hepatocellular carcinoma (HCC) remains unclear and needs to be further explored.
Methods: qRT-PCR, western blot and immunofluorescence was used to investigate the expression of Eag1 mRNA and protein in HCC specimens. LM3 and Huh7 cell lines were chosen for gain or loss of Eag1 function studies both *in vitro* and *in vivo*. We also performed a drug combination experiment to investigate the clinical role of Eag1 in the treatment of HCC.
Results: In this study, we found that Eag1 was overexpressed in HCC tissues and was associated with a poor clinical prognosis. In vitro and in vivo experiments showed that Eag1 could promote the proliferation of HCC by inhibiting the ubiquitination of SKP2 and promoting cell cycle progression. Our research also revealed that Eag1 could promote the migration and invasion of HCC by promoting cell pseudopod formation. Furthermore, we found that astemizole, an Eag1 inhibitor, could promote the anti-tumor effects of doxorubicin on HCC.
Conclusion: Our study demonstrated that Eag1 could accelerate cell proliferation through the SKP2/p21/p27 axis, and promote the invasion and migration abilities of cells by remodeling the cell cytoskeleton. As Eag1 plays an important role in HCC progression, the combined use of astemizole and doxorubicin might be a novel prospective therapy for liver cancer.

P-483

Methylations of SOCS family are recurrent predictors in liver transplantation for hepatocellular carcinoma

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Liver transplantation (LT) is one of standard treatment for hepatocellular carcinoma (HCC), however, the recurrence is the major challenge. Therefore, it is necessary to identify some effective predictors for the recurrence. Recent studies reported that methylation of (Suppressor Of Cytokine Signaling 1-3) SOCS1-3 is associated with HCC recurrence and overall survival. Accordingly, we detected methylation 12 CpG islands of SOCS1-3 from 83 HCC samples treated by LT with bisulfite sequencing. The results demonstrated that SOCS1(chr16:11349081-11348955) had most aberrant methylation, in the recurrent group. After univariate and multivariate cox regression, the results indicated that methylation on SOCS1(chr16:11 349011),SOCS1(chr16:11350299), SOCS2(chr12:93963982) and Hangzhou criterion were independent risks for recurrence. Thus,they can work with Hangzhou criterion to constitute an ideal predictor of the recurrence.Then ,we utilized these factors to construct a recurrent predictor.C-index of the predictor is 0.745. As a result, the methylation alternation CpG islands of SOCS familiy may serve as a useful marker to screen the suitable HCC candidates to undergo LT operation and predictors of the prognosis of HCC patients with LT treatment.

P-484

Usefulness of evaluating response to neoadjuvant therapy in selection of hepatocellular carcinoma patients for liver transplantation in the era of novel criteria

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Background: Complete pathological response (CPR) to neoadjuvant therapies is considered as surrogate for cancer cure in patients undergoing liver transplantation for hepatocellular carcinoma (HCC). The aim of this study was to critically evaluate the prognostic role of CPR in liver transplantation for HCC.
Method: A total of 222 HCC transplant recipients were included in this retrospective observational study. Incidence of recurrence and patient survival at 5 years were the primary and secondary outcome measures, respectively. Competing risk analyses were applied to evaluate recurrence incidence. Propensity score matching was performed to compare the outcomes of patients after neoadjuvant treatment with and without CPR. Prognostic models with and without CPR were compared with respect to Bayesian information criterion (BIC).
Results: Of 127 patients after neoadjuvant treatment, CPR was achieved in 32 (25.2%). Baseline recurrence risk according to tumor characteristics was lowest in patients with CPR, followed by treatment naïve-patients and patients without CPR. Adjusted for confounders, CPR did not have any significant effect on tumor recurrence (exp[β]=1.34, 95% confidence interval 0.37-4.85; p=0.660). No significant net reclassification improvement was noted following addition of CPR to existing criteria (range: -0.018 to 0.056; p 0.478 - 0.546). Addition of CPR to selection criteria based on morphological features and alpha-fetoprotein did not improve their predictive performance (ΔBIC 8.85-10.28). As compared to treatment-naïve patients, recurrence risk was increased in patients undergoing neoadjuvant treatment not achieving CPR in subgroups within Milan criteria (p=0.016), AFP model ≤2 points (p=0.021), and within Warsaw criteria (p=0.007). Five-year incidence of recurrence in propensity score-matched patients with and without CPR were 14.0% and 15.9%, respectively (p=0.661), with corresponding survival rates of 73.2% and 67.4%, respectively (p=0.329).
Conclusion: Complete pathological response to neoadjuvant treatment has no prognostic significance in liver transplantation for HCC. Bridging therapies in low-risk patients may increase the risk of recurrence.

P-485

Factors affecting prognosis and outcome in live donor liver transplantation for hepatocellular cancer: Is there a pattern beyond patient selection criteria?

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Introduction: Liver transplantation (LT) remains the best treatment option for hepatocellular carcinoma (HCC). Patient selection is crucial and debated ever since the emerging of the Milan criteria in 1996. As live donor LT being more routinely performed worldwide, numerous new and/or expansions of the original criteria have been suggested to allow more patients to benefit from this superior treatment modality. This study aims to contribute to ever-growing data in search for better coverage of patients with acceptable outcomes.
Material and method: Medical recordings of 196 adult patients who underwent LT for HCC among 733 patients transplanted between July 2009 and October 2018 in our institution, were retrospectively reviewed. Patients were classified by Milan and UCSF criteria. Survival times, as well as tumor, liver disease, and recurrence related data, were recorded for each patient and the outcomes were statistically analyzed.
Results: Factors significantly affecting recurrence and survival were histologic differentiation, number and the size of the tumor and the presence of vascular invasion. Serum alpha-fetoprotein levels did not significantly affect outcomes. Among the patients exceeding both Milan and UCSF criteria, having a total tumor size of less than 160 mm was significantly associated with better outcomes (p=0.007).
Conclusion: In conclusion, HCC patients having tumors with vascular invasion, poor differentiation, exceeding 6 in number and 160 mm in total diameter demonstrate higher recurrence rates and worse outcomes.

P-486

A new pathological scoring system predicting post-hepatectomy survival for hepatocellular carcinoma

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Background: It is helpful to explore a simple staging system predicting the post-hepatectomy survival in patients with resectable hepatocellular carcinoma (HCC).
Materials and methods: This study enrolled a training cohort of 187 HCC patients and a validation cohort of 101 patients undergoing hepatectomy. Survival analysis was performed to define subsets of patients with discriminated prognosis.
Results: Microvascular invasion was present in 28 among the 187 patients (15.0%) of the train cohort, and was associated with significantly decreased post-operative survival ($p< 0.05$). Cox regression analysis showed that microvascular invasion and poor tumor differentiation were the two independent prognostic factors ($p< 0.05$). A new prognostic model based on two pathological predictors was established as: Pathology Score (p-score) =1.18* Poor Differentiation + 1.11 * Microvascular Invasion. Accordingly, all patients were categorized into three groups: low-risk group (p-score=0, n=90), intermediate group (1< p-score< 2, n=78), and high-risk group (p-score>2, n=19). The prognosis was significantly different among three groups (p< 0.001). In the validation cohort (n=101), the staging system (p-score) also functioned well predicting post-hepatectomy survival (p=0.006).
Conclusions: The two pathological predictors-based simplified HCC staging system (p-score) is easy to use at the bedside, and can effectively predict survival for HCC patients who has undergone partial hepatectomy.

P-487

ACSL4 promotes hepatocellular carcinoma progression via c-Myc stability mediated by F-box and WD repeat domain-containing 7

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Background: Long chain acyl CoA synthetase 4 (ACSL4) has been shown to be overexpressed in multiple cancer types, including hepatocellular carcinoma (HCC). However, its function and the underlying molecular mechanisms in HCC are still not fully elucidated.
Method: RT-qPCR and immunohistochemistry were used to detect ACSL4 expression in HCC and adjacent tumor tissues and HCC cell lines. Functional analysis of ACSL4 in HCC
was performed in vitro and in vivo. Co-immunoprecipitation and western blot were used to detect signaling pathways affected by ACSL4 and validate the c-Myc stability.
Results: ACSL4 was frequently upregulated in HCC samples and associated with poor prognosis. Moreover, ectopic ACSL4 expression facilitated the proliferation of HCC cells, whereas ACSL4 knockdown resulted in decreased cell growth in vitro and in vivo. Mechanistically, ACSL4 stabilized the oncoprotein c-Myc via ubiquitin-mediated degradation of c-Myc. ACSL4 depletion attenuated phosphorylation of c-Myc(S62) and decrease the stability of c-Myc via upregulation of F-box/WD repeat-containing protein 7 (FBW7), an E3 ubiquitin ligase of c-Myc. Also, c-Myc degradation by ACSL4 depletion was blocked by knockdown of FBW7 ubiquitin ligase or proteosomal inhibitor MG132. The effects of ACSL4 silencing were partially reversed by FBW7 knockdown. Likewise, c-Myc depletion using siRNA or its inhibitor 10058-F4 inhibited cell growth ability mediated by ACSL4 elevation.
Conclusion: Our data revealed that ACSL4 promotes HCC progression via c-Myc stability mediated by FBW7. ACSL4 may be a potential therapeutic and prognostic target for HCC.

P-488

Out-of-Milan HCC criteria and worse intention-to-treat results following liver transplantation

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Milan criteria are widely used for liver transplantation (LT) selection in hepatocellular carcinoma (HCC) but have been recognized to be too restrictive. Out-of-Milan criteria are increasingly being adopted. Our aim was to analyse if LT waitlisted Out-of-Milan HCC patients have different outcome than Milan patients. Retrospective study including all consecutive patients with HCC admitted in the waiting list for LT between January 2012 and January 2015. We included 177 patients, 146 of which eventually transplanted. Downstaging was achieved in the Out-of-Milan cases (n=34) before waitlisting. From diagnosis to last follow-up 29% patients died. Survival at 1 and 5 years from diagnosis was 93% and 75%, respectively in the within-Milan group compared to 91% and 61% in the Out-of-Milan group (p=0.03). Treatment failure occurred in 20% of cases due to tumour progression in the WL (44%), death on the WL (20%) and HCC recurrence post-LT (9%). Out-of-Milan criteria was the only variable predictive of treatment failure remaining in the multivariate analysis

with a HR of 1.7 (IC 95% 1.34-4.55 p=0.01). Out-of-Milan criteria are associated with a higher intention-to-treat LT failure from time of inclusion in the WL. However, survival ratesare still greater than 50% at 5 years of follow-up.

Conclusion: LDLT remains an important treatment option for HCC. More accurate diagnostic modalities should be employed to identify patients with mixed tumours. With proper patient selection, LDLT outcomes post-LT for HCC remains comparable to DDLT.

P-489

Living-donor liver transplantation (LDLT) versus deceased-donor liver transplantation (DDLT) for patients with hepatocellular carcinoma: our 20 year experience

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Background: Liver transplantation (LT) remains the optimal curative treatment for cirrhotics with hepatocellular carcinoma (HCC). LDLT was introduced to overcome organ scarcity, particularly in Eastern countries where organ donation rates are low. Some centres however, have noticed a higher rate of HCC recurrence following LDLT. While some factors associated with recurrence were attributed to patient selection, others report a correlation between recurrence and graft regeneration. We report our 20-year experience with LDLT versus DDLT for HCC in a multi-ethnic Singaporean population.
Method: Adult LTs for HCC performed at the National University Hospital, Singapore from 1997 to 2017 were reviewed. All LDLTs were right lobe grafts. Univariate, multivariate as well as survival analyses were performed for recurrence and overall survival.
Results: A total of 85 patients underwent LT for HCC (63 DDLTs and 22 LDLTs) All DDLTs were whole grafts with the exception of 1 patient who received a right-lobe split graft. Mean natural model for end-stage liver disease (MELD) score was 15.1 ± 7.3, and mean Child-Pugh score was 7.8 ± 2.4. There were 9 (11.4%) recurrences. No differences in recurrence were noted with either the Milan or University of California San Francisco (UCSF) criteria (p=0.522). All patients (n=3) who were transplanted out of UCSF criteria had tumour recurrence (p< 0.001). An unusual explantation histology was associated with tumour recurrence (p< 0.001). Three recurrences had a HCC-cholangiocarcinoma overlap, while 1 had a focus of sarcomatoid carcinoma. There were no statistically significant differences in recurrence (p=0.112) between the 2 groups, but DDLT patients appeared to have a slightly better overall survival, though this did not reach statistical significance (p=0.069).

P-490

Effect of chronic restraint stress on Hepatocellular Carcinoma (HCC) metastasis in mice

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Background: Hepatocellular Carcinoma (HCC) is one of the most common cancers and a leading cause of death worldwide. Numerous animal studies indicate that Chronic Restraint Stress(CRS) could accelerate tumor growth and invasion via β-adrenergic signaling pathway. Besides, β-blockers can reverse the effects of chronic stress. However, the role of chronic stress in HCC is not well understood.
Method: We established two kinds of mouse metastasis models and CRS model to validate our hypothesis:
(1) Pulmonary Metastasis Model of Mice H22 through tail vein injection;
(2) Liver Metastasis by injection of H22 in spleen. Then these ten- to 12-week-old female BALB/c mice were randomized to two treatment groups:
(1) no-stress control group (n=5) and
(2) CRS group (n=5). The mice in CRS group were stressed daily for 4h and sacrificed 21d after tumor cell (H22) injection. Besides, we selected different concentrations of Epinephrine (E, β-AR agonist) or ICI 118,551(ICI, specific β2-AR antagonist) to incubate with SMMC-7721 cells for 24,48,72h to study the proliferation, invasion and migration ability.
Results: CRS group (n=5) were found with more metastatic lesions comparing with control group (n=5) both in Pulmonary Metastasis Model and Liver Metastasis Model by spleen injection. β-AR agonist could promote invasion and migration of HCC cells, and β2-AR antagonist could inhibit proliferation, migration and invasion of HCC cells.
Conclusion: Chronic restrained stress (CRS) could accelerates HCC metastasis in mice model, and this effect may be interrupted by β2-blockers.

P-491

Effects of terlipressin and somatostatin on liver function after major hepatectomy

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Background and aims: Posthepatectomy liver failure after major hepatectomy is a serious complication and caused by increased portal pressure and flow. Splanchnic vasoactive agents such as terlipressin or somatostain are known to decrease portal pressure. The aim of this study was to investigate the effects of terlipressin and terlipressin on postoperative liver function after major hepatectomy.
Methods: A total of 245 patients with HCC who underwent major hepatectomy were enrolled. After excluding 27 patients with morbidity. 218 patients were divided into four groups: control (n=72), terlipressin (n=64), somatostatin (n=48), and combination (terlipressin+ somatostatin, n=34). Propensity score matching was used to balance basic characteristics between different groups. Alanine transaminase, bilirubin, and prothrombin time were determined after operation.
Results: In terlipressin-control comparison, the postoperative ALT, PT and TB of the patients on POD 1, 3, 5 and peak within one week did not differ statistically between terlipressin versus control group. The similar results were also observed for somatostatin versus control. Compared with the control, combination group showed a worse liver function after operation: higher ALT at POD5 (140±113 U/L vs. 78±57U/L, P=0.011), longer peak PT and PT at POD 3 (15.0±2.7S vs. 13.7±2.0S, P=0.025) and POD5 (13.9±2.2S vs. 12.9±1.7S, P=0.034), and higher peak TB and TB at POD 3 (41.3±34.3μmol/L vs. 23.7±13.8μmol/L, P=0.017) and POD5 (39.9±40.7μmol/L vs. 20.8±12.6μmol/L, P=0.025). No significant difference of ascetic leak was detected between different groups.
Conclusion: Neither somatostatin nor terlipressin improved the liver function recovery after major hepatectomy. The combination of somatostatin and terlipressin appeared to delay liver function. Furthermore, somatostatin and terlipressin decreased ascetic leak after operation.

P-492

Tumor markers at the time of liver transplantation: reliable predictors of hepatocellular carcinoma recurrence after locoregional treatment

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Prediction of the hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) is important for clinicians to make a treatment decision. Alpha fetoprotein (AFP) and protein induced by vitamin K absence-II (PIVKA-II) are useful tumor markers for HCC. We conducted a study of 158 HCC patients underwent liver transplantation after locoregional treatment to clarify when is optimal time point to assess HCC recurrence from serum tumor maker.
We retrospectively recruited data of AFP and PIVKA-II at various time points; at the time of LT, pre-LT maximum, pre-LT minimum, maximum after last LRT. Also we found cutoffs of two markers for HCC recurrence and assessed hazard ratio (HR) of cutoffs adjusted with cancer staging on explanted pathology, Esmond grade, liver function and total number of pretransplant LRT. AFP at LT (cutoff 20 ng/mL; HR 3.67, 95% CI 1.86-7.25), maximum AFP after last LRT (cutoff 75 ng/mL; HR 2.60, 95% CI 1.36-4.99) were independently predictive for HCC recurrence. PVIKA at LT (cutoff 2.22 mAU/mL; HR 2.22, 95% CI 1.05-4.67), maximum PIVKA after last LRT (cutoff 130 mAU//mL; HR 2.38, 95% CI 1.16-4.89) were also significantly associated with HCC recurrence. Pretransplant maximum level or degree of decline of both tumor markers were not significant factors.
Current study demonstrated that AFP and PIVKA at the time of LT were reliable predictors of hepatocellular carcinoma recurrence after locoregional treatment regardless of maximum pretransplant values. Clinicians can rely on the current level of tumor markers at the time of LT.

P-493

Glutamine synthetase is a potential biomarker in evaluation of regorafenib treatment for HCC

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Background: Glutamine synthetase(GS) is frequently reported as a diagnostic biomarker for hepatocellular carcinoma (HCC), it was found with high sensitivity and efficiency. GS reflect a metabolic status of tumor, in this study, which makes it possible to be a potential biomarker in evaluating the efficacy of HCC treatment.
Methods: 4 patients were divided into sensitive group and non-sensitive group according to the expression of raf1, vegfr2, pS6 and p-erk. The tumor from each patient were established for patient-derivedxenograft model (n=6). The concentration of GS in serum of mice was used to assess the performance of GS in evaluating the treatment of regorafenib for HCC.
Results: The tumor volume of HCC patients in sensitive group is significantly smaller than non-sensitive group (p=0.018). But in non-sensitive group, the tumor volume showed no statistical differences during regorafenib treatment. We also found in sensitive group, the concentration of GS in pdx mice greatly decreased comparing with the GS concentration in pdx mice before regorafenib treatment. Correlation analysis showed the change of GS and tumor volume during regorafenib treatment presented with a same tendency (r2=0.64).
Conclusion: During the treatment of regorafenib for HCC, the concentration of GS is a potential evaluated biomarker. Further studies are need to prove the efficiency of GS in evaluation of regorafenib treatment.

P-494

Sirolimus-based immunosuppression improves outcomes in liver transplantation candidates with hepatocellular carcinoma beyond the Milan criteria or the Hangzhou criteria

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Background: We investigated the effect of sirolimus-based immunosuppression on the outcomes of liver transplantation (LT) candidates with hepatocellular carcinoma (HCC).
Method: We retrospectively analyzed 148 HCC patients who underwent LT in our hospital from January 2014 to December 2016. The patients were divided into the sirolimus group (61 cases) and non-sirolimus (control) group (87 cases). Disease-free survival (DFS) and overall survival (OS) after tumor recurrence were compared using the Kaplan-Meier method.
Results: The sirolimus group achieved a better OS compared to the control group while the DFS had no statistical difference. Subgroup (Milan Criteria-based or Hangzhou Criteria-based) analyses revealed that patients exceeding, rather than meeting the Milan criteria or the Hangzhou criteria benefited from sirolimus (exceeding Milan criteria: HR, 0.403; 95% CI, 0.202-0.805; p=0.006; exceeding Hangzhou criteria: HR, 0.402; 95% CI, 0.187-0.864; p=0.014). There was no statistical difference in the OS between sirolimus group or control group that meeting the Milan criteria or Hangzhou criteria.
Conclusion: Sirolimus may improve outcomes in LT patients with HCC beyond the Milan criteria or the Hangzhou criteria.

P-495

A novel irradiation-driven compound based on organoplatinum metallacage is effective in multimodality therapy for liver cancer via killing cancer stem cells

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Background: Liver cancer is a risky cancer with high mortality. Cancer stem cells play a pivotal role in tumorigenesis and cancer recurrence. Photodynamic therapy is an effective treatment for many diseases including cancer due to these advantages, including high efficiency, minimally invasive character, fewer side effect, etc.
Methods and results: By using multicomponent coordination-driven self-assembly, we obtain compound A, which integrates chemotherapy and PDT. CCK8 assay in liver CSCs shows, the IC50 value of Compound A treating group (103.9 ± 43.1 nM) upon irradiation, was much lower than that in the group of chemotherapy (1036.1 ± 340.0 nM) or PDT(1772.2 ± 167.0 nM) alone. Annexin V-FITC/PI assay shows that that compound A treating group has a high proportion of apoptosis cells. By performing FCM assays, the level of ROS and the ration of red-JC-1 of CSCs increase significantly after treating with Compound A. Apoptosis related proteins such as cleaved-caspase 3 were also detected by western blot, which is according with the former results.
Conclusion: Compound A can effectively kill liver CSCs. It can serve as an efficient alternative treatment.

P-496

Functional role of anillin actin binding protein in the development of hepatocellular carcinoma

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Background: Agents designed to block cytokinesis can inhibit proliferation of cancer cells. Anillin actin binding protein (ANLN), a cytokinesis-related proteins, is involved in cell abscission during cytokinesis. We aimed to study the role of ANLN in hepatocellular carcinoma (HCC) and explore its potential as an anti-cytokinesis agent for HCC therapy.
Methods: Using the TCGA database, we evaluate the expression of ANLN and its association with patient survival time in hepatocellular carcinoma database. qRT-PCR and immunohistochemical analysis were performed to detect the expression of ANLN in 65 pairs of HCC tissues. ANLN specific siRNA were used to silence gene expression to study the role of ANLN in proliferation, cell cycle and apoptosis in HCC cell lines. We performed confocal microscopy to identify the function of ANLN in cytokinesis. Additionally, protein interactions were detected and validated with immunofluorescence and co-immunoprecipitation assay.
Results: ANLN was highly overexpressed in HCC tumor tissues and increased expression of ANLN was associated with shorter survival times of patients with cancer. We found knockdown of ANLN reduced cell proliferation, arrested cell cycle and induced apoptosis in HCC cell. Immunofluorescence results demonstrated that knockdown of ANLN resulted in cytokinesis defect and multinucleate cells. Besides, we performed confocal microscopy to identify location of ANLN during cytokinesis and found ANLN colocalized with Aurora kinase B, a cytokinesis-regulatory protein, in midbody. Further, knockdown of ANLN in HCC cells impaired Aurora kinase B redistribution at the midbody during cytokinesis.
Conclusion: Our study demonstrates that ANLN plays an important role in the cytokinesis and growth of HCC cell, implying that it might be a promising therapeutic target in HCC.
Keywords: HCC, ANLN, cytokinesis

P-497

Aminoacylase-1 is a potential biomarker for hepatocellular carcinoma in predicting survival outcome

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Background: Our previous work has found that aminoacylase-1 (ACY1) plays a tumor suppressive role in hepatocellular carcinoma (HCC), however the prognostic value of ACY1 on overall survival and disease-free survival of HCC is still unclear.
Methods: Immunohistochemistry assay was used to investigate ACY1 and E2F5 expression in 74 HCC tissues, and prognostic value of ACY1 in HCC patients was explored.
Results: Immunohistochemical results indicated that ACY1 expressed lower in HCC tissues than in matched adjacent tissues ($p< 0.05$). ACY1 expression was positively correlated with E2F5 expression in HCC tissues ($r=0.506$). Tumor-free survival rate of higher ACY1 patients is better than the patients with lower ACY1 patients ($p< 0.01$). But there is no statistical difference on the overall survival rate ($p > 0.05$).
Conclusion: ACY1 was positively correlated with E2F5 in HCC tissues, and ACY1 was a potential prognostic marker for HCC.

P-498

De novo malignancy after liver transplantation: a single center experience

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Introduction: There are many reports about solid organ transplantation recipients appear to have a higher risk of malignant tumor. It caused by suppressed immune system fail to surveillance malignant transformation. De novo malignancy after transplantation is the most common cause of late mortality. The aim of the study is to describe of experiences of de novo malignancy of major liver transplantation in South Korea.
Method: From March 1988 to March 2018. 1793 Adult liver transplantation was performed in Seoul National University Hospital.

We reviewed the causes of death and de novo cancer status of these cases retrospectively.
Results: A total of 27 de novo cancers were diagnosed among the 1793 recipients. There are 12 cases in 875 hepatocellular carcinomas (HCC) cases and 15 cases in 918 non-HCC cases. De novo cancer is not a main cause of death in an initial 5 years period, but after 5-year follow-up, is the main cause of death after liver transplantation. The most frequent cancers developed after liver transplantation was lymphoma (25%), second is gastric cancer (18%). And de novo hepatocellular carcinoma in non-HCC cases was found in 2 cases.
Conclusion: Liver transplant recipients were at increased risk for developing de novo cancers. We should check-up cancer surveillance on this patient more strictly.

P-499

Posttransplant lymphoproliferative disorder after liver transplantation in patients with low level of FK506

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Background: Posttransplant lymphoproliferative disorder (PTLD) is serious complication of solid organ transplantation. The most important risk factors for PTLD are EBV status at time of transplantation, type of transplanted Forgan and duration and type of immunosuppressive regimen.
Case: A female-52 year old patient underwent living donor liver transplantation for advanced liver cirrhosis and chronic hepatitis B in May 2017. Her EBV IgG was positive at the operation. Immunosuppressive regimen was basiliximab, tacrolimus, mycophenolate mofetil and steroid.
Steroid was discontinued at postoperative 10 days due to duodenal ulcer bleeding, mycophenolate was stopped due to leukopenia at postoperative 20 days. Since 40 days after surgery, her FK level was between 2 and 4 ng/ml, there was no evidence of rejection. During the follow up, several ovoid mass and nodules in small bowel mesentery was recognized in the abdominal CT exam. Explorative laparotomy was performed and 5 masses were located in the mesentery of jejunum. Pathological diagnosis was postransplant lymphoproliferative disorder.
Conclusions: Even low dose of immunosuppression, seropositive for EBV, PTLD can be developed. Frequent regular follow up was mandatory in liver transplantation.

P-500

The function of LIF in the development and treatment of hepatocellular carcinoma

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Leukemia inhibitory factor (LIF) is the most pleiotropic member of the interleukin-6 family of cytokines, which showed paradoxically opposite effects in different cell types. However, the effect of LIF in HCC is still unknown. We explored the function of gene LIF in hepatocellular carcinoma by analyzing the express of LIF in HCC samples who underwent LT and testify the function of LIF gene, including proliferation, invasion, and apoptosis in vitro. The results showed The expression of LIF gene in tumor tissue was significantly higher than that in para-tumor. The higher expression of LIF is associated with poor relapse in patients who received liver transplantion. LIF activate JAK1/2, then transducing mainly through STAT3 and AKT-mTOR downstream. Then, LIF can enhance tumor growth, invasion and reduce apoptosis in vitro. Enhanced LIF signaling promote cancer stem cell gene expression. The effect of LIF can be blocked by JAK inhibitors and LIF-blocker. In conclusion, LIF mainly showed tumorigenesis and metastasis stimulating effects in HCC cell lines. Overexpression of LIF indicating poorer prognosis. Inhibiting LIF signaling can be more efficient by blocking JAK signaling, rather than LIF-blocking or single down-stream pathway inhibitors, which could be a potential therapy target in clinical practice.

P-501

Comparison of two eras in liver transplantation for hepatocellular carcinoma

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Introduction and aim: Our Department analyzed 1000 liver transplantations (LT) in 2012, since then experience in hepatocellular carcinoma (HCC) treatment improved.
The aim is analysis of HCC patients characteristics and outcomes after LT before and after 2012.
Material: There was 1030 transplantations between 1989-2011 (group A) and 961 between 2011-2017 (group B),
HCC was indication in group A: 107 and B: 137 respectively. Patients with pretreatment in group A: 42 (38,89%) and B: 39 (28,47%); (p=0,0851)
Females in group A / B: 35 (32,41%) / 37 (27,01%); (p=0,3569)
Age median A: 55 (51-60), B: 58 (53-62); (p=0,0003)
Etiology in group A - B: HCV 69 (56,35%) - 102 (57,98%), HBV 36 (26,52%) - 48 (30,25%), EtOH 9 (7,56%) - 20 (11,05%), others 5 (4,2%) - 11 (4,98%) (p=0,5633 chi-square)
Results:
Tumor number in group A vs B: median 2 (1-3) vs 1 (1-3) p=0,05
Biggest tumor diameter [mm] in group A vs B: median 35 (21-50) vs 30 (20-40) p=0.0581
Total tumor diameter [mm] in group A vs B: median 35 (21-50) vs 30 (13-50) p=0.0568 Wilcoxon
Locoregional therapy in group A - B: liver resection 13 (26,00%) - 3 (5,66%), cryoablation 2 (4,00%) - 0, RFA 14 (28,00%) - 18 (33,96%), TACE 21 (42,00%) - 18 (60,38%) (p=0,012 chi-square)
Angioinvasion in group A vs B: 34 (31%) vs 27 (21%) (p=0.35 chi-square)
Survival rate in group A vs B: 1 year 0.92 vs 0,86, 2 years 0,82 vs 0,80, 5 years 0,61 vs 0,59 (p=0,9159 log-rank)
Conclusions: Our experience in HCC treatment leads to qualification of older patients, but with more preferable tumor morphology. Pretreatment rate didn't change significantly, but its type does. Long term effect didn't change significantly and is very good. Comparisons between patients before and after 2012 can lead to selection bias, matching techniques are recommended.

P-502

CDCA5, transcribed by E2F1, promotes hepatocellular carcinoma cell proliferation and tumorigenesis via the Akt pathway

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Cell division cycle associated 5 (CDCA5) is a key molecular for the interaction between cohesin and chromatin in interphase. It is overexpressed in many cancers and works as prognostic marker in these cancers. The role of CDCA5 in hepatocellular carcinoma (HCC) still need to be investigated. At present, the results indicate that the expression of CDCA5 was increased in HCC tissues compared to paired normal tissues and the patients with higher CDCA5 suffered a poorer overall survival. Cell proliferation and tumorigenesis were suppressed and cell apoptosis was increased with the knockdown of CDCA5, indicating a vital role of CDCA5 in liver cancer. And E2F1 could induce the expression of CDCA5 and CDCA5 was directly transcribed by E2F1 by Luciferase reporter assay and chromatin immunoprecipitation. Furthermore, CDCA5 influenced cell behavior by inactivating the Akt pathway. These findings forecast that CDCA5 plays an crucial role in HCC progression.

P-503

Tumor recurrence treatment after liver transplantation

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Background: Recurrence of cancer after liver transplantation (LT) for malignant liver tumors is a challenging disease, as it is burdened by the aggressiveness of tumoral growth under immunosuppression.
Method: In a series of 577 liver transplants performed in 506 patients, 212 had a liver tumor. All were diagnosed as Hepatocarcinoma (HCC) by radiological tests, although one resulted to be a cholangiocarcinoma, and another one a carcinosarcoma. Recurrence ot primary tumor was recorded, for patients who survived more than 3 months after transplantation.
Results: Out of 190 patients transplanted for the diagnosis of HCC, 17 had a tumor recurrence (9%). Two were not HCC. Three patients are alive at 62, 44 and 26 months of transplantation.
Recurrences affected the lung in 10 patients, liver in 6, liver hilum lymph nodes in 4, peritoneum in 3; and retroperitoneal lymph nodes, kidney, subcutaneous, adrenal and bone, 1 of each,
Different combinations of mTOR inhibitors and sorafenib were used as medical treatment. One case was treated with percutaneous ablation, later resected; and another one with chemoembolization, both because of hepatic recurrence.
Four recurrences were resected, all as R0, but three of them recurred again; the other one had a liver resection of segment 7 60 days ago, 60 months after LT. The other resections were lesser omentum, liver segment 5, and pelvic tumor in rectovesical pouch.
Mean survival since transplantation was 27.5 months (range 4-62).
Conclusion: Recurrence of liver malignancies after liver transplantation represent a severe disease with worse evolution and outcome than in non-transplanted patients, due to the need of immunosuppression.

Poster Round II, Session 1, 2, 3: Pathology

P-504

Endothelial cell cytoskeleton rearrangement (ECCSKR) and endothelial to mesenchymal transition (EndoMT) in liver allografts following acute rejection (AR): its significance on the liver fibrosis

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Background: Endothelial cell (EC) cytoskeleton is critical for EC adhesion and permeability. CSKR initiates permeability and influx of leukocytes which in turn leads to increased cytokine expression that stimulates EndoMT. First, we evaluated the impact of AR on the development of ECCSKR and EndoMT, and then showed their influence on the development of liver fibrosis.
Methods: A total of 66 patients were included in the study. Of 66 recipients 37 had AR episodes (Group 1) while 29 did not have AR (Group 2). To show the presence of CSKR and the development of EndoMT in ECs, paxillin, CD31, α-SMA, and TGF-β were studied. The intensity of leukocytes and macrophages were graded and highlighted with CD68, TNF-α, and TGF-β. Follow-up biopsies were analyzed for the development of LF during 18 months after biopsy.
Results: The development of ECCSKR and EndoMT was found to be higher in Group 1 than Group 2 (p< 0.01). Compared to patients without ECCSKR (0.5±0.4) and EndoMT (0.6±0.5) , the mean number of AR episodes was higher in recipients with ECCSKR (1.3±1.1) and EndoMT (1.1±0.8) (p< 0.01). Patients who developed ECCSKR (90.3%) and EndoMT (86%) showed a higher incidence of LF than recipients who did not develop ECCSKR (23%) and EndoMT (16.7%) (p< 0.001). Both TNF-α and TGF-β expression showed a positive correlation with the ECCSKR and EndoMT (p< 0.001). Overall 10-year graft survival for patients with ECCSKR and EndoMT were 71% and 75% respectively, while it was 94% and 93% respectively for recipients without ECCSKR and EndoMT (p< 0.01).
Conclusion: EC activation during AR induces ECCSKR and EndoMT. With the development of ECCSKR, EC barrier may disrupt and permit leukocyte infiltration with large amounts of cytokines. ECCSKR and the mesenchymal transition of ECs with increased cytokines together induce graft loss due to the early development of LF.

P-505

Inflammation and fibrosis is observed in 34% of clinically stable adult liver transplant recipients

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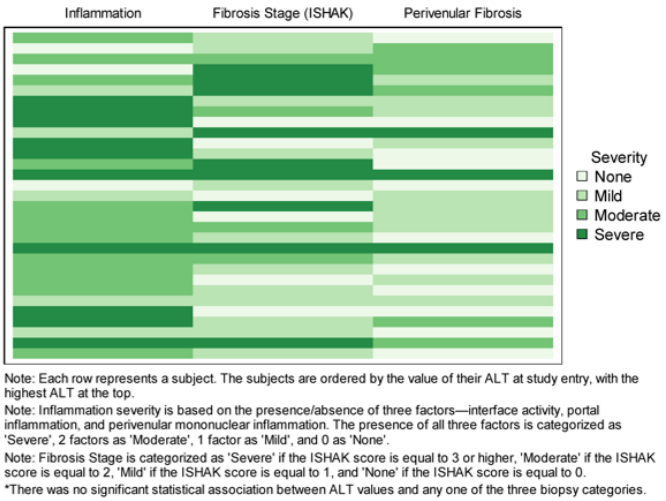
Body: OPTIMAL is a 7-center immunosuppression withdrawal (ISW) study in non-autoimmune, non-HCV adult liver transplant recipients ≥3 yrs post-transplant (tx) (NCT02533180). Subjects underwent a screening liver biopsy to exclude unfavorable histology and potentially identify tissue biomarkers of tolerance.
Methods: 91 biopsies have been performed. To meet histologic eligibility, biopsies had to be absent of or have mild portal and/or interface inflammation, and/or fibrosis; and be absent of centrizonal and perivenular inflammation, arteriopathy, and bile duct changes (damage, ductopenia or biliary epithelial senescence). Histologically eligible and ineligible subjects were compared using Fisher´s exact or Wilcoxon rank sum tests.
Results: 31/91 subjects were ineligible due to inflammation (n=17) and/or fibrosis (n=9), or bile duct damage (n=3), or arteriopathy (n=3). Figure 1 shows the distribution of inflammation and fibrosis in the ineligible subjects based on their study entry ALT value. No significant differences were observed between the 2 groups in terms of cause of liver failure, sex, race, immunosuppression type (CNI alone or CNI plus a low dose MMF or prednisone), time post-tx, ALT, GGT, or donor type, age, or sex. Eligible subjects were significantly older at tx (56 vs. 48, p=0.0030) and enrollment (64 vs. 54, p=0.0006), and had a higher frequency of steatohepatitis (52% vs. 10%, p=0.0001). The presence of steatohepatitis was associated with older age (at tx, p=0.0056; at enrollment, p=0.0015).



Note: Each row represents a subject. The subjects are ordered by the value of their ALT at study entry, with the highest ALT at the top.
Note: Inflammation severity is based on the presence/absence of three factors—interface activity, portal inflammation, and perivenular mononuclear inflammation. The presence of all three factors is categorized as 'Severe', 2 factors as 'Moderate', 1 factor as 'Mild', and 0 as 'None'.
Note: Fibrosis Stage is categorized as 'Severe' if the ISHAK score is equal to 3 or higher, 'Moderate' if the ISHAK score is equal to 2, 'Mild' if the ISHAK score is equal to 1, and 'None' if the ISHAK score is equal to 0.
*There was no significant statistical association between ALT values and any one of the three biopsy categories.

[Figure 1. Ineligible Subject Biopsy Findings]

Conclusion: 1/3 of biopsies from long-term, stable liver transplant recipients harbored subclinical inflammation and/or fibrosis. Increased recipient age at tx and enrollment, but not time from tx, correlated with histologic eligibility. Eligible biopsies were also more likely to have steatohepatitis and coincide with increased age. The natural history and significance of these biopsy findings is unknown. We plan to further analyze correlations of these observations with study outcomes.

P-506

Pathology of incidental hepatocellular carcinoma in explanted livers and their prognostic significance

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Background: The impact of incidentally detected hepatocellular carcinoma (iHCC) in explanted livers on the prognosis of the patients undergoing liver transplantation (LT) remains controversial.
Methods: Explant pathology reports of all adult patients who underwent LT in our centre between August 2009 and March 2018 were reviewed for detection of iHCC. Detailed pathology of identified iHCC and the outcomes of these patients were studied.
Results: The study included 748 adult LT including 159 deceased donor and 545 living-related LTs. The primary indication for LT was HCC in 147 patients. Among the remaining 601 patients, HCC was detected in the explanted livers of 34 patients. Four of these 34 patients were found to have HCC on review of pre-LT imaging and were classified as "Missed HCC".
31 were classified as iHCC constituting 4.1% of all adult LT. There were 27 men and 4 women with median age of 54 years. NAFLD (43.3%), and viral hepatitis (26.7%) were the most common etiologies. Median (range) of number of HCC nodules were 1(1-5) and median (range) HCC nodule size was 10 (3-35) mm. Majority of iHCC were well differentiated tumor (73%) and micro-vascular invasion was present in only four patients (13%). All but one patient (96.7%) had iHCC within Milan criteria. Five-year cumulative overall survival was 96.7%. No tumor recurrence was observed in the iHCC cohort over median follow-up of 16 months (6-65 months).
Conclusions: Incidence of iHCC in explanted livers is low and those not visualized on pre-operative imaging are early-stage tumors that do not adversely impact medium term prognosis. Further long-term followup is necessary to clearly evaluate the need for post-transplant surveillance in this cohort.

P-507

Etiology of liver dysfunction after transplantation in children with metabolic disorders

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Background: The prognosis for children with metabolic disorders (such as urea cycle disorders) after liver transplantation (LT) is said to be good. We examined the pathogenesis of liver dysfunction observed soon after LT in recipients with metabolic disorders at the National Center for Child Health and Development.
Patients and methods: Of 106 children (under 18 years old) with metabolic disorders who underwent LT at our center, 36 patients who underwent liver biopsy within 60 days after LT were enrolled. The underlying diseases were urea cycle disorders (14 cases), methylmalonic acidemia (11 cases), Wilson disease (3 cases), mitochondrial hepatopathy (3 cases), and others (5 cases). The median age was 1 year 2 months. The reasons for biopsy were liver dysfunction (30 cases), ascites (5 cases), and infection (1 case).
Results: The main findings of graft liver biopsy were diffuse steatosis (21), rejection (7), infection (5), and others (3). Of 21 cases

of graft biopsy showing steatosis, all the donor livers originally showed no steatosis or only mild steatosis. The liver function improved immediately after biopsy in 18 of 21 cases that showed diffuse steatosis. Continuous liver dysfunction and graft liver steatosis was seen in only one case.
Conclusions: The major cause of liver dysfunction soon after LT in recipients with metabolic disorders was steatosis. Steatosis might have been due to the excess load on the graft liver from sudden normalization of metabolic pathways after LT, and it was considered to be transient. The risk of rejection soon after LT was low in recipients with metabolic disorders.
It is important to take a liver biopsy and examine the cause of liver dysfunction to avoid administration of excess immunosuppressant and select the right therapy for recipients with metabolic disorders.

P-508

Combined liver and kidney transplant in recurrent acute intermittent porphyria

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Background: We report a rare case of Acute Intermittent Porphyria (AIP) successfully treated with combined liver and kidney transplantation (CLKT). Early evaluation for liver transplantation (LT) should be considered in select patients.
Case description: A 58-year-old-woman diagnosed with AIP at 40-years-old in 1999 with acute attacks characteristic of intermittent abdominal pain, peripheral neuropathy, and syncope. Urine porphobilinogen was elevated (98.7 mg/24hrs, normal 0-4). Mutation analysis by DNA sequencing identified a missense mutation, R173W in HMB-synthase gene alleles. Delta aminolevulinic acid was elevated (31.4 mg/24hrs, normal 0-7). Initially, hematin infusions were initiated as needed with symptomatic improvement. Ten years later, acute attacks were more frequent prompting infusions twice weekly. She subsequently developed Stage 4 CKD, significant iron overload (ferritin 1,101 ng/mL, normal 10-300), elevated hepatic venous pressure gradient (15 mmHg, normal 5-10) consistent with portal hypertension, elevated liver enzymes, and splenomegaly. Phlebotomy was discontinued due to precipitation of acute attacks. Liver biopsy showed increased iron deposition without inflammation or fibrosis. Successful CLKT was performed in 2018. No signs or symptoms of hepatic artery thrombosis. Post-operative course was uncomplicated with clinical and biochemical resolution.
Discussion: Impaired hepatic enzymatic activity of porphobilinogen deaminase is responsible for effects in AIP. Indications for LT include recurrent, medically nonresponsive acute attacks impairing quality of life (QOL), acute life-threatening attacks of AIP, and poor venous access limiting hematin use. Progressive renal dysfunction prompted transplant evaluation resulting in successful CLKT in this case. LT has been successful in most cases, immunosuppressive therapy well tolerated with improved QOL. To-date there were 10 cases of LT outside the United States (US). This case is probably one of the first reported successful cases of LT in the US. In conclusion, prompt evaluation for LT in select patients with AIP should be considered before permanent or irreversible damage occurs.

Poster Round II, Session 1, 2, 3: Radiology/Interventional Radiology/Molecular Imaging

P-509

Non-invasive diagnosis model for pancreatic cystic tumors based on machine learning-radiomics using contrast-enhanced CT

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Background: To establish and validate a radiomics diagnosis model for classification of three subtypes of the pancreatic lesion, including intraductal papillary mucinous neoplasm (IPMN), solid-pseudopapillary neoplasm (SPN) and pancreatic cystadenoma (PCN).
Methods: The contrast-enhanced (CECT) images and clinical parameters of 134 pathological proven pancreatic cystic tumor patients were retrospectively collected, including IPMN (n=40), SPN (n=47) and PCN (n=47). All patients were randomly split into the training cohort (n=90) and independent validation cohort (n=44). A total of 468 radiomics features were extracted. The highly inter-correlated radiomics features were excluded, and recursive feature elimination (RFE) algorithm was used for further feature selection. Supporting vector machine (SVM) and random forest (RF) methods were used to construct the diagnosis model based on selected features. The diagnosis accuracy in the training set and validation set was calculated to evaluate the performance of both diagnosis models.
Results: Eighty-two radiomics features (inter-correlation coefficient of less than 0.75) were selected. Sixteen radiomics features, and eight clinical parameters, including age, gender, tumor location, tumor number, ALT, AST, CEA and fasting blood glucose, showed a significant difference between IPMN, SPN and PCN. Utilizing the RFE algorithm, six radiomics features and six clinical parameters were demonstrated essential for model construction. An SVM model with a linear kernel was constructed showing diagnosis accuracy of 82.2% in the training dataset and 81.8% in the validation dataset. The built RF model showed diagnosis accuracy of 100% and 81.8%. Both SVM and RF model can identify IPMN, SPN and PCN with high diagnostic accuracy.
Conclusion: Our study suggests CECT-based radiomics model can serve as a diagnostic tool for preoperative diagnosis for IPMN, SPN and PCN patients in a non-invasive, convenient and accurate way, thus facilitating evidence-based medical decision making.

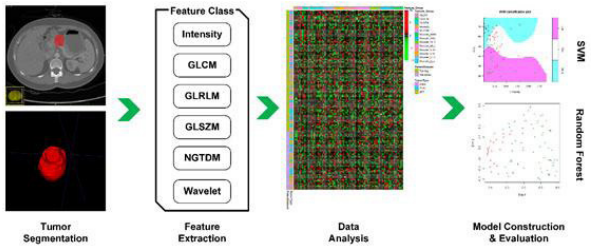


Figure 1 Radiomics Procedure

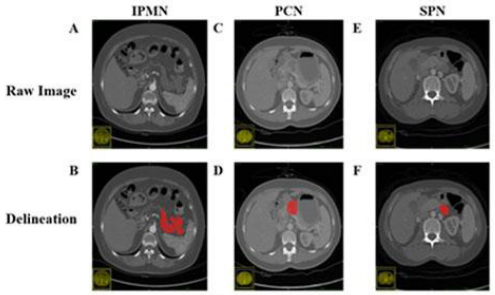
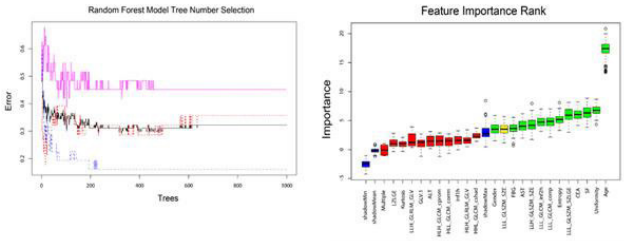


Figure 2 Raw CT Image and Delineation



[Figure]

P-510

Hepatic venous angioplasty in pediatric liver transplantation

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Background: Our aim in this study was to evaluate long-term efficiency of hepatic venous balloon angioplasty (BA) and stent placement (SP) for hepatic venous outflow obstruction (HVOO) in pediatric liver transplantation (LT).
Methods: From January 1999 to September 2016, 262 pediatric patients underwent LT at our hospital. Ten were diagnosed with HVOO, which included 8 living donor grafts and 2 split liver grafts. BA and SP were used in management of these 10 patients with HVOO. After intervention, Doppler ultrasound (DUS) was the major follow-up modality for comparing efficiency of BA and SP.

Results: The incidence of HVOO was 3.8% (10 of 262) in our pediatric LTs. Of the 10 HVOO cases, 5 had SP, 3 had BA once, 1 had BA twice, and 1 had BA twice along with SP. The patent hepatic vein was maintained after a mean follow-up of 7.4 (range, 0.04e17) years. Recurrent rate of HVOO after BA was 42%. Neither recurrent HVOO nor stent migration occurred after SP and throughout long-term follow-up.
Conclusion: Hepatic venous SP was found to be more effective and safe than BA for treatment of HVOO in pediatric LT for long-term follow-up.

P-511

Clinical usefulness of gadoxetic acid-enhanced MRI for evaluating biliary anatomy in living donor liver transplantation

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Purpose: To determine the incremental value of T2-magnetic resonance cholangiography (T2-MRC) added to hepatobiliary-phase-MRC (T2+HBP-MRC) for evaluating biliary anatomy in living donor liver transplantation (LDLT), including evaluation of the clinical utility of T2+HBP-MRC for surgical planning.
Materials and methods: 276 donors who underwent T2 and gadoxetic acid-enhanced MRI before right hemihepatectomy for LDLT between January and December 2016 were retrospectively enrolled. Two reviewers evaluated biliary anatomy classification using T2-MRC in the first session and T2+HBP-MRC in the second session. The sensitivity, specificity, and confidence level (5-point scale) of T2-MRC and T2+HBP-MRC for variant biliary anatomy were evaluated. The agreement rates between MRC and operative cholangiography for each biliary anatomy classification and the underestimation rates for multiple bile duct openings (BDOs) for both MRC techniques were evaluated.
Results: Of the 276 donors, variant biliary anatomy was observed in 36.2% (100/276). T2+HBP-MRC showed a significantly higher sensitivity for diagnosing variant biliary anatomy than T2-MRC alone (99.0% [99/100] vs. 89.0% [89/100], p=0.006), with better observer confidence level (4.9 ± 0.3 vs. 4.6 ± 0.7, p< 0.001) and inter-observer agreement (kappa, 0.902 vs. 0.730). Compared with T2-MRC alone, T2+HBP-MRC provided significantly higher agreement with operative cholangiography in biliary anatomy classification (98.6% [272/276] vs. 89.9% [248/276], p< 0.001), and significantly lower underestimation rate for multiple BDOs (5.8% [16/276] vs. 9.4% [26/276], p=0.002).
Conclusion: In the diagnosis of variant biliary anatomy and the provision of information for accurate surgical planning, T2+HBP-MRC is more useful than T2-MRC alone.

P-512

Imaging diagnosis of biliary complications of ABO-incompatibility in living donor liver transplantation

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Background: To evaluate the imaging findings of biliary complications in patients with ABO-incompatible (ABOi) living donor liver transplantation (LDLT), with emphasis on ultrasound and MR cholangiography results, and to evaluate clinical outcomes.
Methods: A retrospective analysis of 34 patients with ABOi LDLT from December 2009 to March 2018 was enrolled in the study. After LDLT, patients were followed up daily for two weeks and every three months after discharge. MRI was scheduled if ultrasound imaging results or clinical presentation suggested biliary complications. The types of biliary complications on MRI were classified into type A (diffuse) and type B (anastomotic stenosis).
Results: In routine ultrasound follow-up, 8 (23%) patients had abnormalities including diameter of IHD larger than 3mm or fluid collection. Eleven patients (32%) were found to have abnormal liver function in suspected biliary problems. Finally, Final MRI confirmed that 5 patients (15%) were type A, as known as diffuse ischemic ABOi cholangitis and 3 of them requested intervention treatment, including ERBD and PTCD. Type B biliary anastomotic narrowing was found in 7 patients (20%) and all of them received further intervention treatment.
Conclusion: Typical ABOi diffuse irregular IHD dilatation was found in 15% of patients and intervention was required in the case of abscess formation or recurrent cholangitis. However, even with intervention management, their results are not satisfactory. Doppler ultrasound diagnosis of biliary complications is always under estimation. MR cholangiography is necessary for clinically suspected biliary complications. In addition, the differential diagnosis of biliary complications is mandatory for interventional procedures.

P-513

Pre-operative CT and sequential surgeon-lead intra-operative Doppler measurements can predict the need for interposition vein grafting in pediatric liver transplantation for biliary atresia

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Background: Atretic portal vein (PV) in biliary atresia (BA) can complicate liver transplantation (LT). Our protocol includes sequential intra-operative Dopplers performed by the surgeon at four time-points during LT(after portal reperfusion, arterial anastomosis, bile duct reconstruction, abdominal closure) to repeatedly assess graft vascularity and take corrective measures. We present our experience of dealing with atretic PV during LT and means of predicting the need for interposition vein grafting (InVG).
Methods: Children who needed InVG during LT for BA were identified from a prospective database. Preoperative CT scans were reviewed for possible predictors for InVG. Intra-operative decision-making and postoperative outcomes were analysed.
Results: 118 children underwent their first LT for BA between Jan 2010 and June 2018. 18 (15%) children needed InVG interpositioned between the recipient SMV and graft PV. Median (Inter-quartile-range) age in the study cohort was 11 months (9,12), median weight 7 Kg (5.5, 9) and median GRWR 4.0 (3.0,4.5).
10 children underwent primary InVG due to findings of atretic PV with poor flow. Six children underwent standard portal anastomosis initially, which was converted to InVG following intra-operative Doppler showing absent portal flow or flow less than 10cm/sec. Children in these two groups recovered well with no mortality though the conversion group had higher transfusion requirement. Two children needed re-exploration for PV thrombosis within 48 hours following standard portal anastomosis and were converted to InVG. One child in the third group died due to sepsis related complications.
Consistent indicators on preoperative CT scan for the need of InVG were PV diameter less than 4mm, presence of large draining coronary vein and a hepatic artery larger than PV.
Conclusion: Careful review of pre-operative CT and repeated surgeon-lead intra-operative Doppler measurements can help identify high-risk portal vein anastomoses and aid decision-making to convert to an InVG.

P-514

Tips placement after orthotopic liver transplantation (OLT): still building the "niche". Preliminary results of a single centre experience

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Background: Data on TIPS placement after OLT are still limited,but the following issues seem to be challenging:
1. Technical feasibility might be compromised due to anatomical changes after transplant;
2. Potentially enhanced neurological and renal toxicity under immunosoppression;
3. Long term survival is still unclear and may be affected by the leading indication for TIPS.
Aim: Evaluate the outcome of TIPS procedures after OLT at out Centre.
Methods: Since 2002,11 pts have undergone TIPS placement after OLT at our center.This population was prospectively followed until last clinical visit,reOLT or death.
Results: The clinical features of the population are summarized in **Table 1**.All HCV(+ve) pts developed a recurrent HCV infection(36%) while,in the remaining,a vascular disorder occurred:SOS/VOD-45%;PVT- 18%.Indications for TIPS were:Refractory ascites(RA)-45% and Clinically Significant Portal Hypertension(CSPH) without RA-55%. In the latter,time to TIPS was shorter-151.5 d[16-316]- than in the others-104 d[19.7 - 188.3];log rank=0.6.This data may reflect the trend to anticipate p-s shunt insertion before refractory ascites arise.All of the stents were covered with a median size of 8 mm.The procedure was technically feasible in 9 pts and only in two(18%) a second attempt was necessary.Onset of HE was an isolated event(9%). None developed renal failure or worsening of pre-existing mild impairment.Four pts underwent re-OLT(CSHP-33%;RA-40%).The median OS was:10.1 y[5.8-14.1]and dropped to 7.4 y[3.7-11.2]when re-OLT pts were censored.Finally,the median OS(included re-OLT)was stratified according to the main indications for TIPS: the course of pts with RA was significantly worse than in the others (RA group-4.7y[1.2-8.3] vs CSPH group-14.2y[10.2-18.3];log rank=**0.04**).
Conclusion: Our study suggests a satisfactory technical feasibility of TIPS after OLT.None developed renail failure.The rate of HE was very low;therefore,the potential effect of CNI on neurological complication seems to be not relevant.In pts who developed RA and without any perspective of re-OLT,indication for TIPS should be accurately weighted given the poorest outcome observed in this category.

Baseline clinical characteristics of the population	
Male: n-%	9- 81%
Age: median [IC]	60 [48-64] y
Main blood group (A): n-%	6- 55%
Meld at OLT: median [IC]	20 [10-28]
Indication to OLT: (n-%)	
• ESLD	6- 55%
• HCC	5- 45%
Etiology of liver disease: n-%	
• HCV	4- 36%
• HBV	2- 18%
• Alcohol	3- 27%
• Others	2- 18%
Recurrence of primary liver disease: n-%	4- 36% (all HCV)
Vascular disorders: n-%	
• VOD/SOS	5- 45%
• PVT	2- 18%
Re-OLT: n-%	4- 36%

[Baseline clinical features of the population]

P-515

Comparison of PV- and HV- based semiautomated liver segmentation for estimated volume of right hemiliver graft in potential live liver donor

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Background: Preoperative estimation of graft weight is a mandatory step before living donor liver transplantation (LDLT). There are several methods of the hepatic segmentation for estimation of right hemiliver graft volume in computed tomography (CT) hepatic volumetry. The purpose of our study is to compare the reproducibility and accuracy of portal vein (PV)- and hepatic vein (HV)- based surgical planning using semiautomated liver segmentation program for the assessment of estimating graft volume using actual graft weight as a standard of reference in live liver donors.
Method: This retrospective study was approved by our Institutional Review Board and the requirement for informed consent was waived. A total of 52 live liver donor candidates who underwent preoperative liver CT were reviewed. Two radiologists performed the hepatic segmentation using a semiautomatic analysis program based on the PV and HV territory (CTV_{PV} and CTV_{HV}), independently, to obtain the estimated volume of right hemiliver graft (GV_{PV} and GV_{HV}). Inter-observer agreements of CTV_{PV} and CTV_{HV} were assessed using intraclass correlation coefficients (ICC) and Bland-Altman analysis. The accuracy of liver graft estimation was assessed by absolute difference (AD) and percentage of AD (%AD) between preoperatively estimated graft weight and intraoperatively measured graft weight.
Results: Inter-reader ICC for CTV_{PV} (0.995[95% confidence interval:0.991 to 0.997]) was higher than that for CTV_{HV} (0.951[0.917 to 0.972]). Inter-reader repeatability was -0.62± 15.93g (bias±1.96 SD)(95% limits of agreement:-31.85g to 30.60g) for CTV_{PV} and -13.45 ± 43.23g (-98.18g to 71.28g) for CTV_{HV}. Both of CTV_{PV} and CTV_{HV} showed similar accuracy in liver graft estimation (AD = 83.61±66.80g [65.01g to 102.2g] for GV_{PV} vs. 70.43±55.66g [54.93g to 85.93g] for GV_{HV} [P=0.0685]; %AD = 12.31±10.61% [9.35% to 15.26%] for GV_{PV} vs. 10.48±9.49% [7.83% to 13.12%] for GV_{HV} [P=0.0587]).
Conclusion: CTV_{PV} showed higher reproducibility with similar accuracy for estimation of right hemiliver graft volume, compared with CTV_{HV}.

P-516

Microvascular invasion in hepatocellular carcinoma: is it predictable with quantitative CT parameters?

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Microvascular invasion (MVI) is well known to negatively influence outcomes following surgical treatment of hepatocellular carcinoma (HCC). The aim of this study was to investigate whether quantitative measurements of dynamic computed tomography (CT) could be useful in predicting MVI in HCC.
Two hundred surgically proven HCCs from 125 patients, who underwent to liver transplantation (LT) or surgical resection were retrospectively analyzed. We measured regions of interest (ROIs) of lesions and areas of adjacent liver on pre-contrast, arterial, portal, and equilibrium phase images. Enhancement profiles were analyzed and compared with histopathological references of MVI.
Of the 200 HCCs, 77 (38,5%) had evidence of MVI on histopathological analysis. There was no statistically significant difference in percentage attenuation ratio - PAR (defined as 100 x ratio of attenuation of adjacent liver to that of the lesion) between HCCs

with MVI and those without MVI in portal (median attenuation ratio, 114.7 for MVI and 115.8 for no-MVI) or equilibrium (median attenuation ratio, 126.7 for MVI and 128.2 for no-MVI) phases. There was also no statistically significant difference in relative washout ratio - RWR on portal and equilibrium phases between HCCs with MVI and those without MVI (realtive washout, 15.0 for MVI and 8.2 for no-MVI on portal phase, and 31.4 for MVI and 26.3 for no-MVI on equilibrium phase). Attenuation change in nodules with and those without MVI also had no statistically difference (attenuation change, 35.28 for MVI and 29.62 for no-MVI on arterial phase, 8.56 for MVI and 8.39 for no-MVI on portal phase, and 14.56 for MVI and 14.81 for no-MVI on equilibrium phase).
There was no relation of preoperatively dynamic CT quantitative parameters with prediction of MVI for HCCs. All tumor characteristics failed to predict MVI.

P-517

Long-term recanalization of complete biliary enteric occlusion by magnetic compression anastomosis in living donor related liver transplant patients: radiologic, endoscopic and pathologic correlation

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Background: High grade biliary strictures and occlusions after right lobe living donor liver transplantation (RLDLT) are a significant challenge for treatment endoscopically and percutaneously. Magnetic compression anastomosis (MCA) may offer an effective, minimally invasive treatment for refractory high grade benign biliary strictures and occlusion. Magnetic compressive forces lead to gradual tissue necrosis within the magnets while tissue healing occurs simultaneously at the edge of the magnet. We present two cases of magnetic recanalization of complete occlusions at the biliary enteric anastomosis in RLDLT with radiologic, endoscopic and pathologic correlation.
Materials and methods: Two RLDLT patients with completely occluded biliary enteric anastomosis refractory to conventional treatments underwent magnetic compression recanalization. MCA was performed with Neodymium Iron Boron magnets. The Roux limb magnet was placed with the assistance of endoscopy and the biliary side magnets were placed using the existing PTC access.
Results: Within four weeks of the MCA procedure, successful recanalization of the biliary-enteric anastomosis was confirmed by cholangiogram and endoscopy. Magnets were allowed to pass through the GI tract. Either a 4Fr Kumpe catheter or 8Fr biliary drain were left in situ for access in the event of recurrent biliary stricture. Patients initially presented with recurrent biliary sepsis. After MCA recanalization of the biliary enteric anastomosis, there was reduction in the number of hospitalizations and severity of biliary sepsis.
Due to recurrent primary biliary cholangitis, repeat liver transplant was performed 33 months after MCA. The recanalized biliary-enteric anastomosis on the explant was patent. Hematoxylin and eosin staining of the anastomosis demonstrated expected changes at the biliary anastomosis with denudation of intestinal mucosa in continguity with bile duct wall.
Conclusion: Magnetic compression anastomosis can durably recanalize complete biliary enteric occlusion in living donor liver transplant patients and represents an attractive, minimally invasive management option for refractory benign strictures and occlusions.

P-518

Magnetic compression anastomosis for the treatment of biliary anastomotic stricture after orthotopic liver transplantation

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Background: Magnetic compression anastomosis (MCA) is a revolutionary, minimally invasive method of performing choledochocholedochostomy without using surgical techniques in patients with biliary anastomotic stricture(BAS). Herein, we describe cases of MCA for complete BAS after orthotopic liver transplantation(OLT), which could not be treated with conventional ERCP or PTBD.
Patients and methods: All patients had percutaneous biliary drainage before MCA, and took cholangiography through PTBD and ERCP simutaneously. One magnet was delivered through the percutaneous trans-hepatic biliary drainage tract into the superior side of the obstruction, and the other one was advanced through the papilla endoscopically into the lower bilary duct stump. After magnet approximation and recanalization, biliary stents was placed for 6 months at least.
Results: A total of 6 patients(aged 49±6.6 years, 4 men) with BAS underwent MCA from January 2012 to June 2018. The Stricture length was 2±1.9mm, and re-canalization was achieved in all cases with 12±2.4 days. Multiple plastic stents (2 cases) or fully covered self-expansion mental stent (4 cases)were inserted into the new fistula after re-canalization. There was no recurrence after 3-64 months of stent-free follow-up in 4 cases.
Conclusion: The MCA technique is a revolutionary method of performing choledochocholedochostomy interventionally in patients with BAS, for whom the conventional procedures not available.

P-519

Virtual reality and 3D printing applications in split liver transplantation

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Virtual reality (VR) and 3-dimensional printing are complementary technologies that generate high fidelity representations of physical objects. These capabilities are well suited to enhance operations that involve complex anatomy and spatial orientation such as split liver transplantation. Using commercially available products, we generated both VR and 3-D printed models of cadaveric and living donor split liver candidates for a pediatric recipient with situs inversus anatomy.
High-resolution computed tomography imaging was obtained for donors and the recipient and DICOM files uploaded to segmentation software (IQQA®, EDDA Technology, Inc). Multi-component 3D digital objects were generated through a semi-automated process to define critical anatomic structures. After segmentation, 3D models were exported in stereolithography (STL) file format for use in VR platform (Samsung HMD Odyssey) and for 3D printing. For the donors, the left lateral segment graft was separated along with corresponding vasculature and printed on fused deposition (Ultimaker s5) and stereolithography (Formlabs Form 2) printers. The VR models allowed for simulation of split liver grafts superimposed on the model of the recipient with situs inversus anatomy. The VR experience enhanced case planning with respect to graft orientation and vascular reconstruction for the primary surgeons and served as a useful teaching adjunct for fellows and residents. The 3D models of the graft were printed to scale using hybrid materials to approximate the physical properties of the artery, veins and parenchyma. The patient was ultimately transplanted with a split liver graft from a cadaveric donor and the models generated post hoc with high degree of fidelity to the transplanted graft.
Virtual reality and 3D printing are promising adjuncts for complex transplant cases and can be generated with commercially available products.

P-520

A novel combined surgical and interventional radiological treatment of complete biliary anastomosis obstructions after right lobe living donor liver transplantation

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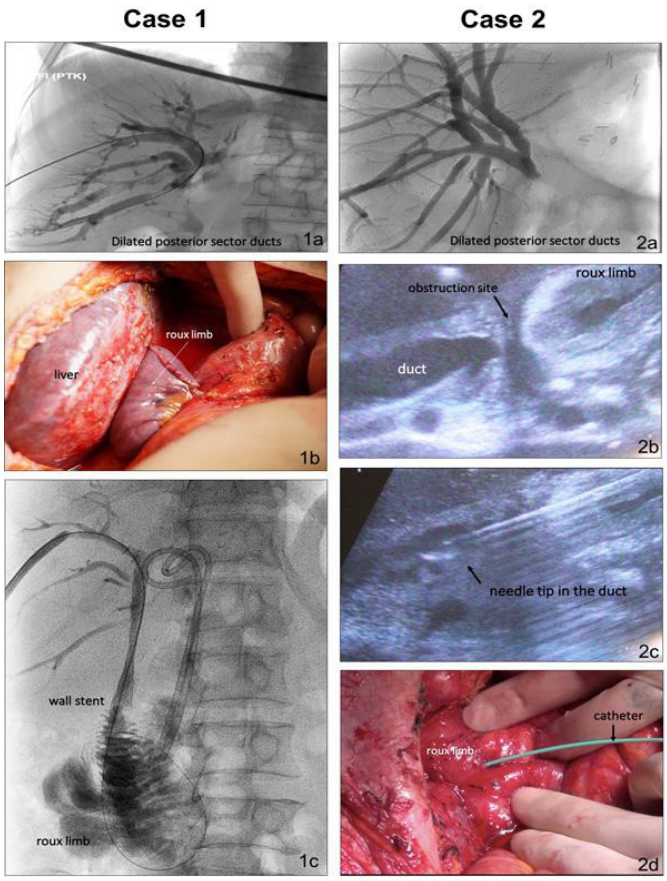
Despite much efforts to avoid biliary anastomotic stenosis, the incidence is still high after partial liver transplantation. Endoscopic, percutaneous and/or surgical approaches are used to reinstitute biliary flow. Here, we present a novel approach including complementary use of surgical and interventional modalities to treat anastomotic obstruction when percutaneous interventional attempts fail to overcome the problem. Two liver recipients presented with posterior sector duct obstruction at 9 and 12 months after transplant. Interventional specialist was invited to operating theater and joined to surgical team.
Case 1: 56y female. Following mobilization of right liver graft, from inferior surface of liver, nearest posterior sector branch was punctured under ultrasound. Guide wire was advanced to exit from the orifice of previous percutaneous drainage catheter. Then, an anastomosis between Glisson´s capsule and jejunal roux limb was performed over catheter. Postoperative period was uneventful. One month after, biliary stent was placed between the punctured biliary branch and the anastomosis to reinforce liver parenchyma in-between.
Case 2: 46y male. After identifying previous jejunal roux limb, under perioperative USG, needle was inserted from outside in the jejunum wall and passed through the fibrotic tissue blocking the anastomotic site and into the dilated duct. Then, guide wire was advanced to exit from the external orifice of previous percutaneous catheter. Proximal end of wire was routed into the lumen of roux limb. Puncture site on jejunum was secured using a single stich. Two days after the operation, biliary stent was placed following balloon dilatation of the obstructed site.
At 16 months of follow-up, both recipients have stable function with normal liver enzymes.
Conclusion: In the situation that difficult dissection at the liver hilum is encountered and a redo hepaticojejunostomy is deemed impossible, complementary surgical and interventional treatment strategies could be safely applied.



[Pre and postoperative images of Case 1 and Case 2.]

P-521

Transjugular intrahepatic portosystemic shunt for the treatment of veno occlusive disease after liver transplantation: single center experience with long term follow-up

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Backround: Veno Occlusive Disease (VOD) is a rare and life threatening vascular disease, usually seen after hematopoietic stem cell transplantation, but reported also in liver transplant (LT) recipients. Treatment is based on the use of supportive measurements (diuretics, paracentesis) or employment of anticoagulants and profibrinolitic-antithtrombotic agents like defibrodite. Recently the role of Transjugular Intrahepatic Portosystemic Shunt (TIPS) has been proposed in patients not responsive to medical treatment, however few data is available on efficacy and long term follow-up.
Aim: We present our experience in using the TIPS as treatment for VOD in LT recipients not responsive to medical treatment.
Materials and methods: Retrospectively charts of all adults LT recipients who underwent TIPS creation in a single centre, using ePTFE covered stent, in the period between 2004 and 2018 were reviewed; in 3 cases TIPS was performed as rescue treatment for VOD not responsive to medical treatment.
Results: Patients characteristics are reported in Table 1. All patients had histological diagnosis of VOD. Technical success of TIPS was 100%. No immediate or delayed complications were reported. Clinical success was achieved in all 3 patients. No patients had post-TIPS encephalopathy. TIPS revision in the follow up was performed in 2 out of 3 patients. Until today all patients are still alive and in good clinical conditions with a follow-up of 120, 39 and 17 months respectively.
Conclusions: In our experience TIPS creation was associated with good clinical outcome and low complications rate in the long term in LT recipients with VOD not responsive to medical treatment.

Patient/ Age	Gender	Cause of the LTx	Clinical presenta-tion	Type of immunso-suppres-sion	Time of the diagnosis after LT(days)	PSG before TIPS (mmHg)	PSG after TIPS (mmHg)	Outcome	Follow-up post-TIPS (months)
1 - 61 y/o	Male	HCC+HBV cirrosis	Refractory ascites	Tacroli-mus	60	17	7	Alive	120
2 - 46 y/o	Female	CBP	Refractory ascites	Tacro-limus + Azathio-prin	150	15	5	Alive	39
3 - 59 y/o	Female	Hepatic Congenital fibrosis	Refractory hydrotho-rax	Tacroli-mus	140	10	5	Alive	17

[Table 1.]

P-522

A case of migration of cyanoacrylate into portal vein after living donor liver transplantation

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Gastroesophageal varices bleeding is a major complication and carries a high mortality in patients with liver cirrhosis. Endoscopic injection of N-butyl-2-cyanoacrylate mixed with lipiodol has been used for hemostasis of bleeding gastric varices. We present a case of migration of injected cyanoacrylate to portal vein after living donor liver transplantation (LDLT).

A 53-year-old man presented with fever and abdominal pain 3 weeks after LDLT. He had received LDLT due to recurrent bleeding of esophageal and cardiac varices. Tissue adhesive (lipiodol and cyanoacrylate) was injected to cardiac varices 2 months before LDLT. Abdominal CT scan before LDLT showed high attenuation material (lipiodol/cyanoacrylate adhesive) in coronary veins with no evidence of portal vein thrombosis. However, CT scan 3 weeks after LDLT revealed high attenuation material in main portal vein. Fever and thrombocytopenia persisted. Liver enzymes were mildly elevated. Transsplenic portal vein stent was placed due to protrusion of tissue adhesive into main portal vein after obliteration of gastroesophageal varices. After portal vein stent placement, fever and thrombocytopenia has been improved and portal vein flow was intact. Treatment of gastroesophageal varices using tissue adhesive is relatively safe. However, migration of injected cyanoacrylate to portal vein should be remembered as a complication caused by tissue adhesive even after LDLT.

Poster Round II, Session 1, 2, 3: Short and Long-Term Patient and Allograft Outcomes

P-523

Associated balance of risk score - comprehensive complication index for the prediction of long-term survival after liver transplantation: starting from the ABC

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Background: In past years, several scoring systems were developed to predict early post-LT graft function. However, many of them showed poor efficiency in predicting long-term survival. Moreover, the necessity to devise a user-friendly score represents another obstacle. Indeed, a number of existing scores are composed of several, difficult to find, variables. Recently, the pre-LT Balance of Risk (BAR) and the post-LT Comprehensive Complication Index (CCI) have been created, but their external validation and integration in this setting is lacking.
This study aims to create a user-friendly score system based on the combination of a limited number of pre- and immediately post-liver transplant (LT) independent variables, in order to accurately predict long-term graft survival after LT.
Method: A Training Set was created, composed of 1,262 retrospectively analysed first-LT performed in four European Centres (Brussels, Rome Sapienza, Ancona and Padua). A Validation Set from the Karolinska Institute (N=520) was also obtained, with the intent to externally validate the results of the Training Set.
Results: The Associated Balance of risk-Comprehensive complication index (ABC) was generated in the Training Set, based on the combination of HCV status, BAR and CCI. At internal validation, the ABC showed the best performances when the risk of five-year graft loss was investigated, with an area under the curve (AUC)=0.80. The external validation confirmed the superiority of our score (AUC=0.70).
Conclusions: The ABC score shows excellent ability to predict the risk of five-year graft survival. Its predictive power is superior to the other pre- and post-LT scores. (ClinicalTrials.gov NCT03723317)

P-524

Life expectancy (LE) and loss-of-LE in HCC patients receiving liver transplantation versus hepatic resection

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Background: Both liver transplantation(LT) and hepatic resection(HR) provide potential cure for patients with hepatocellular carcinoma (HCC).Meta-analyses suggest the overall and recurrence-free survival of patients receiving LT were longer than those receiving HR.However, differences in baseline characteristics and non-negligible selection bias might still be explanatory to the above results.
Materials and methods: We conducted a population-based retrospective cohort study, retrieving information from the interlinkages of Taiwan Cancer Registry, Taiwan Mortality Registry, and Taiwan's National Health Insurance Research Database (NHIRD). The target population was patients with diagnosis of HCC and liver cirrhosis who underwent either LT or HR as the primary treatment during 2000 through 2010, and followed up till the end of 2011. Age-, sex, and calendar year of diagnosis were matched to simulate corresponding referents for the two groups for extrapolation to life time and estimation of LE and loss-of-LE.
Results: The study cohort consists of 11503 patients in HR group and 454 patients in LT group. Higher proportion of patients in the LT group had the diagnosis of hepatitis B/C virus and alcoholic related liver cirrhosis, however, more patients in the HR group had co-morbidities, such as diabetes mellitus, hypertension, coronary artery disease and renal impairment. Average age and 5-year survival were 54.4±7.6 years and 72.5% for patients receiving LT, while those of resection group were 59.2±12.0 years and 47.4%. Although life expectancy(LE) of LT was 11.61±0.15 years, which was higher than resection group (7.42±0.04), the loss-of-LE were similar, or, 14.34±0.15 and 14.81±0.04 years, respectively, indicating a potential lead time bias.
Conclusion: The health benefits of LT over HR under lifetime horizon seem to diminish after adjusting for different age distribution, or, lead time bias. More studies are warranted to corroborate the above hypothesis.

P-525

Interstitial glucose metabolism in deceased donor liver allograft during the first week after transplantation - the microdialysis study

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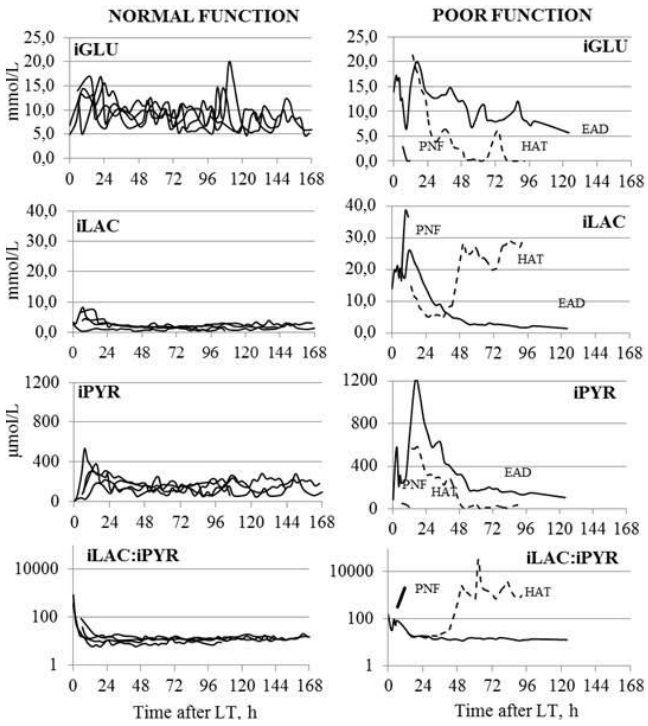
Background: Early allograft dysfunction(EAD), primary non-function(PNF) as well as vascular complications are the leading causes (up to 50%) of early post-transplant graft losses and mortality. The patterns of interstitial graft glucose metabolism, measured with microdialysis technique, may be better reflect the value of ischemic graft injury, including hepatic artery thrombosis (HAT), than routine biochemistry and coagulation tests.
Object: To identify the association between graft interstitial glucose (iGLU), lactate (iLAC), pyruvate (iPYR) concentrations, initial graft function and clinical outcomes during the first week after liver transplantation(LT).
Materials and methods: "Prospective non-randomized observational clinical study of glucose metabolism patterns in the liver graft for early diagnosis of its dysfunction after transplantation" was started in March 2018. After graft reperfusion hepatic microdialysis catheter (MDialysisAB, Sweden) was inserted in parenchyma. The samples of interstitial fluid were collected continuously during the first post-transplant week and iGLU, iLAC, iPYR concentrations were measured every 2-3 hours (MDialysisAB, Sweden). EAD and PNF were diagnosed with Olthoff, 2010 Criteria and UNOS Criteria, respectively.
Results: Seven LT from standard criteria brain-dead donors were performed. Organs were preserved in histidine-tryptophan-ketoglutarate solution with cold ischemia time 8 - 12 hours.Four different cases of post-transplant course were identified: normal graft function(n=4), EAD(n=1), HAT(n=1) and PNF(n=1).
Dynamics of graft interstitial parameters presented at the Graph1. The differences between normal values and in the cases of HAT, PNF, EAD reached 10-1.000 times.



[Normal (left column) and Poor (right column) graft function - iGLU, iLAC, iPYR, iLAC:iPYR ratio]

All patients with normal graft function are still alive (2-6mo follow-up). Patients with PNF, HAT and EAD died on 1, 5 and 23 day after LT, respectively.
Conclusion: Monitoring of interstitial glucose and its metabolites concentrations is a powerful method for initial graft function assessment and vascular complications diagnosis early after LT.
Disclosure: This study was supported by the Russian Science Foundation (grant#17-75-10010)

P-526

The association of insurance coverage with outcomes of liver transplantation in the United States

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Background: The outcomes of liver transplantation may vary according to socioeconomic factors.
Aim: To assess the association of outcomes of liver transplant (LT) candidates and recipients with the type of insurance payer.
Methods: The U.S. Scientific Registry of Transplant Recipients was used to select adults (18+) waitlisted for LT (2001-2017); patients were followed until March 2018.
Results: 177,862 LT candidates with complete data were included: 54.1±10.4 years, 64% male, 39% with chronic hepatitis C (CHC) with or without alcoholic liver disease (ALD), 19% ALD alone, 17% non-alcoholic steatohepatitis; 16% had hepatocellular carcinoma (HCC). Furthermore, 59% were primarily covered by private insurance, 21% Medicare, 16% Medicaid. After listing, 56% of candidates were eventually transplanted (mean wait 229 days), 22% dropped out of the list, and 4.5% improved. In multivariate analysis, being covered by Medicare (odds ratio (OR) (95% confidence interval) 0.80 (0.77-0.83)) or Medicaid (OR=0.74 (0.71-0.77)) was independently associated with lower chance of receiving LT (reference: private insurance). Other factors adjusted for age, gender, ethnicity, education level, MELD score, and listing status, included pre-LT hepatic encephalopathy (OR=0.85 (0.82-0.89)), having ALD (OR=0.81 (0.78-0.86); reference - CHC) or HCC (OR=2.36 (2.25-2.47)). Post-LT mortality was 11.6% at 1 year, 20.1% at 3 years, 26.8% at 5 years, 41.6% at 10 years. Both Medicare (adjusted hazard ratio (aHR)=1.21 (1.15-1.26)) and Medicaid (aHR = 1.17 (1.11-1.24)) were independently associated with higher post-LT mortality. Other predictors of post-LT mortality, in addition to age, gender, race, and MELD score, were earlier year of LT (0.93 (0.92-0.94) per year), pre-LT type 2 diabetes (1.24 (1.19-1.30)), having CHC (1.25 (1.20-1.30)) or HCC (1.17 (1.10-1.25)) (all p< 0.005). The type of insurance coverage was not associated with a risk of graft loss (all p>0.05).
Conclusions: Liver transplant candidates covered by Medicare or Medicaid have poorer waitlist outcomes and higher post-transplant mortality.

P-527

Liver transplantation for non-resectable hepatic alveolar echinococcosis: to be continued

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Introduction: Hepatic alveolar echinococcosis (HAE) is a chronic and progressive cystic liver disease caused by Echinococcus multilocularis. Hepatic alveolar echinococcosis (HAE) can invade adjacent tissues and make distant metastasis. Transplantation is an alternative in patients with non-resectable liver lesions. We presented our liver transplantation (LT) cases for HAE at previous ILTS annual meetings. Here we present new cases added to the series and report the follow up results of previous cases.
Patients and methods: Patients undergoing LT for HAE at our institution during the last 7 years were investigated. Patient demographics, clinical findings, lesion localizations, kind of LT, intra-postoperative complications and outcome were noted. Kaplan-Meier test was used to analyse survival and mortality.
Results: A total of 48 LT in 46 patients were done between November 2011- November 2018. Living donor liver transplantation (LDLT) was performed in 36 patients (78.2%) and deceased donor liver transplantation (DDLT) was performed in 10 patients (21.8%). Median follow-up was 40.1 months (6-91 months). Survival rates for 1,3, and 5 year were 76%, 70% and 69%, respectively. Rejection developed only 2 patients and 15 died during follow-up. Most of the mortalities occurred in the first 6 months. The most common cause of death was postoperative sepsis (7 patients). The most important factors affecting outcome were intraoperative bleeding and postoperative infectious complications.
Conclusion: LT for HAE is a valuable option in non-resectable HAE cases. Survival rates are acceptable.

P-528

Recipient sex interacts with primary diagnosis to affect liver transplant graft survival

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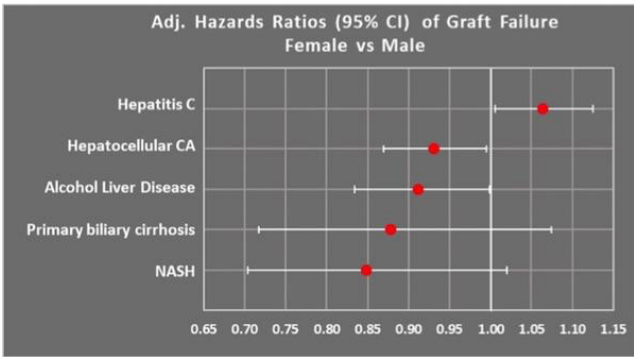
Background: While recipient sex is a commonly studied risk factor in liver transplantation, findings have been contradictory. We hypothesized that different causes of liver disease portend differential risks for male and female recipients. We aimed to evaluate differences in risk for graft loss following liver transplantation by recipient sex and primary liver disease.
Methods: The 2002-2017 UNOS database was queried for all primary liver-only transplants. We evaluated the effect of recipient sex and primary liver disease on graft survival adjusted for characteristics of the recipient and donor. Cox proportional regression (CPR) was used to test interactions between recipient sex and primary disease and derive adjusted hazard ratios (AdjHR).
Results: 27,141 females (33%) and 54,825 males (67%) underwent a first liver transplant during the study period. One, five, and ten-year graft survival rates were 86%, 73%, and 60% for females and 87%, 71%, and 57% for males. A significant interaction between

sex and primary disease was detected (p< 0.0001) indicating that sex modified the risk associated with specific primary diseases. Separate CPR models for the most common primary diseases demonstrated that recipient female sex was significantly protective in alcoholic liver disease (AdjHR:0.91, 95%CI:0.83-0.99, p=0.046) and hepatocellular carcinoma (AdjHR:0.93, 95% CI:0.82-0.99, p=0.035), but significantly detrimental in hepatitis C cirrhosis (AdjHR:1.06, 95%CI:1.01-1.13, p=0.031).

Conclusion: The impact of recipient sex on liver transplant graft survival varies depending on the primary cause of liver disease. While female sex is protective in alcoholic liver disease and hepatocellular carcinoma, it is associated with increased risk in hepatitis C cirrhosis. Additional work to characterize the mechanisms of these sex-related survival differences is essential to identify modifiable factors and improve outcomes.



[Hazard Ratios of Graft Failure by Sex and Primary Liver Disease]

P-529

Liver transplantation from octogenarian donors: Analysis of The European Liver Transplant Registry (ELTR)

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Background: Although the impact o thef donor age on liver transplantation (LTx) results has been evaluated in many studies, there are not recommendations for using an old graft. An advanced donor age alone is not a contraindication for LTx, however additional factors can affect the results of LTx from old donors. The aim of this study was to investigate the role and impact of "borderline aged" liver grafts on patient and graft survival rate after deceased LTx.

Methods: The study covers 76971 primary, full-size and adult LTx performed between 2000 and 2017 in adult (≥18 years) recipients and collected in the ELTR.

Results: After excluding the missing data 2,780 recipients of octogenarian grafts (≥80 years)-Oct-Group were compared with 74,140 recipients of young grafts (18-79 years)-You-Group. The 1-, 5-, 10- and 15-year patient survival was 84.3%, 67.6%, 46.5% and 33.5% in the Oct-Group and 85.5%, 72.6%, 59.9% and 47.4% in the You-Group, respectively (p< 0.001). The 1-, 5-, 10- and 15-year graft survival was 79.2%, 61.8%, 41.5% and 29.0% in the Oct-Group and 82.0%, 68.4%, 55.4% and 43.1% in the You-Group, respectively (p< 0.001). In the multivariate analysis significant risk factors of graft loss were: donor age (HR1.01,p< 0.001), total ischemia time (HR1.19 and 1.28 for more than 8h and 12h respectively,p< 0.001), recipient age (HR1.01, p< 0.001) and male sex of the recipient (HR1.12,p< 0.001). In the sub-analysis hepatitis C virus (HCV) positive recipients from Oct-Group had significantly worse 5-year graft survival (49.6%) compared to HCV positive recipients from You-Group (61.3)%, HCV negative recipients from Oct-Group (65.1%) and from You-Group (70.5%), p< 0.001.

Conclusion: The advanced donor age is a risk factor for inferior long-term patient and graft survival. The adequate policy is needed to allocate "borderline aged" liver grafts in order to minimize the increased risk of graft loss.

P-530

Domino liver transplants from donors with mutant transthyretin amyloidosis (ATTR): a single center experience

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Background: Mutant transthyretin amyloidosis (ATTR) is a rare, clinically heterogeneous disease characterized by heritable mutations that lead to misfolding of transthyretin (TTR) protein and multisystem disease. Liver transplantation (LT) is the most definitive option to halt disease progression. Explanted livers from ATTR patients maintain intact function and structure and therefore can be used in sequential liver transplant, otherwise known as domino liver transplant (DLT). DLT recipients are at risk of developing acquired amyloidosis due to the production of abnormal TTR by the donor liver.

Method: In this case series, we describe the clinical outcomes of DLT recipients at our center.
Results: Eleven DLT recipients were followed between January 1985 and October 2018, ten of whom, underwent DLT from ATTR donors at our center. At time of transplant, the average age was 68 (62-71) and the average MELD was 15 (8-22). The 5 year patient-survival was 82%, comparable to the overall 5-year survival in our program (79.6%). Three patients developed new onset peripheral neuropathy attributed to amyloidosis at an average onset of 8 years after transplant
(7-9). One patient was re-transplanted after 11 years due to debilitating peripheral neuropathy attributed to acquired amyloidosis.
Conclusion: DLT expands the donor pool and allows transplantation of older recipients with low MELD scores, who might not otherwise attract a donor. The patient-survival is comparable to the general transplant population, however acquired amyloidosis remains a risk that should be clearly discussed with potential transplant candidates. More data is needed to identify risk factors for acquired amyloidosis in this population.

P-531

Reduced eGFR 15~29 ml/min per 1.73 m² and persistent massive ascites after living donor liver transplantation are life threatening for recipients

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Background: Recipients with estimated glomerular filtration rate (eGFR) < 15 ml/min per 1.73 m² on renal replacement therapy (RRT) after living donor liver transplantation (LDLT) are associated with significant mortality. Sequential kidney transplantation (SKT) is a well-established measure for these patients on RRT. However, a recipient with reduced eGFR, not on RRT after LDLT, is also risky in mortality. We try to assess and share our remedies for these recipients with reduced eGFR.
Methods: We retrospectively reviewed adult primary LDLT recipients without SKT from 2005 January to 2018 June after exclusion of early death (< 14 days). The demographics and median data were collected from 3 months before LDLT and 2 weeks to 3 months after LDLT. The eGFR of renal function were stratified as I ≥ 90, II 60~89, III 30~59, IV 15~29, and V < 15 ml/min per 1.73 m². Significant factors by multivariate regression were exposed as relative risk (RR) and 95% confidential interval (CI). The other receiving SKT were as SKT group.
Results: The 975 recipients were included as non-SKT group. Two pre-operative factors as sepsis 3.434 (2.318-5.088, p< 0.001) and hepatocellular carcinoma 1.981 (1.323-2.968, p< 0.001) and four post-operative as eGFR IV 11.969(5.485-26.117, p< 0.001), persistent massive ascites (PMAS) 1.731(1.090-2.749, p=0.020), total bilirubin 1.822 (1.099-3.022, p=0.020), and asparate-transaminase 1.507(1.018-2.229, p=0.040) were significantly identified. There was no survival difference between eGFR I, II, and III. However, eGFR IV had the highest risk for mortality and worst survival in combined with PMAS. Conversely, the SKT group including 4 patients with eGFR IV not on RRT and 6 patients with eGFR V on RRT was all 100% survival.
Conclusion: Recipients with eGFR IV 15~29 and PMAS between 2 weeks and 3 months after LDLT are very high risk for mortality. SKT is an effectively life-saving remedy.

P-532

Long-term outcomes of patients with pre-tranplant portal vein thrombosis after living donor liver transplantation: experience from a high volume center

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Background: As high as 25% of pre-transplant candidates have portal vein thrombosis (PVT) and its incidence and severity are well-correlated with the degree of hepatic decompensation. Novel techniques for portal reconstruction during living donor liver transplantation (LDLT) gives the transplant surgeon numerous options to curtail challenges in establishing adequate portal inflow especially in patients with high grade PVT, but long-term outcomes of these patients are limited and contrasting.
Methods: 1,530 consecutive LDLT's were performed from June 1994 to June 2018 at Kaohsiung Chang Gung Memorial Hospital. Preoperative PVT was diagnosed using combined CT/MRI and was graded using Yerdel's classification. A total of 122 (8%) patients with pre-transplant PVT were analyzed and long-term outcomes were compared against patients without PVT.
Results: Of the 122 patients with pre-transplant PVT, 97 (80%) were adults while 25 (20%) belonged to the pediatric population. Grade 1 PVT was noted in 64 (52%), grade 2 in 44 (36%), grade 3 in 9 (7%) and grade 4 in 5 (4%) patients. Physiologic or portal to portal inflow reconstruction was achieved in 107 (88%) patients while non-physiologic inflow reconstruction was done in 15 (12%) patients, majority of which utilized an engorged spontaneous portosystemic shunt. Re-thrombosis rate for this study was 5% while the rate of

post-transplant portal vein stenosis was 7%. Overall 9-year patient survival was 85% vs. 84% in patients without PVT.
Conclusion: LDLT is safe and equally effective in patients with pre-transplant PVT with comparable long-term survival outcomes when compared to those without PVT. In high volume centers, pre-transplant PVT is no longer considered as a contraindication for LDLT except in patients with grade 4 PVT without a sizable collateral vein.

P-533

30-day readmission after living donor liver transplantation: risk factors, causes and outcomes

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Background: Complications following liver transplantation may be potentially serious and require readmission. Most reports on readmission have been about after deceased donor liver transplantation (DDLT). We aimed to determine the risk factors, rate, and outcomes of readmissions within the first 30-days after living donor liver transplantation (LDLT) and its potential impact on outcomes.
Methods: Medical records of 855 consecutive patients who underwent LDLT (12/ 2011 - 09/2018) at our center were reviewed. Ninety patients were excluded owing to pediatric recipients (n = 58) and death (n = 30) or retransplantation (n = 2) within the same hospital admission. Transplant- and non-transplant-related factors were collected during the index admission and potential readmissions.
Results: Sixty-eight patients (68/765; 8.9%) were readmitted within 30-days after LDLT, for a total of 95 readmissions (average, 1.4 readmissions per patient) and a median hospital length of stay of 4 days. The most common reasons for readmission within first 30 days after discharge were infection (52.5%), acute cellular rejection (18%), and renal insufficiency (11.3%). Risk factors for readmission included high MELD score, acute-on-chronic liver failure, preoperative renal dysfunction, presence of diabetes and albumin < 2.5 g/dL. Readmissions within 30 days were associated with decreased graft and patient survival.
Conclusion: Infection represents the most common reason for 30-day readmissions after LDLT. Readmission are associated with inferior recipient outcomes and represent a significant resource utilization. These data confirm that further efforts are needed to predict and circumvent preventable causes for readmission to improve health care costs and outcomes after LDLT.

P-534

The prognostic impacts of donor gender in deceased donor liver transplantation for hepatocellular carcinoma

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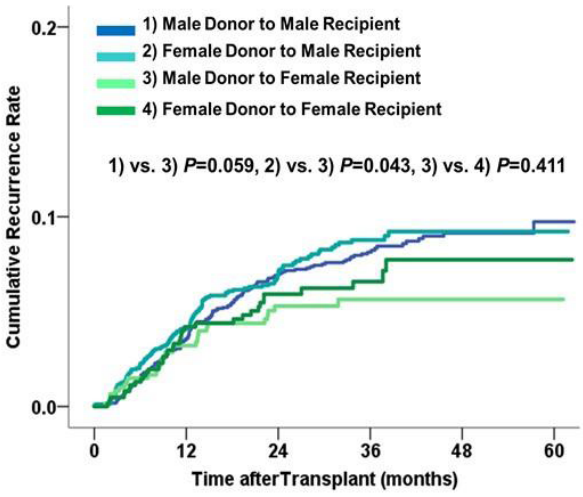
Background: Hepatocellular carcinoma (HCC) is a significantly male predominant cancer. Sex hormonal signal is considered to play some roles, although exact underlying mechanisms are not fully understood. Recently, the favorable influences on recurrence in female donor to male recipient was reported in living donor liver transplant (LDLT). This study aimed to investigate the influence of donor and recipient gender on HCC recurrence in deceased donor LT.
Methods: This study included adult patients who underwent deceased donor LT for HCC and were registered in the scientific registry of transplant recipients (SRTR) between 2012 and 2015. Donor and recipient characteristic difference according to gender as well as prognostic influence of donor and recipient gender combination were evaluated.
Results: Of 5,842 patients, 4,543 were male (77.8%) and 1,299 were female (22.2%). The number of male donors were 3523 (60.3%) and female donors were 2,319 (39.7%). Male donor to male recipient (MtoM) was 2,884 (49.4%), male donor to female recipient (MtoF) was 639 (10.9%), female donor to male recipient (FtoM) was 1,659 (28.4%), and female donor to female recipient (FtoF) was 660 (11.3%), respectively. The median tumor size/number/median AFP/ vascular invasion rate/poorly differentiation rates of MtoM, MtoF, FtoM, FtoF were 2.5cm/2/8.0/15.7%/7.9%, 2.2cm/1/10.0/14.4%/6.4%, 2.5cm/1/8.0/16.6%/8.1%, and 2.4cm/1/10.0/13.7%/6.4%, respectively. The Kaplan-Meier Curves according to the combination of genders were shown in Figure 1. The competing risk cox-regression analyses showed that hazard ratio of MtoF LT was 0.64 (95%CI; 0.42-0.98) (P=0.043).
Conclusion: In deceased donor cohort, male donor to female recipient had remarkably better prognosis which was controversial to the reported results in LDLT.



[Figure 1]

P-535

Fibrinolytic shutdown is associated with thrombotic and hemorrhagic complications and poorer outcomes after liver transplantation

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Introduction: Detrimental consequences of hypofibrinolysis, also known as fibrinolytic shutdown (FS), have recently arisen, and its significance in liver transplantation remains unknown.
Methods: To fill this gap, this retrospective study included 166 adults who received transplants between 2016 and 2018 for whom baseline thromboelastography was available. Based on percent (%) clot lysis 30 minutes after maximal amplitude, patients were stratified into 3 fibrinolysis phenotypes: FS, physiologic fibrinolysis, and hyperfibrinolysis.
Results: FS occurred in 72% of recipients, followed by physiologic fibrinolysis 20% and hyperfibrinolysis 8%. Intra- and postoperative venous thrombosis events occurred exclusively in recipients with FS phenotype. Intraoperative thrombosis occurred with an overall incidence of 4.8% and was associated with 25% in-hospital mortality. Incidence of postoperative venous thrombosis within the first month was deep venous thrombosis/pulmonary embolism 4.8% and portal vein thrombosis/hepatic vein thrombosis 1.8%. Massive transfusion of >20 units packed red blood cells was required in 12% of recipients with FS, compared to none in the other 2 phenotype groups (P = 0.014). Multivariable analysis identified 2 pre-transplant risk factors for FS: platelet count and nonalcoholic steatohepatitis/ cryptogenic cirrhosis. Recursive partitioning identified a critical platelet cutoff value of 50 × 109/L to be associated with FS phenotype. Hyperfibrinolysis phenotype was associated with the lowest 1-year survival (86%), followed by FS (95%) and physiologic fibrinolysis (97%). Infection/multisystem organ failure was the predominant cause of death; in the FS group, 1 patient died of exsanguination, and 1 patient died of massive intraoperative pulmonary embolism.
Conclusion: There is a strong association between FS and thrombo-hemorrhagic complications and poorer outcomes after liver transplantation.

P-536

Fibrinolytic shutdown is associated with intraoperative bleeding and thrombosis during visceral transplant

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Background & objective: Cirrhosis is characterized by a precarious balance of hemostasis. Concerns for detrimental consequences of hypofibrinolysis, also known as fibrinolytic shutdown, have recently arisen, and its significance in visceral transplant remains unknown.
Design & setting: To fill this gap, this retrospective study included 49 adult visceral transplants: 35 multivisceral; 10 isolated intestine; 4 modified-multivisceral, performed between 2010-2018 in a single university hospital, for whom baseline thromboelastography was available. Based on % clot lysis 30 min after maximal amplitude, patients were stratified into 3 fibrinolysis phenotypes: fibrinolytic shutdown, physiologic fibrinolysis, and hyperfibrinolysis.
Results: Fibrinolytic shutdown occurred in 57% of recipients, with higher incidence in multivisceral (69%), compared to isolated intestine (30%) or modified-multivisceral (25%) (P=.04). Fibrinolytic shutdown was associated with an increase in both intraoperative thrombosis and hemorrhage. Intraoperative thrombosis (18%) occurred only with MVT, and accounted for 36% of in-hospital mortality. Fibrinolytic shutdown was also associated with a remarkable increase in the cumulative perioperative thrombotic risk. Logistic regression identified pretransplant platelet count as a risk factor for fibrinolytic shutdown [OR 0.9, 95% CI (0.99-0.998); $\chi 2$=7.8, P=0.005). Porto-mesenteric vein thrombosis (PVT) was associated with intraoperative thrombosis in the fibrinolytic shutdown group (OR 7 [1.099-40.43]; $\chi 2$=5, P=0.04). In a predictive model (Table), coexistence of PVT and fibrinolytic shutdown increased the likelihood of intraoperative thrombosis to 50%.
Conclusions: This study reveals fibrinolytic shutdown ton be a dominant and clinically important feature of the hemostatic imbalance in recipients undergoing MVT.

Portal Vein Thrombosis	Fibrinolytic shutdown	Probability for Intraoperative thrombosis
No	No	3%
Yes	No	12%
No	Yes	18%
Yes	Yes	50%

[Predictive model for pretransplant risk factors associated with intraoperative thrombosis]

P-538

Immediate versus delayed kidney implantation in combined liver-kidney transplantation: single center, observational study

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Introduction: Patients with combined liver-kidney transplantation (LKTx) are at the risk for poorer outcomes when compared to LTx and KTx alone. Posttransplant renal failure secondary to hypotension and vasopressor usage may cause worse outcomes.
Method: 54 LKTx were performed at our center between 2016-2018. All kidneys were placed on hypothermic pulsatile pump prior Tx: 23 simultaneous KTx (at the time of LTx) and 31 delayed KTx (later time as a second operation). 74% (40/54) were on pretransplant renal replacement therapy (RRT) and continued intraoperatively in 90% (36/40) of the cases. In all patients kidney was transplanted in the right pelvis through a separate incision. Delayed kidney graft function (DGF) was defined as need of RRT in the 1st week after KTx.
Results: The median (min-max) CIT of simultaneous and delay KTx was 9.7 (7.6-14.5) and 23.2 (13.4-49.2) hours respectively (P< 0.001). The rate of DGF of 9% (2/23) in simultaneous KTx and 16% (5/31) in delayed KTx was statistically similar (P=0.4213). Dialysis dependence at 90 days was similar 4% (1/23) in simultaneous KTx versus 6% (2/31) in delayed KTx (P=0.7386). No difference in survival at 1 year was reported between simultaneous and delayed KTx of 96% (22/23) and 97% (30/31) respectively (P=0.8291).
Conclusion: If indicated by intraoperative patient's conditions, delayed KTx is a safe and clinically preferred alternative to simultaneous LKTx.
Reference:
1. Ciancio G et al. Favorable Outcomes with Machine Perfusion and Longer Pump Times in Kidney Transplantation: A Single-Center, Observational Study. Clinical and Translational Research 2010; 90 (8):882-890.
2. Ekser B et al. A novel Approach in Combined Liver and Kidney Transplantation with Long-term Outcomes. Ann Surg 2017; 265 (5):1000-1008.

	Simultaneous KTx n= 23	Delayed KTx n=31	P value
Preoperative			
Age	60 (32-74)	60 (22-76)	0.4621
Caucasian	18 (78%)	25 (81%)	0.8297
Male	12 (52%)	18 (58%)	0.6666
BMI	27 (18-36)	25 (20-36)	0.1279
Pre-transplant RRT	17 (74%)	23 (74%)	0.9814
Pre-Transplant hospitalization	7 (30%)	14 (45%)	0.2723
MELD	25 (10-43)	26 (15-45)	0.3360
TIPS	2 (9%)	7 (23%)	0.1758
Redo	1 (4%)	3 (10%)	0.4596
PVT	2 (9%)	2 (6%)	0.7555
Etiology NASH AIH PBC/PSC Viral ETOH other	 10 (43%) 0 1 (4%) 7 (30%) 2 (9%) 3 (14%)	 10 (32%) 2 (6%) 2 (6%) 7 (23%) 3 (10%) 7 (23%)	0.8108
CAD	4 (17%)	4 (13%)	0.6462
Hx of A fib	3 (13%)	7 (23%)	0.3723
DM	10 (43%)	14 (45%)	0.9020
HTN	16 (70%)	20 (65%)	0.6971
Intraoperative			
Intraoperative RRT	16 (70%)	29 (94%)	0.0194*
Surgery time	7.5 (5.5-14)	4.3 (2.31-10.6)	<0.0001*
Crystalloids	5100 (2000-10,000)	4500 (1700-14000)	0.2575
Albumin 5%	1750 (500-4000)	1125 (0-3000)	0.0208*
>10 units pRBC	10 (43%)	14 (45%)	0.9020
pRBC	9 (0-31)	9 (0-50)	0.9093
FFP	5 (0-22)	4 (0-38)	0.9160
Plts	2 (0-6)	2 (0-8)	0.9485
Cryo	0 (0-4)	1 (0-4)	0.2477
Amicar	4 (17%)	12 (39%)	0.0898
Vasopressin/Phenylephrine at the end	11 (48%)	18 (58%)	0.4556
Epinephrine/Norepinephrine at the end	4 (17%)	7 (23%)	0.6396
Post-reperfusion syndrome severe	7 (30%)	12 (39%)	0.7889
DCD	4 (17%)	4 (13%)	0.6462
DRI	1.4 (1.2-1.9)	1.5 (1.2-1.8)	0.7199
CIT liver	5.3 (4-8.5)	5.5 (2.4-9)	0.7133
CIT kidney	9.7 (7.6-14.5)	23.2 (13.4-49.2)	<0.0001*

[Immediate versus Delayed Kidney Implantation in Combined Liver-Kidney Transplantation]

P-539

Efficacy of telemedical interventional management in patients with liver transplantation - a pilot study

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Introduction: Recently, the survival rates of liver transplantation in our country are still lower than western countries, one of the important reasons is that the postoperative management and follow-up system were defective. That was lack of health education and patient's self-management ability was poor. We aimed to investigate the efficacy of our remote patient management intervention on rapid recovery, mortality and morbidity in patients with liver transplantation.
Methods: The telemedical follow-up management trial in perioperative liver transplantation was a prospective, randomised, unmasked. The patients received liver transplantation in the First Affiliated Hospital of Xi'an Jiaotong University, Shaanxi Province, China. The donors were derived from DCD. Patients were randomly assigned using a secure web-based system to either telemedical follow-up management 2 weeks plus usual follow-up or to usual follow-up only. Quantitative data were presented as mean ± SD. All statistical measurements were performed using SPSS 20.
Results: Between Jan, 1, 2015, and Oct, 31, 2018, 110 patients were randomly assigned to telemedical management (n=60) or usual follow-up (n=50). Of these 110 patients, 52 in the telemedical management group and 50 in the usual follow-up group started their assigned care. The hospitalization days, hospital costs and hospital readmission rate in 30 days of telemedical management group were markedly lower than that in usual follow-up group (16.31±3.57 vs 19.12±8.45, 382502.36±35115.42 vs 408190.11±85904.12, 0.08±0.269 vs 0.24±0.431, p< 0.05). There were no difference between the two groups of age, MELD score, operation time, blood loss, transfusion amount. The death rate was 1.92%(1/52) in the telemedical management group compared with 8%(4/50) in the usual follow-up group.
Conclusions: The trial suggests that the telemedical follow-up management intervention in patients of liver transplantation, could promote rapid recovery, shorten hospitalization days, reduce hospital costs and incidence of early complication, that is important to improve long-term survival rate in patients.

P-540

Donor-recipient size mismatch has no impact on outcomes after deceased donor whole liver transplantation: a single center analysis

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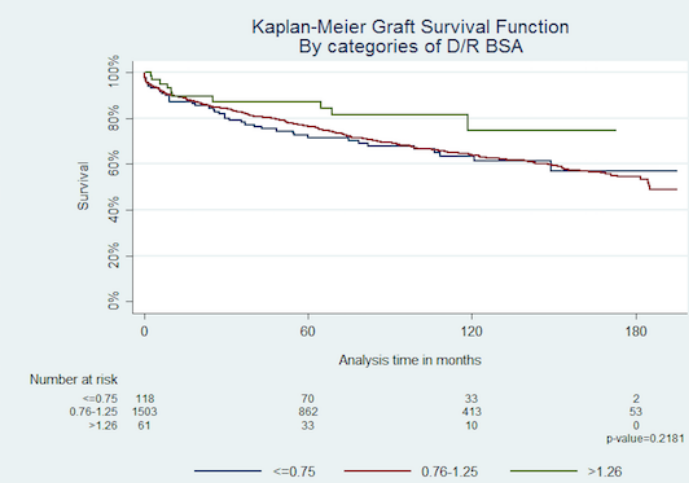
Background: Assessment of donor size by demographic variables is an important part of deceased donor evaluation prior to liver transplantation (LT). Lack of liver volumetric assessment in deceased donor LT forces transplant surgeons to correlate weight and height of donors and recipients, despite poor correlation with liver volume.
Methods: From August 2016-August 2018, consecutive liver grafts in adult LT at our center were weighed before implantation. Donor body surface area (BSA) was the best predictor of liver weight in this cohort and was used as the surrogate for liver size in a larger cohort of 1785 adult LTs. The impact of donor/recipient (D/R) BSA ratio of 1785 adult LTs (July 2001-Dec 2017) was evaluated on outcomes. Early allograft dysfunction (EAD) and graft survival were the primary endpoints. Transplants with D/R BSA ratio < 0.76 and > 1.25 were considered to have significant D/R size mismatch. Cox Proportional Hazard and multivariable logistic regression controlling for relevant donor and recipient variables were used to determine relative risk of graft failure and EAD respectively.
Results: There were 123 (7%) transplants with D/R BSA ratio < 0.76 and 68 (4%) with D/R BSA ratio > 1.25. EAD was numerically higher (41%) in transplants receiving livers from larger donors. When stratified by D/R BSA ratios (< 0.76, 0.76 - 1.25, >1.25), EAD and 1-year graft survival were comparable between the three study groups (25% vs. 28% vs. 41%; $P = 0.06$) and (86% vs. 89% vs. 90%; $P = 0.49$) respectively. Upon multivariable analysis there was no difference in the hazard for 1-year graft failure ($P = 0.72$) and in adjusted odds ratios for EAD ($P = 0.22$).
Conclusion: In whole liver transplants, donor-recipient size mismatch has no adverse impact on short- and long-term outcomes.



[Kaplan-Meier Graft Survival Function by Categories of D/R BSA]

P-541

Survival benefit of profound tumor necrosis by locoregional therapy before living donor liver transplantation for hepatocellular carcinoma

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Background: Nowadays, liver transplantation (LT) has been an established curative treatment for hepatocellular carcinoma (HCC) associated with end-stage liver cirrhosis. However, numerous efforts remains to be done to improve long-term outcome of patients after LT for HCC. Locoregional therapy that treats HCC during the time period awaiting LT emerged as an attractive strategy to reduce the risk of tumor progression in the waitlist and possible HCC recurrence after LT. The study aimed to analyze the beneficial effect of locoregional therapy on the outcome of patients with HCC upon living donor liver transplantation (LDLT), and to provide additional information for decision-making in therapeutic strategy for patient with HCC.
Methods: A total of 289 patients who had been undergone LDLT for HCC between August 2004 and March 2017 in the transplantation institute were retrospectively reviewed. The clinicopathological features of the patients regarding HCC status and locoregional therapy prior to LT were analyzed to determine the impact of pre-transplantation therapy on the outcome of patients.
Results: Overall, 240 patients (83%) had been treated by locoregional therapy before LT. The incidence of HCC recurrence had no significant difference based on pre-transplantation locoregional therapy. The HCC recurrence-free survival (RFS) regarding pre-transplantation locoregional therapy was also no significant difference, in which the 5-years RFS were 89.4% *versus* 90.6% in patients with locoregional therapy *versus* without locoregional therapy, respectively. Based on the histological examination of explanted hepatic tumors, patients who had profound tumor necrosis (≥60%) induced by pre-transplantation locoregional therapy had significant better RFS as compared with those without profound tumor necrosis (< 60%). The 5-year RFS were 96.2% *versus* 86.9%, respectively. (p=0.026)
Conclusion: The actual advantage for locoregional therapy has not been clearly demonstrated in terms of recurrence and survival after LDLT unless certain degree of tumor necrosis induced by pre-transplantation locoregional therapy could be obtained.

P-542

Donor polymorphisms predict the risk of fibrosis after liver transplantation

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Background and aims: Liver fibrosis (LF) is becoming a common indication after liver transplantation (LT). Some genes polymorphisms have been reported as genetic biomarker for LF or cirrhosis. However, relatively little is known regarding those polymorphisms effect after LT. In this study, we aim at evaluating the association between donor gene polymorphisms and LF among Chinese patients after LT.
Patients and methods: A total of 232 patients undergoing LT were included. Twenty-three single nucleotide polymorphisms closely associated with LF were genotyped and analyzed.
Results: Seven donor polymorphisms (rs430397, rs909253, rs2856718, rs1052133, rs1695, rs12304647, rs1800630) were found to be significantly associated with LF after LT by univariate analysis. In multivariate analysis, donor rs1052133, rs12304647 and rs1800630 genetic variation (OR = 0.42, p = 0.014; OR=3.48, p=0.003; OR=2.97, p=0.007), blood tacrolimus levels at maintenance (more than 2 years after LT) >7ng/ml (OR =7.48, p < 0.001), and post-transplant diabetes mellitus (OR = 7.50 p = 0.001) were identified as independent risk factors of LF.
Conclusion: Donor rs1052133, rs12304647 and rs1800630 polymorphisms are associated with an increased risk of LF after LT and has a potential clinical biomarker for the prediction of LF after LT.

Table The risk factors of fibrosis after liver transplantation

Donor SNP characteristic		Univariate OR (95% CI)	Univariate P*	Multivariate OR (95% CI)	Multivariate P*
rs430397	C/C				
	C/T	/	1		
	T/T	/	1		
rs909253	G/G				
	G/A	0.91 (0.36-2.26)	0.832		
	A/A	3.0 (1.17-7.67)	0.022		
rs2856718	T/T				
	C/T	0.52 (0.25-1.11)	0.092		
	C/C	0.40 (0.13-1.25)	0.115		
rs1052133	G/G				
	C/G	7.54 (2.53-22.47)	<0.001	9.84 (2.39-40.37)	0.002
	C/C	7.5 (2.18-25.81)	0.001	5.19 (0.96-28.04)	0.056
rs1695	A/A				
	G/A	0.36 (0.14-0.90)	0.029		
	G/G	3.71 (0.50-27.28)	0.198		
rs12304647	A/A				
	A/C	2.91 (1.41-6.01)	0.004	3.89 (1.26-11.98)	0.018
	C/C	2.67 (0.76-9.41)	0.127	7.56 (1.03-55.22)	0.046
rs1800630	C/C				
	C/A	1.86 (0.89-3.89)	0.102	2.55 (0.73-8.86)	0.141
	A/A	3.89 (1.02-14.81)	0.047	16.56 (1.91-143.23)	0.011
Recipient characteristic					
Age >55 yr		3.06 (1.37-6.82)	0.006		
TAC at maintenance >7 ng/ml		3.98 (1.70-9.33)	0.002	6.30 (2.03-19.57)	0.001
HCC		0.43 (0.20-0.93)	0.031		
PTDM		2.99 (1.26-7.06)	0.013	6.68 (1.84-24.19)	0.004
BMI >24		0.44 (0.19-1.01)	0.053		

CI, confidence interval; TAC, tacrolimus; HCC, hepatocellular carcinoma; PTDM, post-transplant diabetes mellitus; SNP, single nucleotide polymorphism;
p* value was calculated from univariate logistic regression test; p# value was calculated from multivariate logistic regression test.

[The risk factors of fibrosis after liver transplantation]

P-543

Liver transplantation for cholestatic liver diseases in adult - a single centre experience from the Eastern world

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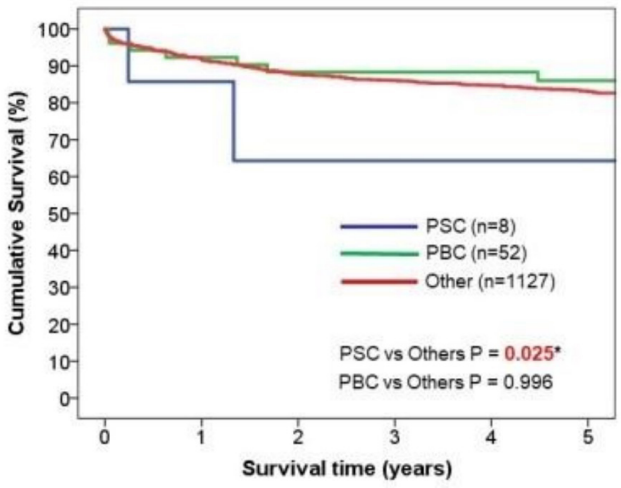
Introduction: Liver transplantation is an established therapy for primary cholestatic liver diseases including primary sclerosing cholangitis (PSC) and primary biliary cirrhosis (PBC) but it is uncommon in the Eastern world. We reviewed our single centre experience of LT for primary cholestatic liver diseases.
Method: Retrospective study of a prospectively collected database of all LT at the Department of Surgery, Queen Mary Hospital, Hong Kong was performed.
Result: From 1991 to 2018, 1187 patients underwent LT in our hospital. 52 patients (4.38%) had PBC and 8 (0.67%) had PSC. All PSC and PBC patients received prednisolone as part of the immunosuppressive regimen. For the PSC group (n=8), 2 (25%) had associated inflammatory bowel disease (IBD). 2 patients (25%) developed recurrent PSC. 2 patients (25%) required retransplantation, one for hepatic artery thrombosis and one for recurrent PSC. For the PBC group (n=52), 33 (63.5%) underwent DDLT and 19 (36.5%) underwent LDLT. None underwent retransplantation. The 1-year, 3-year and 5-year graft survival was 85.7%, 64.3% and 64.3% for PSC group, 92.3%, 88.3% and 86.0% for PBC group and 91.9%, 86.0% and 83.1% for the others group (*p=0.025* for PSC vs others, *p=0.996* for PBC vs others). The respective 1-year, 3-year and 5 year patient survival was 100%, 80% and 80% for the PSC group, 92.3%, 88.3% and 86.0% for PBC group, 92.9%, 87.0% and 84.5% for the others group. (*p=0.958* for PSC vs others, *p=0.783* for PBC vs others) (Figure 1)



[The 1-year, 3-year and 5-year graft survival of the PSC, PBC and the others group]

Conclusion: LT is associated with good long term outcome for primary cholestatic liver diseases and our results are comparable with Western world. However, recurrent PSC remained an important issue as it occurred in 25% of our study population and the optimal immunosuppressive regimen for the PSC patients are yet to be identified.

P-544

Donor hepatectomy time and implantation time increase the risk of non-anastomotic biliary strictures and allograft dysfunction after liver transplantation

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During static cold storage, livers are preserved at 4-6°C. However, this temperature is not reached during donor hepatectomy time (time needed to remove the liver from the donor body). Additionally, an abrupt rewarming of the liver occurs in the recipient whilst vascular anastomoses are being performed (implantation time). Consequently, during donor hepatectomy and implantation, grafts are exposed to subnormothemic ischemia. We hypothesized that these two surgical times trigger early complications such as Early Allograft Dysfunction (EAD) and Non-anastomotic biliary Strictures (NAS). All deceased, adult liver transplants performed between 1/2000-12/2016 were considered. The effect of donor hepatectomy and implantation time on the risk of EAD/NAS was investigated in multivariable logistic and Cox regression, respectively. An interaction analysis assessed if the effect of these surgical times varies when Donation after Circulatory Death (DCD) grafts are transplanted. Median (IQR) or numbers (%) are given. Out of 917 liver transplants, 247 (27%) developed EAD and 106 (12%) developed NAS. Donor hepatectomy time was 35 minutes (26-46), implantation time was 80 minutes (69-95). Implantation time was independently associated with EAD (adjusted OR:1.15, 95%CI:1.07-1.23, p< 0.0001), while donor hepatectomy time was non-influent. Both portal vein anastomosis time (adjusted OR:1.26, 95%CI:1.12-1.42, p=0.0001) and hepatic artery anastomosis time (adjusted OR:1.13, 95%CI:1.04-1.22, p=0.005) were risk factors of EAD. DCD grafts were not more vulnerable to implantation time. Donor hepatectomy time was independent risk factor for NAS (adjusted HR:1.19, 95%CI:1.04-1.35, p=0.01), while implantation time, vena porta anastomosis time and hepatic artery anastomosis time were not. DCD grafts had a four-fold increased risk of NAS but were not more vulnerable to the effect of hepatectomy time. During procurement, efforts should be made to shorten donor hepatectomy time and to optimize organ cooling. During implantation, graft abrupt rewarming should be prevented and the liver quickly reperfused

P-545

Liver retransplantation in adult recipients: Analysis of the Netherlands Organ Transplant Registration (NOTR)

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Background: Liver retransplantation (re-LT) accounts for up to 22% after primary liver transplantation (LT), and using donor livers for retransplantation can only be justified by successful outcome. The aim of this study was to examine the incidence, long-term outcome, and risk factors for re-LT in the Netherlands.
Method: A total of 2387 adult recipients with 2778 LTs, between 1979 and 2017, were respectively analyzed. Patient survival rates for primary LT, first, second, and third or fourth re-LT were compared. Survival rates after first re-LT according to the time interval between primary LT and first re-LT (0-30 days, 31-365 days, and >365 days) were analyzed. Multivariate analysis was performed to investigate predictors associated with retransplantation after primary LT.
Results: Of 2778 LTs, 336 (12.1%) were first, 43 (1.5%) were second, and 12 (0.5%) were third or fourth re-LT. The 5-year patient survival rates for primary LT, and first, second, and third or fourth re-LT were 74.0%, 70.8%, 63.3%, and 57.1%, respectively (P = 0.10). Survival after re-LT according to the time interval between primary LT and re-LT showed no significant differences (P = 0.12). Recipient age (≤60 years) (HR = 2.08, P < 0.001), donor after circulatory death (DCD) (HR = 1.78, P = 0.001), and cold ischemia time (CIT) >9 hours (HR = 1.48, P = 0.003) were significant risk factors for retransplantation after primary LT.
Conclusion: Good clinical outcome after first re-LT and acceptable survival after multiple re-LT were shown. Third and fourth re-LT can be justified with proper patient selection. Recipient age, DCD, and CIT were identified as risk factors for retransplantation.

P-546

Impact of MELD-Na course (Delta MELD-Na) on outcome after liver transplantation

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Background: Currently, MELD Score listing is state of the art for liver transplant recipients. Our department could show by our own institutional data and confirmed by an Eurotransplant cohort that dynamic MELD deterioration (Delta MELD) during waiting time has a significant impact on postoperative survival. Aim of this study was to analyze the risk prediction of posttransplant survival by adding recipient Sodium values to Delta MELD (Delta MELD-Na).
Method: More than 22000 patients of the UNOS data base were analyzed, who were transplanted in the US from 2012 to 5/2016. MELD-Na was calculated according to this formula
MELD - Na - [0.025 × MELD × (140 - Na)] + 140(na ranges from 125-140)
Delta MELD-Na was defined as MELD-Na at listing minus MELD-Na at transplantation: Delta MELD=MELD-Na (ON) - MELD-Na (TX)
Delta MAX was the highest MELD-Na deterioration between two observation time points.
Delta LAST was the alteration between forelast and last observation before transplantation.
Results: 69.7% of patients showed a stable MELD Na during waiting time for transplantation with a maximum increase of 4 points. In 15.4% of patients an increase of 5-9 points was observed. Further 14.8% of patients showed an increase of 10 and more points.
Statistical significant factors for posttransplant survival were MELD Na ON (p=0.007), MELD Na TX (p=< 0.001) and Delta MELD-Na and Delta MELD-Na MAX (both p=< 0.001). Delta MELD-Na LAST did not show statistical significance (p=0.35).
Conclusion: A severe deterioration of MELD- Na during waiting time results in significantly poor posttransplant survival in liver transplantation. Also temporary deterioration during waiting showed similar risk.

P-547

Body composition and morbidity following orthotopic liver transplantation - the value of quality over quantity

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Background: The significance of preoperative body composition is in the spotlight of interest in various diseases. Here we assessed the role of sarcopenia and myosteatosis as prognostic factors following orthotopic liver transplantation (OLT).
Method: The data of 225 consecutive OLT recipients from a prospective database were analyzed retrospectively (05/2010-01/2018). Computed tomography-based lumbar skeletal muscle index-L3SMI, visceral adipose tissue area-L3VAT and mean muscle attenuation-MA were calculated preoperatively using a segmentation tool (3DSlicer). Patients with sarcopenia (low L3SMI), visceral obesity (high L3VAT) and myosteatosis (low MA) were identified using predefined sex-specific cutoff values. Parametric- and non-parametric tests as well as uni- and multivariable logistic regression were used to determine the association of body composition profiles with outcome.
Results: The cutoff values of myosteatosis resulted in a good stratification of patients into low- and high-risk groups in terms of major morbidity (Clavien-Dindo-CD≥3b). Myosteatotic patients had significantly higher complication (90-days CCI 68±32 vs. 44±30, p< 0.0001) and early allograft dysfunction rates. These patients spent significantly longer time at the ICU and in hospital. The estimated costs were 44% higher compared to patient with superior muscle quality. Significant correlation was found between MA and various outcome parameters (ICU, hospital stay, CCI, costs). Cutoff values for the other body composition parameters failed to identify high risk patients and did not correlate with outcome. Multivariable analysis identified myosteatosis as an independent prognostic factor for major morbidity (2.432 OR, 1.319-4.486, p=0.004). Adding myosteatosis to the well-established Balance of Risk-BAR score resulted in the increase of the prognostic value for morbidity compared to the original BAR-score (Area-under-the-curve 0.710 vs 0.677).
Conclusion: Our results suggest the superior predictive value of muscle quality (myosteatosis) over quantity (sarcopenia) in terms of morbidity following OLT. Myosteatosis might be a valuable easy to assess novel parameter in already established outcome prediction tools.

P-548

Barriers to medication adherence in individuals post-liver transplant and with chronic liver disease: a comparison of paediatric and adult services

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Background: Barriers to medication adherence in those post-liver transplant and with chronic liver disease (LTLD) remain poorly understood. There are limited data regarding whether these barriers are different across the lifespan.
Methods: The purpose of this study was to describe medication adherence and barriers to adherence in individuals with LTLD. Eighty-three individuals (aged 12-50 years, mean= 20.0 years, SD= 7.8, 49% female) completed a questionnaire assessing adherence and medication coordination (medication storage, preparation time, type of medication, forgetting and routine). Responses were then compared between individuals aged ≤17 years and those ≥18 years.
Results: Only a third of each group reported preparing medication in advance, mainly using a pillbox. Patients ≤17 years were more likely to report that their parent/carer coordinated their medication (77%) than those ≥18 years (47%, with 45% preparing independently and the remaining 8% sharing the responsibility). Adherence was higher (90%) in patients ≤17 years than those ≥18 years (70%). Half of both groups acknowledged sometimes running out of medication, and 26% and 27% respectively reported taking their medication more frequently in the weeks running up to clinic. Most patients (77% ≤17 years and 67% ≥18 years) had a routine for taking their medication, but 55% and 45% respectively acknowledged that they sometimes forget their medication. Routine change was barrier to adherence in 48% of each group. Of particular concern was the finding that a fifth (20% and 18% respectively) reported intentional non-adherence (that on occasions they actively choose not to take prescribed medications).
Conclusion: Medication routines and barriers to successful adherence are similar in individuals aged ≤17 years and those ≥18 years. This highlights the importance of considering these factors in young adults as well as adolescent patients, in line with evidence that neurodevelopmental changes observed during adolescence continue well into the 3rd decade of life.

P-549

Delta neutrophil index as a new mortality predictor after liver transplantation

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Background: Infection is a frequent complication of both acute and chronic liver disease. Patients with liver disease have been shown to display numerous defects in the immune system, including impaired monocyte and neutrophil function. And, these infections are independently associated with poor outcomes after liver transplantation. Our objective was to evaluate the delta neutrophil index DNI), a new inflammation marker, as a predictor of survival after liver transplantation (LT).
Methods: We retrospectively evaluated the records of 712 patients who underwent LT from January 2010 to February 2018. This observational study was conducted by using a database analysis of Severance and Gangnam Severance Hospital, Yonsei University College of Medicine. DNI was checked at pre-transplantation, post-operative 1, 7, 14, and 30 days. Other clinical characteristic variables were analyzed. Statistical analysis was performed by using the T-test or chi-square test, and logistic regression analysis.
Results: Among 712 recipients, there were 500 males and 212 females. There were 277 deceased donor liver transplantations and 435 living donor liver transplantations. The mean MELD score was 16.7 ± 9.4 (0 ~ 48). There were 125 mortality cases (17.8%) after liver transplantation. Mean DNI was 1.61 at pre-transplantation, 3.94 at post-operative 1 day, 2.67 at post-operative 7 days, 1.61 post-operative 14 days, and 1.64 post-operative 30 days respectively. In multivariate analysis, DNI at post-operative 7 and 14 days were revealed as an independent prognostic factor for mortality after liver transplantation (p=0.040 and p< 0.0001).
Conclusions: The DNI is a simple and reliable predictor of patient mortality after liver transplantation.

P-550

Impact of recipient age in Combined Liver-Kidney Transplantation (CLKT): caution is needed for elderly patients ≥70 years

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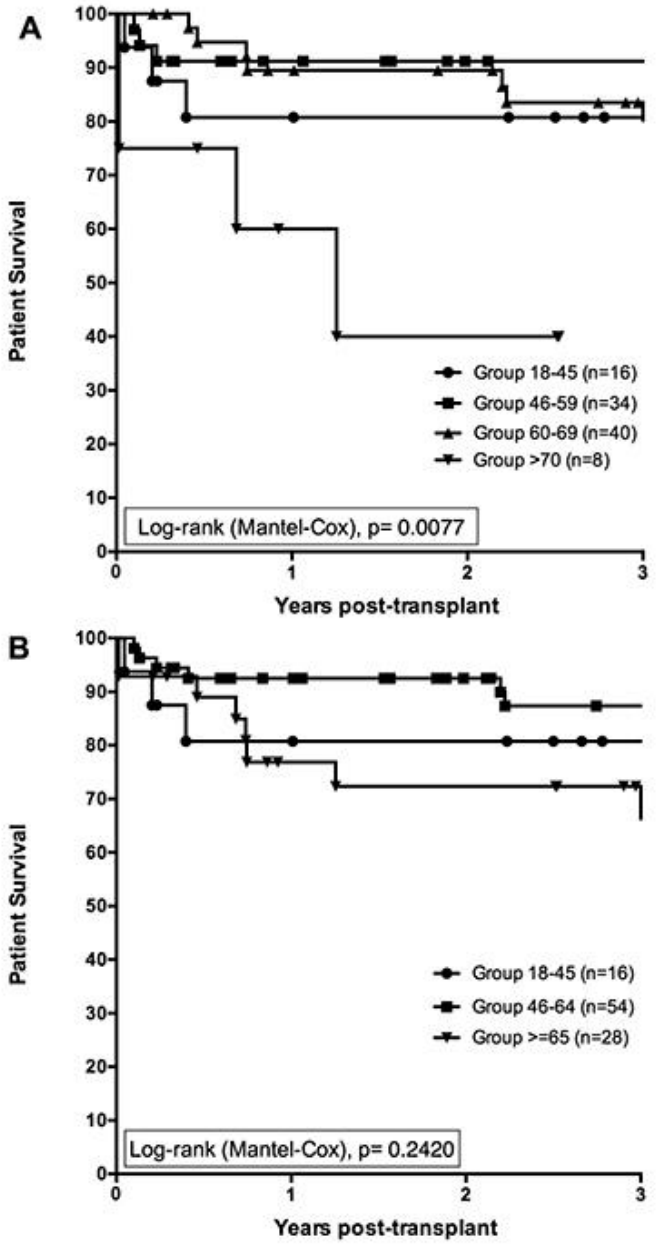
Background: Recent SRTR analysis showed that recipients ≥70 years account for 2.6% of all liver transplant alone (LTA) and do as well as younger LTA recipients, if selected carefully. Although the rate for elderly recipients in CLKT is similar (2%, 104/5194), no national or center-based data is available how elderly recipients perform after CLKT.

Methods: After we showed excellent outcomes in CLKT using delayed KT (Indiana) Approach, we now routinely delay the kidney portion of CLKT (mean CIT 53±14hours, range 20-83). Between 2007-2018, 98 CLKT were performed using the Indiana Approach. Recipients were subgrouped based on their age, such as 18-45 (n=16), 46-59 (n=34), 60-69 (n=40), and ≥70 years (n=8). 45 different variables were compared.

Results: Overall more elderly patients receive LTA at Indiana University (IU) compared to SRTR (recipients ≥70 years; 5.2% at IU vs. 2.6% SRTR). The rate of elderly recipients in CLKT at IU was 8.2% (vs. 2% SRTR). In the present study, recipient and donor characteristics were comparable between all age groups, except recipient age as expected (p< 0.01). Although patient survival at 1 and 3-year was similar in age groups 18-45, 46-59, and 60-69, it was significantly lower in recipients ≥70 years at 1-year (60%) and 3-year (40%) (Figure 1A). Recent SRTR data which compared recipient age < and >65 years in CLKT showed similar outcomes. To replicate the SRTR survival stratification, we ran an analysis using 18-45, 46-64, and ≥65 years age groups, as controls (Figure 1B). Control analysis showed that patient survival was similar among different age groups, as shown by the SRTR analysis.

Conclusion: Although LTA can be safely performed in selected elderly recipients, extreme caution is needed in recipients ≥70 years undergoing CLKT due to the magnitude of operation and expected poor outcomes.



Legend: The study is important because census.gov reported that projected increase in the population of age group ≥65 years old is 13% by 2020, 48% by 2030 and 74% by 2050. Figure 1B analyzed the same database (as Figure 1A) using different age groups. SRTR database study by *Croome et al. Ann Hepatol 2016;15:870-880* showed similar outcomes < or >65 year-old SLK recipients.

[Figure 1]

P-551

Feasibility of aorta after endarterectomy as middle hepatic vein reconstruction in living donor liver transplantation

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Introduction: Cryopreserved iliac vein, Polytetrafluoroethylene (PTFE) grafts, and cryopreserved aorta without endarterectomy have been used as middle hepatic vein (MHV) conduits for right liver graft in living donor liver transplantation, but each has advantages and disadvantages. In this study, we started to use aorta after endarterectomy (AoE) without any additional patches and checked patency after engraftment.
Method: From January 2015 to June 2018, 111 cases of adult LDLT with modified right lobe grafts using aorta after endarterectomy were performed at Asan Medical Center. Retrospective analysis of patency in these recipients were carried out and compared with control group who received iliac vein (n=436) during the same study period. All vessels were stored and prepared as cryopreservation. Patency of reconstructed MHV was assessed by computed tomography (CT) which was routinely followed at every week during in-hospital stay and at 1, 3, 6, and 12 months after LDLT.
Result: Clinically significant stenosis of MHV requiring interventional stenting was occurred in three patients (2.7%) in AoE group, not significantly different from seventeen patients (3.9%) in iliac vein group (p=0.778). Aorta after endarterectomy showed 3-month patency rate of 91.6% and 1-year patency rate of 63.5%. Mean patency time of MHV with AoE 21.4±1.9 months. When compared to iliac vein group, which demonstrated 3-month and 1-year patency rate as 90.0% and 37.3%, respectively, AoE proved superior patency outcome (p=0.001). Mean patency time of iliac vein was 19.6±2.2 months.
Conclusion: In this study, AoE showed an acceptable outcome and even better patency compared to iliac vein. Clinically significant complication of stenosis or obstruction of MHV was fairly low. Larger diameter with well-matched thickness to MHV branches, not requiring iliac artery patch, is of great advantage in AoE as interposition graft.

P-552

Persistent fibrinolysis shutdown following liver transplantation is associated with early allograft dysfunction: a therapeutic opportunity?

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Introduction: Prolonged fibrinolysis shutdown (SD; resistant to clot breakdown) after resuscitation from shock is associated with increased mortality. The impact of the duration of SD following liver transplantation has not been evaluated. We hypothesize that liver transplant recipients with SD for multiple days following surgery will have a higher rate of early allograft dysfunction (EAD).
Methods: Liver transplant recipients (2015 - 2018) consented for coagulation analysis had blood assayed using a tissue plasminogen activator (t-PA) thrombelastography (TEG). SD was defined by the t-PA TEG threshold of a lysis of 30 minutes(LY30) less than 1.6%, which was previously identified as pathologic in trauma. EAD was contrasted between SD and non-SD recipients.
Results: Sixty patients were included. The median pre-operative model for end stage liver disease (MELD) score was 19 and EAD was present in 22% of patients. Post-operative day (POD) 1 SD was identified in 62% of patients which was reduced to 32% by POD5. SD on POD1 had higher EAD rates (compared to non-SD) but not statically significant (27% vs 19% p=0.456). However, in the 25 patients with POD5 TEGs available, SD was associated with significantly higher rate of EAD (25% vs 0% p=0.041), and all of these patients were in SD on POD1.
Conclusion: Prolonged post-operative SD is associated with a higher rate of EAD in liver transplant recipients. POD1 SD resolved by POD5 in ½ of these patients, none of which had evidence of EAD supporting a potential therapeutic window to treat post-operative SD to reduce EAD.

P-553

The influence of the timing of portal vein thrombosis diagnosis on outcome in liver transplant

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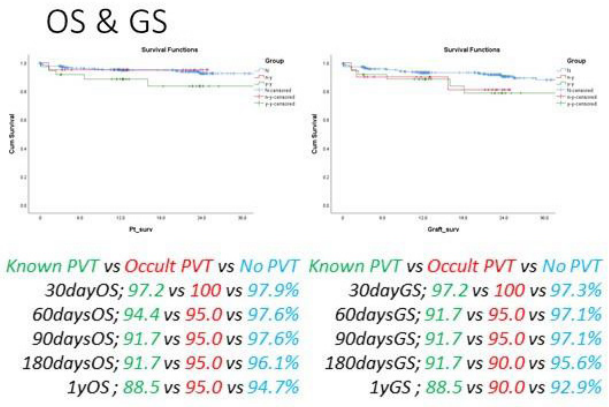
Background: Portal vein thrombosis (PVT) is a recognized poor early prognostic factor in liver transplantation (LT), but there is limited data distinguishing the influence of pre-transplant (known) versus intra-operatively (occult) identified PVT on outcome.
Method: A single center retrospective analysis of a prospectively maintained LT database was performed (Aug. 2014 - Dec. 2016). Supplemented with review of radiology at time of listing and operative findings. Statistical analysis was performed using SPSS (version 22).
Results: In the time period of analysis there were 443 adult LT (including 42 acute/401 chronic, and 20 re-transplantations). 42 patients (9.5 %) were identified to have a PVT at the time of listing, of which 16 were totally occluded (38%). Of this group, interposition graft was required in 7 and 3 needed a venous conduit from the SMV. A further 20 (5.0%) patients had PVT identified at LT, of which one required an interposition graft and the remainder managed by eversion thrombectomy. Median interval between last CT and transplant was 69 (1-696) days. Overall 32 recipients died and 43 grafts were lost. Median follow up 18.2 months. Dividing into three groups of Known (n=42), Occult PVT (n=20), No PVT (n=381): 1 year recipient survival was 89% v 95% v 95% and 1 year graft survival was 89%, 90% and 93%. There were no significant differences. On multivariate analysis of recipient variables: ascites grade 3 (p= 0.020) and a platelet count less than 100 (p=0.013) were identified to be associated with occult PVT.
Conclusion: On this preliminary analysis, no adverse effect of PVT (known or occult) on early one year graft and recipient survival was identified.



[OS&GS_of_3_groups]

P-554

Following up liver transplant recipients - casting the electronic media net

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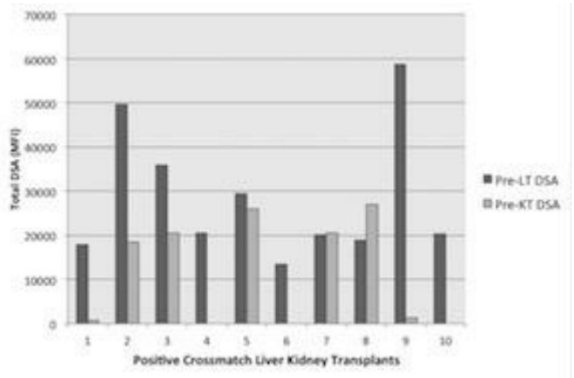
Liver transplant still remains the only curative treatment option for end stage liver disease. Indeed, the numbers of transplants performed in India has grown by leaps and bounds in the last decade. Medical tourism has helped in achieving high numbers. However, maintaing a proper follow up protocol is essential for ensuring long term surveillance of the recipients and early detection of any issues plaguing the recipient. Our centre performs over 250 liver transplants annually, majority being living donor liver transplants.
Almost 50% if our recipients are from other countries, while most of the remaining stay more than 100 km from the transplant center. Maintaining a follow up protocol is essential to keep track of the recipients in the long term.
This study reviews our practice of maintaining such follow up and strives to find out the adherence rate.
Our team has devised a follow up chart, which includes the weight, height, blood pressure, blood test results, tacrolimus trough levels, dosage of immunosuppressive medications The process starts with patient education before discharge and teaching on ways to fill up the chart. Once the patients are discharged from the clinic, they return to their respective place of residence. Patients then fill up the chart after every test and send them to our center by email.

Patients are actively encouraged to use social media- whatsapp, facebook and viber to send us their reports.
There is a dedicated transplant helpline in our center, which can be accessed 24 7.
Using multiple such techniques we have been able to ensure more than 90% long term adherence. Also, any concerns of the recipients are promptly addressed.
The study shows the impact of electronic and social media in long term follow up of transplant recipients.



[Figure]

Figure: Cases 1,5,6 and 7 did not receive plasma exchange. Cases 5, 7 and 8 (without significant decreases in DSA) were re-transplants.

P-555

Positive crossmatch liver kidney transplantation: utility of delaying kidney transplantation

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Significant decrease in circulating anti-HLA donor specific antibodies (DSA) has been observed after liver transplantation (LT). This property of liver allograft can be utilized to lower DSA levels prior to kidney transplantation (KT) by delaying KT. Additionally, this approach may time to lower DSA by plasma exchange in patients with extremely high levels of DSA.
Methods: 10 combined liver kidney transplants with pre-existing DSA were retrospectively studied. All patients had DSA quantified by Luminex solid-phase bead assay immediately preceding LT, and again immediately preceding KT. Kidney allografts remained on continuous hypothermic pulsatile perfusion until KT. Median cold ischemia time for kidney transplants was 48 hours. Plasma exchange was utilized in of 6 of 10 cases with strong positive crossmatch.
Results: A decrease in total Mean Fluorescence Intensity (MFI) of DSA following LT was observed in 8 of 10 by an average decrease of 17,060 (- 56.7%) MFI. In 5 patients, there was negligible amount of DSA detected at the time of KT. Decrease in MHC Class I antibody was significantly higher than that in Class II ($P < 0.05$). Decrease in DSA was comparable regardless of plasma exchange ($P = 0.22$). Patients without significant decrease in DSA had previous transplants. Mild acute cellular rejection was seen in one patient which resolved immediately. There was no incidence of delayed renal graft function and acute humoral rejection. Overall patient survival was 90%.
Conclusions: This series demonstrates that delaying KT allows reduction in circulating DSA after LT and prior to KT with and without plasma exchange. With this approach, excellent clinical outcomes can be achieved in crossmatch positive liver kidney transplantation.

P-556

Is 15mm Hg still the benchmark to aim for in adult living donor liver transplantation?

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Background: Graft hyperperfusion usually presents with prolonged graft cholestasis and coagulopathy. Previously, final portal pressure(PP) > 15mm Hg has been reported to be associated with post-operative hyperbilirubinemia and coagulopathy. With advances in surgical techniques and improved critical care, post reperfusion PP has not been receiving much attention. We wanted to assess the implications of graft PP on patient outcomes in present day practice.
Methods: Retrospective analysis of adult LDLTs from January 2016 to August 2018 was carried out. Postoperative graft functions (peak bilirubin and peak INR) in relation to native and post reperfusion PP was assessed. PP was measured directly from the portal vein prior to explant and post arterial reperfusion.
Results: Data on 272 adult patients (63 females) undergoing their first LDLT were analysed. The mean age (mean+sd) of the patients in all cohorts was 50 years (12), with a mean preoperative MELD of 17(6.6),mean GRWR was 1.0 (0.24). Mean PP before recipient hepatectomy was 17mmHg (4.4) which reduced to a final PP of 11mmHg (2.8) after arterial anastomosis.

Patients were divided into 3 groups according to the final PP (group1: < 10mm Hg (n=83, 30%), group2: 10-15mm Hg (n=175, 64.8%), group3: >15mmHg (n=14, 5.2%)).
Postoperative peak bilirubin showed a sequential increase with increasing final PP and was significantly higher in group 3 [Group1: 7.2mg%(7.1), group2: 9.8mg%(6.3), group 3: 13.6mg%(6.6), p=0.006]. There was no difference in postoperative peak INR in the 3 groups. [Group1: 2.1(0.7), Group2: 2.2(0.4), Group3: 2.4(0.4), p=0.152]. Mean hospital stay increased with higher final PP but did not reach statistical significance [19days(10), 20days(9), 25days(10) respectively, p=0.221].
Conclusion: Higher final PP (>15mmHg) is associated with graft cholestasis. There is a trend towards prolonged hospital stay with higher PP. Aggressive measures to keep PP under 15mm Hg is necessary to improve outcomes after adult LDLT.

P-557

Managing multiple inferior right hepatic veins in right lobe living donor liver transplantation: outcomes after bench reconstruction with a novel technique of ePTFE ‚BOAT' graft

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Background: Optimal outflow reconstruction of right lobe liver grafts (RLG) is essential for good outcome especially when the GRWR is marginal.However variations in number, size and lie of multiple right inferior hepatic veins(RIHV) pose significant technical challenges in reconstruction.
Methods: From 2015 January to 2018 September,out of 766 RLG ,70 had >1 significant RIHV(>4mm). Our techniques included:Type A-(2 veins,good lie < 6mm apart) venoplasty and direct venocaval anastomosis,or Type B-(≥ 2 RIHVs far apart / different lie) reconstruction with Polytetrafluoroethylene(ePTFE) boat graft (14 -16mm non-ringed graft, closed at ends) with RIHVs anastomosed to the lateral side of the graft maintaining their spatial lies,and a slit on the medial side anastomosed to the side of IVC. Recipient outcomes were analysed.
Results: Type A and Type B reconstruction was done for 19 and 51 RLG respectively. 28.5% with multiple RIHVs vs 17% with single or no RIHV had GRWR < 0.8(p< 0.001). The mean CIT was 117± 37mins in Type A and 156±51mins in Type B(p-0.057). Type B had significantly shorter warm ischemia time (51±8.8 mins) compared to the Type A group(56.16±14.72)(p< 0.05). There were no thrombotic complications in either group of recipients at a mean follow up of 2 months. The 1 year patency rate in the Type B group on Doppler Ultrasound was 48/51(94%).There was no complication of ePTFE graft such as migration or fistulisation. *Among the Type A and B groups, the in-hospital mortality was 5% and 8% (p-0.9) and 1 year graft survival was 89.5% and 88% (p-0.8) respectively.*
Conclusion: Our technique using PTFE boat graft for reconstructing multiple RIHVs is safe and effective, and ensures optimum venous outflow reconstruction in such grafts. It has the advantages of shorter warm ischemia time, easy availability, and high long-term patency rate.

P-558

Liver transplantation with sovraceliac aorto-hepatic vs infrarenal revascolarization: multicentric retrospective study

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Introduction: During a liver transplantation (LT), several pathological conditions related to the recipient's hepatic artery do not allow an end-to-end arterial anastomosis; in these circumstances, the arterial inflow can be restored by anastomosing the graft's HA to the abdominal aorta. Aorto-hepatic arterial reconstruction (AHAR) can be performed on the supra-celiac (SC) or the infrarenal (IR) tract of the aorta with or without interposition of an arterial conduit; To date, no data are available in the literature to support which is the most effective and safe techniques .
The objective of the study was to compare the results of infra-renal vs. supra-celiac AHAR, with or without interposition of an arterial conduit in LT patients.
Methodology: AHAR was performed in 120 consecutive LT recipients across six European centers; the incidence of hepatic artery thrombosis (HAT) was considered the primary endpoint.
We retrospectively analyzed the main intra and post-operative parameters and a multivariate analysis was planned to identify the independent predictors of HAT.

Results: In 56/120 (46.6%) cases an infrarenal anastomosis was performed, always using an arterial conduit, while in the other 64/120 (53.4%) cases a supraceliac anastomosis was made, using an arterial conduit in 45/64 (70.3%) cases. The overall HAT incidence was 30.4% in the IR-AHAR vs. 10.9% in the SC-AHAR (p=0.015). No significant differences emerged in the incidence of primary non-function, early allograft dysfunction, biliary strictures, postoperative hospitalization, transfusion of blood products, duration of intervention. Multivariate analysis showed that infrarenal anastomosis was an independent risk factor of HAT (exp(B)=3.535, 95% CI=1.292-9.670, p=0.014). After an average follow-up of 54.52±49 months, graft and patient survival were higher in supraceliac group, although not statistically significant (p=0.061, p=0.129).
Conclusions: In those cases in where an AHAR is necessary, arterial anastomosis using supraceliac aorta significantly reduces the incidence of hepatic artery thrombosis and is therefore recommended.

P-559

Outcome after transplantation of liver grafts from diabetic donors: a national multicenter study

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Background: As the incidence of diabetes mellitus (DM) continues to grow, an increased number of deceased organ donors with DM can be expected. Outcome after transplantation of livers from diabetic donors, however, is not well documented. Also, no studies examined the effect of donor type I versus type II DM on outcome after liver transplantation.
Method: All adult recipients in the Netherlands transplanted with a liver from a diabetic donor (n=69) in the period 2000-2016 were matched with recipients of livers from non-diabetic donors (n=138). Outcomes were 90-day, 1-year, and 3-year graft and patient survival, incidence of primary non-function (PNF), hepatic artery thrombosis (HAT), and non-anastomotic biliary strictures (NAS).
Results: Of diabetic donors, 22 had type I and 37 had type II DM (10 missing cases). Moreover, 11/69 were donation after circulatory death (DCD) and 58/69 donation after brain death donors. Recipients of livers from diabetic donors experienced significantly worse graft survival compared to recipients of livers from non-diabetic donors (90-day: 88.4% versus 96.4%, 1-year: 84.1% versus 91.3%, and 3-year: 78.3% versus 89.1%). Interestingly, NAS occurred less often in the diabetic donor group (4.3% vs. 14.6%, p=0.032), whereas HAT occurred more frequently in these recipients (8.7% vs. 2.2%, p=0.030). There were no differences in outcome after transplantation of livers from donors with type I or type II DM. Noteworthy, transplantation of livers from diabetic DCD donors resulted in favorable outcomes with 91% 3-year graft survival, 100% 3-year patient survival, no PNF or HAT, and only 1/11 recipients developed NAS.
Conclusion: Overall outcome after transplantation of liver donors with DM is inferior compared to transplantation of livers from non-diabetic donors. However, transplantation of livers from selected DCD donors with DM had favorable outcomes and diabetes in a DCD donor should, therefore, not be considered a contraindication for liver donation.

P-560

Risk factors for thrombosis and bleeding in ppediatric liver transplantation in an era of routine postoperative antithrombotic therapy

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Background: Hepatic artery thrombosis (HAT) and portal vein thrombosis (PVT) are serious causes of morbidity and mortality after pediatric liver transplantation. In order to reduce the number of thrombotic complications, routine antithrombotic therapy, consisting of 1 week heparin followed by 3 months acetylsalicylic acid, was implemented in our pediatric liver transplant program in 2003. The aim of this study is to evaluate the incidence of bleeding

and thrombotic complications since the implementation of routine antithrombotic therapy and to identify risk factors for these complications.
Method: In this retrospective cohort study all 200 pediatric primary liver transplantations performed between 2003-2016 were included. Uni- and multivariate logistic regression analysis, the Kaplan-Meier method and Cox regression analysis were used to evaluate recipient outcome. Odds ratios (OR) and hazard ratios (HR) are reported with 95% confidence intervals.
Results: Fifty-six (28%) full size and 144 (72%) partial grafts from 161 (80%) deceased and 39 (20%) living donors were transplanted. HAT occurred in 15 (7.5%), PVT in 4 (2.0%) and venous outflow thrombosis in 2 (1.0%) recipients. Intra-operative vascular interventions (OR 14.4 (3.7-55.7)), recipient age (OR 0.81 (0.69-0.95)) and donor age (OR 0.96 (0.93-0.99)) were significantly associated with post-transplant thrombosis. Clinically relevant bleeding occurred in 37%. Independent risk factors were high recipient age (OR 1.08 (1.02-1.15)), high Child-Pugh scores (OR 1.14 (1.02-1.28)) and intra-operative blood loss in ml/kg (OR 1.003 (1.001-1.006)). Both post-transplant thrombotic (HR 3.4 (1.4-8.5); *P*=0.009) and bleeding complications (HR 2.5 (1.2-5.2); *P*=0.015) increased mortality.
Conclusion: In 200 consecutive pediatric liver transplant recipients receiving routine post-operative antithrombotic therapy we report low incidences of post-transplant vascular complications. Post-transplant routine antithrombotic therapy seems to be valuable for pediatric liver transplant care. The identified risk factors for bleeding and thrombotic complications may facilitate a more personalized approach to antithrombotic therapy.

P-561

20 year survival after liver transplantation and development of a risk score to predict long term survival

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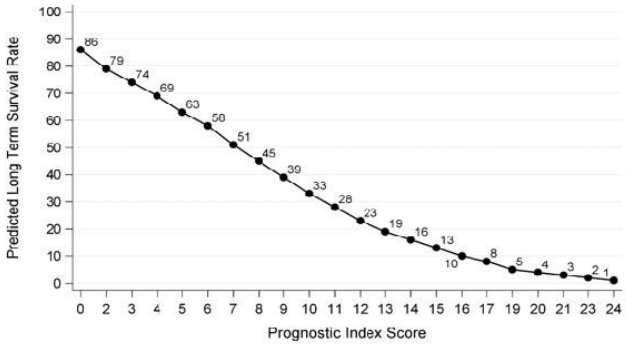
Background: Long-term survival after liver transplant has improved over the years. The aim of this study was, to analyze data of recipients who survived more than 20 years after liver transplantation and to identify variables affecting long-term survival. A risk score was developed based on the variables to characterize a risk profile that is associated with long-term survival.
Method: Prospective review of patients transplanted at the Baylor Simmons Transplant Institute from 1985-2017. Patients that were alive after 20 years were compared to patients who did not survive 1 year post-transplant. A logistic regression analysis was performed.
Results: 1261 patients underwent liver transplant between 1985-1997. Patient and graft survival was 65.8%; 60.1% at 5 years, 52.8%; 48.1% at 10 years and 26.3%; 25.3% at 20 years.
Characteristics of patients surviving 20 years after transplant were: younger age, female, younger donor, less likely to have HCC, required < 5units of PRBCs and more likely to have ACR (Table1).
The final multivariate logistic regression model developed (c-statistics=0.75), revealed that recipient age of 60 years or older, (OR=7.4, CI=3.5, 15.7), HCC diagnosis (OR=7.3, CI=3.0, 17.9), donor age of 50 of older, (OR=4.4, CI=2.4, 8.0), receiving ≥5 units of PRBCs (OR=1.68, CI=1.1, 2.6) and a MELD score of 20 or greater (OR=1.7, CI=1.1, 2.7) were associated with negative long-term survival.
The multivariate regression analysis was used to derive a Long-Term Survival Point Score (0-26). Plotting the Prognostic Index Score against the predicted long-term survival showed: the lower the score the higher the likelihood of a patient surviving long-term and vice versa (Graph 1).
Conclusion: This risk score could be used to predict candidates at the time of listing that have the best long-term survival and aid in discussions with the patient about their predicted outcome.

Table 1: Summary descriptives table by groups of 'Study Group'

	Died within 1 yr post OLTx N=199	Survived at 20 yrs post OLTx N=282	p-value	N
Recipient Sex:			0.011	481
Male	54.8%	42.6%		
Female	45.2%	57.4%		
Recipient Age	52.0 [43.0,61.0]	45.0 [38.0,50.0]	<0.001	481
Recipient Age:			<0.001	481
≤60	74.4%	96.5%		
>60	25.6%	3.55%		
Donor Age	36.5 [20.0,51.2]	26.0 [19.0,36.0]	<0.001	478
Donor Age:			<0.001	481
≤50	74.4%	92.9%		
>50	25.6%	7.09%		
Donor Sex:			1.000	477
Male	62.2%	62.3%		
Female	37.8%	37.7%		
Biological MELD	19.0 [13.0;27.0]	17.0 [13.0;26.0]	0.246	470
Biological MELD:			0.053	470
MELD≤20	57.9%	67.0%		
MELD>20	42.1%	33.0%		
DM:			0.003	217
No DM	86.1%	97.2%		
DM	13.9%	2.76%		
Cold Ischemia Time (hr)	10.1 [6.80;12.6]	9.83 [6.58;13.0]	0.758	463
HCC:			<0.001	481
No HCC	82.4%	97.5%		
HCC	17.6%	2.48%		
PRBC:			0.009	479
<5	46.7%	59.3%		
=> 5	53.3%	40.7%		
ACR:			0.040	481
No ACR	42.2%	32.6%		
ACR	57.8%	67.4%		



[Table/Graph]

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Standardized critical care end points for deceased organ donors improve post-transplant graft function after liver transplantation

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Background: In deceased organ donor management, meeting a bundle of care endpoints (donor management goals, DMG) has been associated with increased organ yield and reduced incidence of delayed graft function after kidney transplantation. (targets: mean arterial pressure: 60 - 110mmHg, central venous pressure: 4 - 12mmHg, ejection fraction > 50%, ≤1 vasopressor, pH: 7.3 - 7.5, PaO2:FiO2 ≥300, sodium ≤155mEq/L, glucose ≤150mg/dl, urine output ≥0.5 ml/kg/h). Donor data, including physiological data and compliance with DMG endpoints, is collected in the prospective DMG registry.
In liver transplantation, the model of early allograft function (MEAF) allows to quantify early allograft dysfunction and can predict one-year survival. The MEAF score (based on AST, bilirubin and INR on postoperative day 3) quantifies graft function between 0 and 10 (a lower score depicts better organ function).
Our aim was to evaluate the impact of meeting DMGs at time of organ recovery on early allograft function after liver transplantation.
Methods: Adult liver recipients transplanted at our center between June 2012 and October 2017 were evaluated based on the number of DMGs met in the donor. DMG data was available for 512 (86%) transplants. Multivariable linear regression was used to assess whether the number of DMGs met, corrected for warm ischemia time and donor risk index, was a predictor of graft function measured by MEAF.
Results: A median of 7 (IQR 6-8) DMGs were met per donor. Adjusting for variables known to determine MEAF, the number of DMGs met prior to organ recovery was independently associated with improved early graft function (Coefficient: -0.128, 95%CI -0.234 to -0.021, P = 0.02; for each DMG met).
Conclusion: This is the first study to demonstrate the beneficial effect of compliance with DMGs on graft function after liver transplantation. The number of DMGs met was associated with improved early allograft function.

P-563

Transplant center perceptions of engagement in organization health literacy

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Introduction: Organizational health literacy (OHL) is an institution´s ability to assist individuals with low health literacy navigate the healthcare system. However, it is unclear how well transplant centers practice the components of OHL pertaining to the complex transplant process. Therefore, we assessed the perceptions of OHL among transplant staff at a tertiary academic hospital.
Methods: A 51-question survey from the Agency for Healthcare Research & Quality was administered to staff at a multi-visceral transplant center from 2/28/2018 to 4/6/2018. Respondents selected “Doing well”, “Needs improvement”, “Not doing”, and “Not sure/NA” toa wide range of questions. 6 questions regarding key components of OHL were included for analysis. A performance ratio was calculated by dividing the number of “Doing well” responses by the sum of “Needs improvement”, “Not doing”, and “Not sure/NA” responses. A ratio < 0.5 was considered as not performing well, as an indication that 50% more staff responded “Needs improvement”, “Not doing”, and “Not sure/NA” compared to ““Doing well”.
Results: 68 staff participated (20% response rate), including nurses (28.3% of total respondents), physicians (20.0%), and coordinators (12.8%), completed the survey. Respondents rated the institution as not performing well in all areas (Table 1). The lowest performance ratios were regarding: having a written health literacy improvement plan (0.09), educating staff in health literacy (0.05), and regularly assessing the health literacy environment of the institution (0.04). Notably, a large proportion of respondents indicated “Not sure/NA” for all questions.
Conclusion: Transplant center staff did not perceive the center performs well regarding OHL. A majority of respondents seemed to be unaware of best practices in health literacy. We plan to create health literacy teams, formulate health literacy improvement plans, and raise awareness of OHL at our center and throughout the transplant community.

Table 1. Perceived institutional performance regarding medication education, and general health education an resources at a tertiary academic medical center.
Note: A performance ratio > 1.5 was considered as performing well.

Agency for Healthcare Research & Quality Survey Question	Doing well (N)	Needs improvement / Not doing (N)	Performance ratio (Doing well vs. Needs improvement/Not doing)
Medication Education			
1. Staff members discuss different methods for remembering to take medicines correctly and offer patients assistance setting up a system (e.g., pill box, medicine chart).	39	16	2.4
2. Clinicians write precise instructions for taking medicine that are easy-to-understand (e.g., "take 1 pill in the morning and 1 pill at bedtime" instead of "take twice daily").	37	16	2.3
3. Staff members connect patients with medicine assistance programs, including helping them fill out applications as needed.	39	18	2.2
4. Staff members assess patients' ability to pay for medicines.	38	21	1.8
General health education and resources			
1. Clinicians help patients choose health improvement goals and develop action plans to take manageable steps toward goals.	36	27	1.3
2. Our practice follows up with patients to determine if their action plan goals have been met.	32	30	1.1
3. All clinicians talk with patients about any educational materials they receive during the visit and emphasize the important information.	33	27	1.2
4. All staff members use audio/video materials and/or visual aids to promote better understanding (e.g., food models for portion sizes, models of body parts, instructional health videos).	19	47	0.4
5. Our practice trains patients to use our patient portal.	12	35	0.3
6. Our practice ensures patients have the equipment and know-how to use recommended audio-visual materials and Internet resources.	12	40	0.3
7. Staff members help patients access adult literacy and math programs.	7	25	0.3

[Table]

P-564

Comparative analysis of bile microbiology and antibiotic susceptibilities between liver transplant recipients and normal population: multicenter cohort study

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Biliary complications are still unresolved problems after liver transplantation (LT), up to 28%-32%, especially in living donor LT. Effective antibiotics should be administered to control the cholangitis, however immunosuppression after LT may have changed the microbiology of infected bile. The aim of this study was to compare bile microbiology and antibiotic susceptibilities between liver transplant recipients and normal population.
Between 2008 and 2017, the microbiologic culture and antibiotics sensitivity tests were compared on the patients who underwent percutaneous trans-hepatic biliary drainage because of biliary complications after LT (n=59) and cholecystectomy under the diagnosis of gallbladder disease (n=271) at multiple centers.
The most frequently isolated microorganisms were similar between two groups; Enterococcus (42.4% vs. 29.4%) followed by Escherichia (22.0% vs. 19.0%), Pseudomonas (16.9% vs. 8.8%), and Klebsiella (10.2% vs. 10.1%). For Enterococcus and Escherichia, two most frequently isolated organisms, gentamycin and imipenem showed similar high sensitivity for both organisms in two groups. According to the period, within or after 6 month of LT, Enterococcus (23.7% vs. 18.6%) was consistently frequently isolated, but others were different; Klebsiella (8.5% vs. 1.7%), Escherichia (3.4% vs. 18.6%) and Pseudomonas (3.4% vs. 13.6%).
The microbiologic culture and antibiotics sensitivity tests were similar between liver transplant recipients and normal population, however there was some difference of frequent isolated microorganisms by the period after LT.

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HIV-positive patients undergoing to liver transplantation: 16 years of experience.

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Background: Despite an increase in survival of HIV patients thanks to improved antiretroviral therapy, many present liver-related disease. LT is the only curative treatment for end-stage liver disease (ESLD) associated or not with HCC.
Patients and methods: From May 2002 to September 2018, in our institution 17 HIV-positive patients (mean age: 47 y. Range: 40-59) underwent cadaveric donor LT for ESLD. Twelve patients were coinfected with HCV, three were HBV-positive and one was HBV+HCV-positive. HCC was associated in 7 cases, all were in Milan Criteria. Pre-OLT plasma HIV 1-RNA level was undetectable, CD4(+) T-cell count > 200 cells/microL for 3 months. Six patients had to stop HAART before OLT because of liver disease severity (n = 2) and for HCC (n = 4). Inclusion criteria followed the Italian Protocol for LT in HIV-positive patients. The patients were treated with the triple immunosuppressive therapy.
Results: The median FU was 35 months (range: 1-108). The median overall survival was 50,6 months (range: 1-180). Overall patient survival and graft survival at 60 months were 42%. The median CD4 T-cell count at OLT was 415/ mmc (range 150-764). HCV recurrence was a common problem before 2013 and was observed in 7 HCV

patients (41%). All HBV patients are alive, while in those transplanted for HCV, 5 died for viral recurrence. Rejection and infection post-OLT was rarely observed. In 50% of death patients, HCV-recurrence was observed. In all patients significant improvement in QOL was observed.
Discussion: OLT in HIV-positive patients is feasible procedure with good results. Early severe HCV recurrence was common before introduction of DAAs. Until 2013 HCV recurrence was a major cause of concern and death. After the introduction of DAAs results in HIV patients are in line with those observed in patients with HBV.

P-566

HIV infection is not associated with increased cardiovascular (CV) risk in liver transplant (LT) recipients: a single centre comparative study

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Background: Cardiovascular diseases(CVD)are currently one of the main causes of morbimortality in HIV-infected patients. Similarly, LT recipients have increased prevalence of CV risk factors post-LT. Our aim was to describe the prevalence of CV risk factors and events in HIV-infected LT patients, compared to HIV-uninfected LT patients.
Methods: We included LT recipients from 2004-2016 from a single center.HIV-infected patients were matched to 2 controls each by age,sex,liver disease etiology,and date of LT, when possible.CV risk factors and events pre-LT and post-LT,demographic and transplant related variables were collected.
Results: DEMOGRAPHICS:A total of 138 LT recipients were included(46 HIV-infected and 92 HIV-uninfected).HCV was the main etiology(84% of HIV-infected and 91% of HIV-uninfected),followed by alcohol. Hepatocellular carcinoma was present in 24% of HIV patients and 35% of non-HIV patients.Mean CD4 cell count at LT was 301(58-1100). Mean follow-up was 5.5years in the HIV vs 6.1years in the non-HIV group.
PRE-LT CHARACTERISTICS: Most patients(85%) in both groups were men.Mean age was younger in the HIV-infected group(47vs 51 years)(p 0,0137). Prevalence of CV risk factors was similar in both groups(HIV vs non-HIV):arterial hypertension(AHT)9% vs11%(pNS), diabetes(22% vs19%,pNS),dyslipidemia(9% vs5%,pNS),smoking(59% vs47%,pNS) and chronic renal disease(CKD)(11%vs 10%,pNS).Body mass index was significantly lower in HIV-infected patients(24.3 vs 27.2,p 0,0004).
POST-LT Outcomes: Incidence of CV events was equally frequent in both groups(11%), but they presented at younger ages in HIV-infected patients(49 vs 54 yrs,p 0,1229). Incidence of CV risk factors was increased as compared to the pre-LT setting, and equally similar between groups:AHT(54% vs 48%, pNS),diabetes (33%vs 41%, pNS),dyslipidemia (26%vs 37%, pNS),and CKD (28%vs22%, pNS). Smoking was significantly more frequent in the HIV group(22% vs 8%, p 0.02).During follow-up, 26% of patients in each group died.
Conclusion: In the post-LT setting,CV risk factors and CV events are not increased in HIV-infected patients,but occur at younger age.An intensive management of risk factors is mandatory.

P-567

Mastery of self-management skills in young people post-liver transplant and with chronic liver disease in the United Kingdom

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Background: Over a third of young people (YP) are perceived to have been transitioned into adult liver clinics with inadequate knowledge of their condition. However, self-management skills of YP post-liver transplant and with liver disease (LD) here in the United Kingdom have yet to be assessed. The purpose of our study was to describe mastery of health-care management in a UK sample of YP with LD, along with levels of anxiety and depression symptoms, and engagement in ´risky´ health behaviours.
Methods: Forty seven young people, aged 17-25 years (m= 19.0 years, SD= 2.5, 49% female) completed the Liver Self-Management Questionnaire (LSMQ), an adaptation of the Developmentally Based Skills Checklist and further modified for YP here in the UK by our service. YP completed the Patient Health Questionnaire (PHQ-9), Generalised Anxiety Disorder Assessment (GAD-7) and questionnaires assessing their medication adherence and level of engagement in risky health behaviours, using an informatics system that facilitates collection of patient-reported outcomes (‚IMPARTS').
Results: Less than half of YP reported consistently managing their liver disease independently (none of the behaviours assessed were completely mastered by the whole cohort). Levels of mastery were comparable to USA peers. Levels of anxiety and depression were elevated relative to healthy peers: 14% had symptoms of depression/

probable depressive disorder, 23% had anxiety. Ten percent of males and 19.2% of females reported ‚hazardous drinking', 15.4% reported smoking (above national norms) and 18% reported not taking their medication as prescribed.
Conclusion: YP in the UK display inconsistency with mastery of health management. Levels of mental health problems, hazardous drinking and smoking are high. This highlights the importance of considering these factors in YP being looked after in adult services and not assuming that all individuals over the age of 18 years have mastered self-management of their condition.

P-568

Telomere length in naïve t cells predicts the prognosis of hepatocellular carcinoma patients after liver transplantation

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Background: Telomere dysfunction were reported working as important role in various cancer, telomere length of peripheral blood were frequently studied and were found be association with cancer risks. However, telomere length varies in different blood cell type. This study focus on assessing the telomere length changes in naïve t cells in hepatocellular carcinoma patients.
Methods: 43 Hepatocellular carcinoma (HCC) patients and 25 healthy controls were concluded in this study. PBMC were isolated from 10 ml peripheral blood, CD4+CD45RA+ naïve t cell were isolated from PBMCs using magnetic beads. DNA were extracted and telomere length were assessed by southern blot.
Results: Telomere length of naïve t cells was shorter in HCC patients than healthy controls (p< 0.001). In 43 HCC patients underwent liver transplantation, 10 (23.3%) patients experienced HCC recurrence in first year. Telomere length of naïve t cells in recurrence group was significantly shorter than non-recurrence group (p=0.007). In all HCC patients after LT, telomere length short group showed a lower tumor recurrence free survival (p=0.038).
Conclusion: Telomere length of naïve t cells is correlated with the prognosis of HCC patients after LT. It might be a potential prognostic marker for HCC patients for LT.

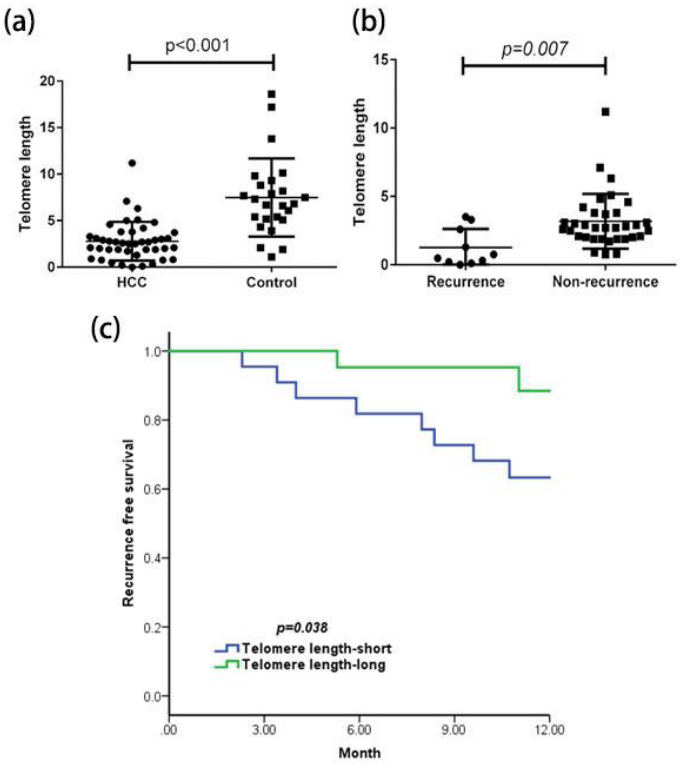

Fig. 1 Telomere length in naive T cells correlated with HCC recurrence after LT
a. Telomere length in naive t cells from HCC patients is significantly shorter than healthy controls. b. Telomere length in naive t cells in recurrence group is shorter than non-recurrence group. c. Telomere length short group showed a lower recurrence free rate than telomere length long group (p=0.038)

[Telomere length in naive t cells was correlated with HCC recurrence after LT]

P-569

Impact on post liver transplant outcomes of response to treatment with terlipressin and albumin in patients with hepatorenal syndrome

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Background: Hepatorenal syndrome (HRS) is a relevant complication of cirrhosis associated with poor prognosis. Terlipressin and albumin are effective in resolving HRS, but it is unclear if response to treatment may improve outcomes after liver transplant (LT) in these patients. The aim of this study was to evaluate the impact of response to treatment on post-LT outcomes in patients with HRS.
Materials and methods: We analyzed 2 cohorts of patients listed for LT at our Centre: a) patients with HRS before LT, treated with terlipressin and albumin and b) patients without HRS transplanted during the study period. Patients with HRS were classified as responders or non-responders to treatment. Patients with previous LT or indication for SLK transplantation were excluded.
Results: 82 patients with HRS were treated with terlipressin and albumin, with a response rate of 52%. Responders had better transplant-free survival (60% vs 33%, p=0.006), longer LT-list waiting time (37 vs 17 days, p=0.041) and lower MELD at LT (23 vs 29, p=0.007). Non-responders showed worse renal function after LT, higher need for RRT (0% vs 26%, p< 0.001) and higher rate of post-LT infections (63% vs 87%, p=0.037) than responders. There was no difference in length of stay, graft dysfunction, immunosuppression between responders and non-responders. Moreover, there was no difference in survival after LT between responders, non-responders and controls. Nevertheless, non-responders had higher incidence of post-LT CKD (60% vs 33%, p=0.019). When a control group was included in the analysis, age (sHR=1.04; p=0.024), diabetes (sHR=1.64; p=0.048), post-LT AKI (sHR=1.81; p=0.012), MELD at LT (sHR=1.03; p=0.028), and no response to treatment were found to be independent predictors of post-LT CKD.
Conclusions: Response to terlipressin and albumin improves renal function and survival before LT. In addition it reduces the the need of RRT and the prevalence of CKD after LT.

P-570

Immunologic monitoring of circulating lymphocyte subsets, HLA-DR+ monocytes and CD64+ neutrophils in DCD liver transplant recipients: a single-center, prospective, observational cohort study

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Background: The clinical significance of circulating lymphocyte subsets, human leukocyte antigen (HLA)-DR+ monocytes and CD64+ neutrophils in the peripheral blood of donation after cardiac death (DCD) liver transplant recipients (LTRs) remains unclear. We examined the efficacy of enumerating these cells for the immunologic monitoring of LTRs.
Method: Blood samples were obtained from different time points, including before transplantation, 1 week, 1 month, 3 months, 6 months and 1 year after transplantation and at diagnosis, and 2 weeks after treating bacteria cultured-proven infection and cytomegalovirus (CMV) infection. Serial flow cytometric analysis was performed using peripheral blood obtained from 86 patients to identify the frequencies and absolute numbers of CD3+, CD4+, CD8+ T cells, CD19+ B cells, CD16+CD56+ natural killer (NK) cells, mean fluorescence intensity (MFI) of HLA-DR+ monocytes and the percentage of CD64+ neutrophils.
Results: Frequencies and absolute numbers of CD3+, CD4+, CD8+ T cells, NK cells, and MFI of HLA-DR+ monocytes were significantly lower but percentages of B cells and CD64+ neutrophils were significantly higher at 1 week after transplantation than other time points (all P< 0.001). These decrease and increase were not correlated with clinical parameters. The frequency of CD64+ neutrophils was significantly higher in LTRs with bacteria infection than in LTRs at 1 week after transplantation (p< 0.05). However, no significant differences were observed between stable LTRs and LTRs with CMV infection. Analysis of the receiver operating characteristic curve adjusted by covariates showed that bacteria infection could be predicted with high sensitivity and specificity by setting the cutoff value of CD64+ neutrophils frequency as 15%.
Conclusion: Circulating lymphocyte, monocyte and neutrophils subsets showed significant and consistent changes in their frequencies after immunosuppression. Of the various immune cells examined, circulating levels of CD64+ neutrophils might be a useful noninvasive immunologic indicator for detecting bacterial infection.

P-571

Predictive factors of early allograft dysfunction and its impact on long-term graft survival

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Introduction: Early allograft dysfunction (EAD), one of the major complications of liver transplantation (LT), is a multifactorial syndrome associated with higher morbidity in the early post-LT period and may compromise graft survival. We aimed to determine predictors of EAD (Olthoff criteria) and assess if EAD had an impact on long-term graft survival.
Patients and methods: All the 1329 LTs performed in our center

between 2007 and 2016 were reviewed retrospectively. LDLT and domino were excluded. Recipient (7 variables), donor (5 variables), intraoperative data (6 variables) and postoperative data (5 variables) were used to assess the predictors of each endpoint (EAD or graft survival). Risk factor variables with P< 0.20 in univariate analysis were included in a multivariate logistic regression model or a Cox model when adequate.
Results: The incidence of EAD was 36% overall and 27% during the last two years, with 10% of re-LT (3.6% in non- EAD, p< 0.0001). Analysis of the study cohort of 1212 LTs revealed 7 independent predictors of EAD: partial graft (RR=2.22, p=0.003), SCOT preservation solution (RR=1.67, p=0.04), D/R graft weight ratio (RR=1.37, p=0.006), MELD score at LT (RR=1.03, p=0.0007), cold ischemia time (RR=1.00, p< 0.0001), recipient age ≥60 yrs (RR=0.73, p=0.04) and combined kidney transplant (RR=0.50, p=0.02). EAD was a strong independent predictor (RR=1.43, p=0.003) of graft survival (79%vs. 91% at 1 year, p< 0.0001), with five other factors: number of transfused blood units (RR=1.02, p=0.002), recipient age (RR=1.02, p=0.0002), donor age (RR=1.01, p=0.007), length of ICU stay (RR=1.01, p< 0.0001) and recipient BMI (RR=0.96, p=0.001).
Conclusion: The incidence of EAD was 36% in our series. Seven independent factors were predictive of EAD. EAD impacted significantly the graft survival even in the absence of re-LT.

P-572

Feasibility of a rapid magnetic resonance protocol to assess body composition profiles in adult liver transplant candidates

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Background: Body mass index (BMI) is a poor marker of obesity and outcomes in liver transplant (LT) candidates. Data suggest that body composition profiling (BCP) may provide more accurate markers of LT risk, but arduous analysis methods limit implementation. We sought to assess rapid magnetic resonance (MR)-protocol feasibility for BCP in LT.
Methods: A prospective pilot study of adults listed for LT (9/2017-3/2018) at an urban, tertiary care facility underwent BCP using a 6-minute MR-protocol at the time of LT listing, with repeat BCP 6 months later. Spearman correlation coefficients assessed associations between BCP and BMI. Wilcoxon rank scores assessed associations between change in BCP by LT status.
Results: Among 28 patients consented, 18 (64.3%) completed baseline BCP (mean age 58yrs, 72% male, 89% non-Hispanic white). Reasons for dropout included LT prior to BCP (n=3), waitlist removal (n=2), critical illness (n=2) and patient time constraints (n=3). Mean BMI was 30.9±15.3 kg/m2, median MELD score was 13 (range, 6-23) and ascites prevalence 23%. Fourteen patients (78%) had repeat BCP after median interval of 172 days (range 78-308 days). 6 (33%) underwent LT. Visceral adipose tissue (VAT) increased by mean 5.5% over time, while subcutaneous adipose tissue decreased by 3.4%. Liver fat fraction (LFF) increased by 8.0 percentage points (pp) in LT recipients vs. 6.4 pp in waitlist candidates though this difference was not statistically significant (p=0.26). BMI was not correlated with LFF (Spearman r= -0.35, p=0.16) or VAT (r=0.34, p=0.18), but correlated strongly with waist circumference (r=0.97, p< 0.0001) and muscle fat infiltration (r=0.76, p=0.0002).
Conclusions: Rapid MR-derived BCP is feasible and demonstrates that body composition changes over time in LT candidates. As anticipated, BMI is a poor marker of underlying fat and muscle volume changes in LT. Future studies will focus on whether BCP aids prediction of LT clinical outcomes.

P-573

Hemiportocaval shunt using a fixed diameter PTFE graft is a safe and effective technique for managing, Small for flow' grafts in living donor liver transplantation

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Background: Portal flow modulation(PFM) in the setting of live donor liver transplantation (LDLT) is utilized to reduce graft hyperperfusion related injury. Hemiportocaval shunt (HPCS) is one technique for PFM, though its technical difficulty and fear of complications such as portal steal and hepatic encephalopathy have prevented its widespread use.
Methods: Data for patients who underwent a HPCS during LDLT between January 2016 and November 2018 was analysed with particular reference to the decision-making process and the post-transplant outcomes.
Results: 17 patients underwent HPCS. Median recipient age was 48 years. Median pre-operative MELD score was 18. Right lobe graft was used in 11 patients, while left lobe and right posterior sector grafts

were used in 3 patients each. Median GRWR was 0.78 (range of 0.56 to 1.1). Seven patients had a GRWR< 0.7.
Prophylactic HPCS prior to recipient hepatectomy was performed in 3 patients anticipating portal hyperperfusion due to a combination of low GRWR (median GRWR of 0.65) and high baseline portal pressure (PP) (median PP 21mmHg). Final median PP in this group was 14mmHg. Fourteen patients underwent HPCS for high post-reperfusion PP (median PP 17mmHg) with normal/elevated portal flow (>60cm/sec).Post HPCS PP in this group reduced to 12 mmHg. Finally,in one patient, high portal flow (150 cm/sec) alone was the indication for HPCS (initial PP:14mmHg, final PP:13mmHg, final portal flow:70ml/sec)
Reversible early allograft dysfunction (Olthoff et al) developed in 5 patients. One patient developed grade 1 encephalopathy with elevated ammonia levels and recovered with medical treatment. Major complications (≥ Clavien grade IIIb) occurred in 4 patients including one mortality. There were no late HPCS related complications.
Conclusion: HPCS using a PTFE graft is a safe and effective technique to manage graft hyperperfusion. Its role in expanding LDLT using low GRWR grafts and preventing early graft dysfunction should be explored.

P-574

Predictive model of morbidity and mortality for simultaneous liver transplantation and cardiac surgery: an innovative proposal

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Background: Patients undergoing combined heart surgery (HS) and liver transplantation (OLT) are characterized by high morbidity and mortality therefore risk stratification becomes key when selecting candidates. Aim of this study was to create a model able to predict morbidity and mortality in patients undergoing combined OLT+HS.
Methods: Between 1/2005 and 8/2018, 1362 patients underwent OLT at our institution. 19 of them underwent OLT+HS (CABG and/or valve surgery). A predictive model was built with binary logistic regression to assess the predictors of mortality and morbidity using Euro score, MELD score and GFR. Three univariate models, rather than one multivariate model, were constructed for each outcome using each of these independent variables. Leave one out cross validation was used to reduce the bias in the resulting models. The overall predicted probability of morbidity and mortality was calculated by averaging the probabilities from the three models. Moreover, the performance of the three univariate models and the final model was assessed using receiver operating curve (ROC) and metrics such as accuracy, sensitivity, specificity, PPV and NPV.
Results: MELD score, Euro score and GFR were significantly associated with mortality and morbidity. The final model had a 94% accuracy to predict mortality and 95 % morbidity, which is higher compared to that observed with any of the univariate models.
Conclusion: The use of this simple score could potentially help selecting patients for very high risk surgery and therefore optimizing outcomes and the use of liver grafts. A multicenter clinical study will be needed to validate the model.

P-575

Prediction of delayed graft function in combined liver-kidney transplantation: an analysis using the UNOS registry

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Background: Delayed graft function (DGF), defined by the need for dialysis within 7 days after transplantation, impacts graft and patient outcomes. This study aims to predict the occurrence of DGF after combined liver kidney transplantation (CLKT).
Methods: We examined adult CLKT transplanted from Jan 01 2003 to Mar 31 2018 in the UNOS registry. Recursive feature elimination on random forest was used to select the top 20 out of 134 variables. Logistic regression models were fitted based on selected variables to predict the occurrence of DGF. Performance of the model was assessed by computing the area under the receiver operating characteristic curve (AUROC) after 10-fold stratified cross-validation.
Results: 6934 adult CLKT were included in this study. The incidence of DGF was 22.14%. Risk factors for DGF after CLKT include donor BMI, cause of death, recipient MELD score, KDRI (Rao), dialysis prior to transplant, life support prior to transplant, days on the waiting list, re-transplant, distance to transplant center, creatinine at transplant, and cause of organ failure. The model AUROC was 0.7139 (95% CI: 0.6829, 0.7447).
Conclusion: This study identified novel risk factors and is the first to date to estimate the development of DGF after CLKT using variable selection via a random forest-based method with subsequent logistic regression. Further study is required to confirm and explore these associations in other kidney transplant populations.

Variables	Odds Ratio	P	95% Confidence Interval	
Donor				
BMI (kg/m²)	1.022913	0.058	0.999221	1.047168
Cause of Death				
Cerebrovascular	2.588586	0.069	0.927721	7.222834
Sepsis	2.071564	>0.001	1.44698	2.965746
Respiratory Failure	2.225221	0.003	1.308524	3.784118
Liver Vascular Thrombosis	11.46357	0.007	1.952454	67.30681
Recipient				
MELD Score	1.023815	0.01	1.005633	1.042325
KDRI (Rao)	1.992037	>0.001	1.435862	2.763645
Dialysis Prior to Transplant	1.883351	>0.001	1.344219	2.638716
Life Support Prior to Transplant	1.771227	0.024	1.077682	2.911103
Days on Waiting List	1.000639	0.014	1.000132	1.001146
Kidney or Liver Re-transplant	2.521822	0.007	1.289411	4.932162
Distance to Transplant Center (mi)	1.000688	0.048	1.000006	1.00137
BMI (kg/m²)	1.022378	0.042	1.000842	1.044376
Creatinine at Transplant (mg/dL)	1.055581	0.089	0.991843	1.123416
Cause of Organ Failure				
Type II Diabetes	1.383284	0.073	0.970143	1.972363
Acute Tubular Necrosis	2.524608	0.027	1.108435	5.750133
Oxalate Nephropathy	3.79927	0.046	1.021178	14.1351
Hepatorenal Syndrome	2.31462	>0.001	1.616305	3.314638
Liver Graft Primary Non- Function	6.244271	0.058	0.939786	41.48917

[Logistic Regression Fitted for Prediction of DGF After CLKT]

P-576

Effect of WeChat-based peer education on medication compliance and quality of life in patients with liver transplantation: a pilot study

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Objective: To explore the effect of peer education intervention using WeChat on improving drug compliance and quality of life in follow-up liver transplant recipients.
Methods: This was a randomized control trial, 63 liver transplant recipients (intervention group=32, control group=31) from the follow-up clinic participated in the study. Participants in control group received routine follow-up outpatient health guidance, patients in intervention group were given peer support intervention on WeChat platform for 6 weeks.Drug compliance and quality of life were evaluated at prior to the intervention, 3, 6 and12 months after the intervention.
Results: In 3 months after the intervention, patients in the intervention group showed significant improvement only in drug regimen compared to participates in the control group (P< 0.01). Significant improvements were found in all aspects of the drug adherence in 6 months after intervention (P< 0.01).In 12 months after the intervention, smaller significant improvements were found (P< 0.05). There was no significant improvement in quality of life in all separate intervals after the intervention.
Conclusion: As a randomized control experiment pilot study, the WeChat-based peer education was found to be effective in improving most aspects of drug compliance in liver transplant recipients in China, the long-term effect and the impact on quality of life are worth to study in the future.

P-577

Liver transplantation in Kazakhstan: two-era experience of the single center

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Background and aim: Liver transplant activity started in Kazakhstan in 2011 and has reached 246 cases at December 2017. A present study was intended to analyze the outcome of the most experienced liver transplant center in Kazakhstan.
Methods: Between December 2011 and December 2017, 88 LDLTs were performed at A.N. *Syzganov´s* National Scientific *Center* of Surgery. All patients were divided to cohorts according to the two periods of experience: early era (2011-2014), 25 patients; and late era (2015-2017), 63 patients. Clinical course and outcomes were retrospectively reviewed.
Results: There were no significantly difference between recipient characteristics. Patients operated on during the second era had significantly better survival (1 year, 90.5; 3 year, 79.6%; vs 1 year, 67.7%; 3 year 63.3; p < 0.05). There was significantly greater use of the right lobe graft during the second era (p < 0.05), as well as the indication for splenectomy was significantly lower (p < 0.05). We also noted decreased number of relaparotomies (p < 0.05).
Conclusion: Over the past 7 years, LT program has been established, and operative techniques used in LDLT have changed dramatically. Patient survival has been improving by increasing the experience.

P-578

Decision tree analysis to stratify and quantify risk of acute cellular rejection following liver transplantation

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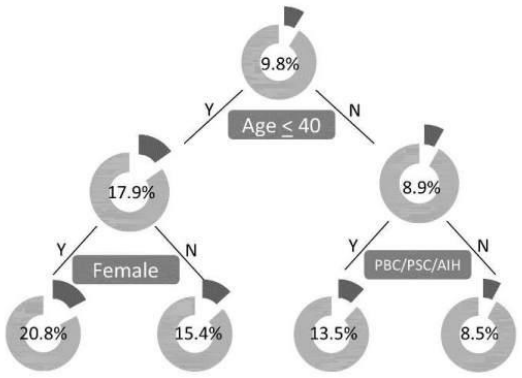
Several clinical factors are reportedly correlated with acute cellular rejection (ACR) after liver transplantation. We used decision tree analysis to develop a tool to stratify and quantify risk of ACR (within 12 months) in LT recipients. Data were from the Organ Procurement Transplant Network (OPTN) STAR files of December 2017. We included LT recipients in the last decade (2008-2017, n = 44872). Decision tree analysis was performed using variables available at LT: Recipient age, gender, ethnicity, etiology of liver disease, HCC, MELD score, BMI, donor age, type of donor (LDLT vs DDLT) and cold ischemic time. Model were built using randomly selected two-third of the recipients (n=29914) and was validated in the rest of the one-third (n=14958). ACR within 6 and 12 months developed in 4474 (10.0%) and 5215 (11.6%) recipients, respectively. The decision tree stratified female gender with age ≤40 as highest risk (20.8 %), male gender with age ≤40 and PBC/PSC/AIH with age >40 as intermediate risk (15.4 and 13.5%, respectively) and non-autoimmune liver disease with age >40 as lowest risk (8.5 %) to develop ACR within 6 months [Figure]. The predictions in the model building set were almost identical to those in the validation set (r^2=0.961, p=0.0198). The risk (odds ratio) of developing ACR in longer post-LT period (12 months) increased 3.0 times for highest risk group, and to 1.8-2.0 times for intermediate risk groups, when compared to lowest risk group (p< 0.0001, respectively). In conclusion, the decision tree model accurately stratifies and quantifies risk of developing ACR within 6 and 12 months post-LT. The model allows physicians to identify patients requiring lower threshold for liver biopsy and those who benefit from intensified immunosupressions to prevent ACR.



[Decision tree for ACR within 6m]

P-579

Liver transplant in Transthyretin (ATTR) familial amyloid polyneuropathy: a single center experience

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Background: Familial amyloid polyneuropathy (FAP) is a rare, clinically heterogeneous disease due to heritable mutations that lead to misfolding of a precursor protein and multisystem disease. Liver transplantation (LT) is the most definitive option to halt disease progression.
Method: In this case series, we describe our experience with patients undergoing LT for FAP.
Results: Seventeen patients with FAP who underwent LT were followed at our center between January 1985 and October 2018 (Fourteen patients underwent LT at our center). Almost two thirds (65%; 11/17) of the patients were of Portuguese origin. Almost half (47%; 8/17) of the patients had at least two systemic manifestations of FAP (neurological, renal or cardiac). Prior to transplant, five patients received a pacemaker and six patients had documented poor nutritional status. The average age at the time of transplant was 42 (26-67). One patient had worsening of peripheral neuropathy after transplant. One patient was re-transplanted after four days due to hepatic artery stenosis. Three patients passed away during the follow-up period. The 5- and 10- year patient survival was 88% and 82% respectively. One patient died 10 years after transplant with severe sepsis. One patient died after 4 years with no cause identified due to loss of follow up. One patient died 5 months after transplant due to multi-organ failure. This patient had peripheral and autonomic neuropathy, poor nutritional status and was wheelchair-bound prior to transplant. Of the 14 transplants performed at our center, 10 livers were sequentially transplanted into another recipient (domino liver transplant).
Conclusion: Consideration of pre-transplant clinical and nutritional status to select suitable transplant candidates could help to further improve the long-term outcomes of FAP patients post LT. The utility of LT in this population is likely to change in the future with the introduction of new pharmaceutical agents.

P-580

Fast track in liver transplantation: six years of a full-fledged ERAS protocol

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Fast track surgery is an enhanced recovery after surgery (ERAS) protocol which has been shown to facilitate hospital discharge, decrease length of stay, improve outcomes and reduce costs. We aimed at designing a comprehensive fast track pathway (OR-to-discharge) to facilitate early recovery after liver transplantation, applying it prospectively to every single patient in a new liver transplant program.
Patients/methods: All patients were included. Balanced general anesthesia, fluid restriction, IVC preservation, temporary porto-caval shunt and thromboelastography were utilized. Oral intake and ambulation were started within hours of ICU arrival. Patients received steroids, tacrolimus and MMF for immunosuppression, using basiliximab induction and delayed start of CNIs in patients with renal impairment. Tacrolimus dosing was adjusted using a Bayesian estimation methodology.
Results: We performed 240 transplants in 236 patients (191♂ /45♀) over 74 months, mean recipient age was 56.3±9.6 years, with mean raw MELD score of 15.5±7.7. The predominant etiologies were alcohol (n=136) and HCV (n=83), with hepatocellular carcinoma present in 130 (55.1%) patients. Nine patients received combined liver and kidney transplant. Mean operating time was 315±64 min with mean cold ischemia times of 279±88 min. Thirty-one patients (13.1%) were transfused in the OR, receiving a mean of 2.4±1.2 units of PRBC. Patient's extubation was immediate (< 30 min) in all but 3 patients. Median ICU length of stay after transplant was 12.7 hours, and median postransplant hospital stay was 4 days (2-76) with 30 patients (14% of discharges) going home by day 2, 87 (40%) by day 3, and 133 (61%) by day 4, which defined our Fast-Track group. Thirty-day-readmission rate was 34.9%, being significantly lower (28.6% vs 44.7% p=0.015) in the Fast-Track group. Patient survival was 87.6% at 1 year and 81.8% at five years.
Conclusion: Fast tracking is feasible and can be applied as the standard of care in liver transplantation.

P-581

Beyond medication education: opportunities for improvement in health education of solid organ transplant recipients

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Introduction: As immunosuppressive medications are crucial to graft and patient survival, transplant centers dedicate significant resources to medication education. However, patient outcomes also depend on general health education. We assessed organizational engagement in these topics at a tertiary academic institution.
Methods: A 51-question survey from the Agency for Healthcare Research & Quality was administered to staff at a multi-visceral Transplant Center from 2/28/2018 to 4/6/2018. Respondents selected "Doing well", "Needs improvement", "Not doing", and "Not sure/NA" toa wide range of questions. 11 questions on medication education, and general health education and resources were included for analysis. A performance ratio was calculated by dividing the number of "Doing well" responses by the sum of "Needs improvement" and "Not doing" responses. "Not sure" responses represented no opinion on institutional performance and were excluded. A ratio greater than 1.5 was considered as performing well, as an indication that 50% more staff responded "Doing well" compared to "Needs improvement" and "Not doing".
Results: 68 staff (20% response rate), including nurses (28.3% of total respondents), physicians (20.0%), and coordinators (12.8%), completed the survey. Respondents rated the institution as performing well in the realm of medication education and access (performance ratios 1.8-2.4), but less well regarding general health education and accessing non-medication related resources (performance ratios 0.3-1.3) (Table 1).
Conclusion: The transplant community in this center is invested in and perceives it is performing well at providing patients medication education and access. There is less confidence in institutional engagement in providing patients with general health education and resources. Staff perceptions will be validated by assessment of patient perceptions, satisfaction, and needs. Together this information may indicate additional opportunities to improve transplant patient outcomes.

P-582

Pregnancy after liver transplantation: a monocentric experience

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Background: Thanks to the innovations in transplant medicine, women undergone to liver transplantation enjoy better health, so that they require living the experience of pregnancy. The purpose of our study is to describe the experience of the Liver Transplantation Unit at "Fondazione Policlinico A. Gemelli" - UCSC in Rome.
Methods: We retrospectively identified all women who had a pregnancy following liver transplantation, reviewing medical records and extracting data on maternal characteristics, pregnancy-related outcomes, neonatal outcomes and long-term patient follow up.
Results: We identified 12 women who had 15 pregnancies following liver transplantation, between 19912015. Mean maternal age at delivery was 32±5 years, while mean transplant-to-pregnancy interval was 11 (±6) years. One pregnancy was conceived following assisted reproductive techniques. There weren't twin pregnancies. Immunosuppressive treatment is carried on with a low-dose scheme. Of the 15 total pregnancies, 9 (60%) delivered preterm, with a range between 25 and 36 weeks of gestation, meanwhile the general gestational age at the delivery was 36.1±3,5 weeks. Of all these, only three presented in spontaneous labour, while 12 (80%) were by elective caesarean. For neonatal outcomes, there were no congenital malformations, one infant needed admission to the NICU. There was no neonatal death. Maternal follow-up at a median of 5.6 years (range 0.2 - 21 years), made up from multidisciplinary team, showed no pregnancy-related complications. A woman breast-fed her child, continuing immunosuppressive therapy with Tacrolimus, without evidence of neonatal changes.
Conclusion: Women undergone to liver transplantation presents low complication rates during pregnancy and should continue immunosuppressive therapy with adequate multidisciplinary assistance.

P-583

Portal vein thrombosis is not a contraindication to liver transplantation

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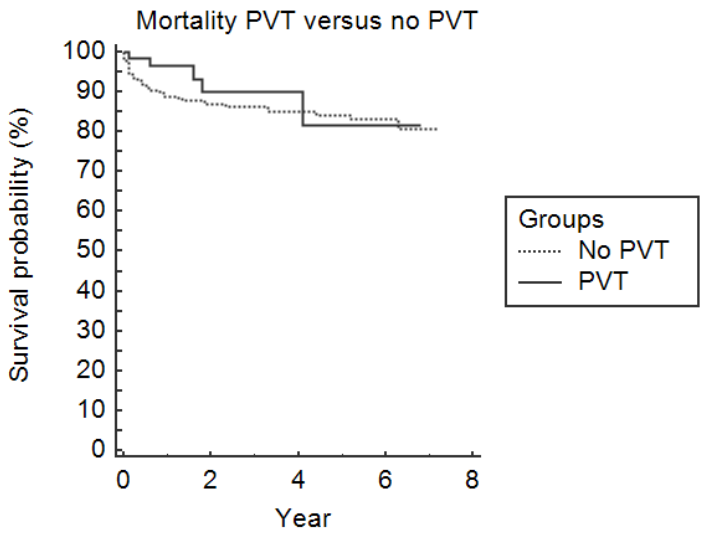
Purpose: Portal vein thrombosis (PVT) is common in the cirrhotic population and no longer considered an absolute contraindication to liver transplantation in most centers.
Methods: Retrospective analysis of 500 consecutive cases of liver transplantation (2011-2018) at a single center. Characteristics and long-term outcomes of patients with portal vein thrombosis (PVT; n=64) were compared with patients transplanted without portal vein thrombosis (noPVT; n=436).
Results: Recipients in the PVT group were older (59 vs 56 years; p< 0.05). There was no statistically significant difference in the 2 groups in the proportion of male patients, BMI, incidence of diabetes mellitus or malignancy, and pre-transplant functional status. The PVT group waited longer for their transplantation (336 vs 228 days; p< 0.05). The mean MELD score was 24 vs 26 (PVT vs noPVT; p=0.13). Similar proportion of recipients in both groups received living donor vs deceased donor grafts. 42% of thrombi were unsuspected on pre-operative imaging and detected intraoperatively, 35.9% were occlusive thrombus and 15.6% had clot extension into the SMV or splenic vein. 63 patients underwent an eversion thrombectomy; in 2 patients, flow could not be reestablished and their graft portal veins were anastomosed to varices in the liver hilum. There were no tumor thrombi on pathological analysis. There was no significant difference in the cold ischemic time, length of hospital stay, or incidence of early graft failure. Patients in the PVT group had a significantly higher rate of post-operative portal vein thrombosis formation (4.7% vs 0.46%; p=0.002). 5-year patient survival were similar between the 2 groups
Conclusion: 12.8% of liver transplants in our center were performed in patients with PVT. Adequate flows can be reestablished in most patients with eversion thrombectomy and long-term survival is comparable with patients transplanted without PVT.



[Mortality PVT vs no PVT]

P-584

Impact of the MELD era in liver allocation in Chile: Are candidates with hepatocellular carcinomas been beneficiated due to the exception points?

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Background: Since October 2011 the MELD score system was adopted in Chile for liver allocation. However there are many circumstances, including Hepatocellular carcinoma (HCC) were the MELD does not reflect mortality or probability to dropout from the waiting list (WL). Our normative assign 20 extra points plus one additinal point per month for candidates with HCC.
Objectives: To evaluate the dropout rate of the waiting list (WL) and survival post - liver transplantation (LT) between cirrhotic patients (CP) listed by MELD scores, patients listed with HCC and patients listed by other exceptions (non-HCC).
Methods: Retrospective analysis of the WL of adult candidates (>15 years old) for elective cadaveric and living-donor LT of in Chile, from October 2011 until December 2017. Analysis of the dropout rate of WL and survival post-LT were carried out including Kaplan-Meier curves compared with log-rank test
Results: In this period, 730 candidates were listed. Mean age was 53.9±12.0 years; 55.8% were men. The principal etiologies were NASH (29.5%), Alcoholic Liver Disease (16.2%) and Autoimmune (11.8%). We analyzed three groups of candidates: CP 301 (41.3%), HCC 195 (26.7%) and non-HCC 233 (32%). We registered 352 LT (48.2%). Mean time in WL was 311 days: 244 days in CP, 381 days in HCC and 313 in non-HCC. The annual dropout rate was significantly higher in CP compared with candidates with HCC, and non-HCC exceptions (45.5%; 33.1% and 29.3%, respectively, p< 0.001). Survival post-LT was 86.1% at 1-year and 84.6% at 5-year, without differences among the three groups (p=0.411).
Conclusion: Exceptions generate inequities in dropout rate, disadvantaging patients without exceptions. Therefore, the extra scoring assignment must be carefully adjusted. Prioritization for LT using the MELD score system has not decreased the dropout rate in Chile (persistent low donor´s rate).

P-585

Renal outcome one year after living donor liver transplantation of patients with pre-transplant hepatorenal syndrome or chronic renal insufficiency

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Purpose: Liver transplantation (LT) is the ultimate curative treatment for end-stage liver disease. However, post-transplant usage of immunosuppressant agents is associated with chronic renal insufficiency (CRI). The aim of this study is to compare the renal outcome of LT patients with pre-transplant normal renal function, hepatorenal syndrome (HRS), and CRI.
Methods: Medical records of adult patients receiving living donor liver transplantation (LDLT) at Kaohsiung Chang Gung Memorial Hospital from July 2008 to September 2017 were reviewed. Patients with pre-transplant renal function impairment were grouped according to the diagnostic criteria of HRS, 12 patients were type 1, 19 patients were type 2, and 44 patients were CRI, respectively. For comparisons, 67 patients with pre-transplant normal renal function were selected using sex and age propensity score match (1:2).
Results: After LDLT, the 1-year mortality were 6% in control group, 8.3% in HRS type 1, 5.3% in HRS type 2, and 13.6% in CRI group respectively (p = 0.515). At the time of liver transplantation, the serum creatinine level of HRS type 2 group was significantly better than CRI group (1.46mg/dL vs 2.32mg/dL, respectively, p = 0.001). But there were no significant differences in creatinine level between HRS type 1 and 2, neither between HRS type 1 and CRI group. One year after LDLT, renal function could be improved to chronic kidney disease (CKD) stage 1 or 2 in 36.4% of patients in HRS type 1 group, 33.3% of patients in HRS type 2 group, and 23.7% of patients in CRI group, respectively (p = 0.420). On the other hand, most of the patients (93.7%) in the control group could maintain in CKD stage 1 or 2.
Conclusion: Patients with pre-transplant HRS had slightly better renal outcome at one year after LDLT than those with CRI. Larger patient number may be warranted.

P-586

Is cell saver mandatory for liver transplantation? Report of more than 500 liver transplants without auto transfusion.

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Background: Liver Transplant program was started in January 2002 in our center, Imam Khomeini Hospital Complex, Tehran, Iran; affiliated to Tehran University of Medical Sciences. We used a brand of Cell Saver infrequently in the first series of 90 patients but no cell saver was used from 2012 when we did more than 50 liver transplants per year.
Method: We did all liver transplants without cell saver and auto transfusion. The main reason was non-availability of the machine set from 2011. Coagulation status was monitored intraoperatively with Rottem system and corrected accordingly.
Results: 544 first liver transplants were done from January 2012 to December 2017. Mean age of the patients was 44.48 years, 60 percent male and average MELD score of 21. The series include acute liver failure and acute on chronic liver failure. 166 patients did not get any transfusion (group 1), 260 patients got 1-4 units of packed red blood cell (group 2), 103 patients 5-9 units (group 3) and 15 patients 10 or more units of packed RBC (group 4). Overall 1 month survival was 89.1%, while in group one it was 95.8%, in group two 90%, in group three 87.4% and in group four 46.7%.
Primary non-function and sever dysfunction was significantly more common in group 3 and 4. Arterial thrombosis was also more common in group 4 and early mortality was increased in a linear correlation with transfusion from 9% in group 1 to 60% in group 4.
Conclusion: Although autotransfusion is a well-known substitute for allotransfusion, there are pros and cons for using cell saver machines in the setup of liver transplantation. This report shows that results of liver transplantation without cell saver can be comparable with transplant programs using this device.

P-587

Fatal skin desquamation syndrome after diseased donor liver transplantation for HBV liver cirrhosis

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Background: Toxic epidermal necrolysis (TEN) or Lyell syndrome is acute immunologic condition, characterized by desquamation of patient's epithelial surfaces, preceded by medication/toxin exposure, usually 4 to 28 days prior onset. By definition it affects more than 30% of the body surface area, as well as conjunctivae and mucosae linings. TEN represents a rare clinical entity on its own, with a frequency of one to two people per million per year. In the liver transplant scenario among the numerous drugs implicated as culprits of TEN, the latter may be a manifestation of a severe form of graft versus host disease (GvHD).
Methods: We present a case of a 57-year old male patient, who underwent deceased donor liver transplantation for HBV-related liver cirrhosis and HCC within Milan criteria. After an uneventful postoperative period, two weeks after discharge, he developed toxic epidermal necrolysis with a lethal end.
Results: Despite Lyell syndrome being our main diagnosis, the background of a recent liver transplantation raised a strong clinical suspicion of a GvHD. Moreover the underlying pathogenic mechanism is the same, namely cytotoxic (CD8+) T-lymphocytes targeting epithelial cells. The differentiation of the two entities through chimerism assay of blood lymphocytes bares no clinical benefit, as there is no proven therapeutic management for either condition. In the liver transplant setting both TEN and GvHD have high mortality rates (60-100%), depending on the severity.
Conclusion: Only a few cases of TEN/GvHD after liver transplantation have been described in the literature. One must recognize these conditions as a possible severe complication with high mortality, regardless of the advanced intensive care management.

P-588

Do extremes of body mass index affect surgical outcomes in a multiethnic Asian cohort?

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Introduction: Liver transplant (LT) in patients with extremes of body mass index (BMI) such as underweight BMI < 18.5kg/m2 and morbid obesity (BMI >40kg/m2 or 35kg/m2 with metabolic syndrome) has been associated with poorer outcomes. However, a more conservative cutoff of BMI >32.5kg/m2 is often used in the Asian population. We reviewed the impact of Asian BMI cutoffs on patients undergoing LT over the last decade.
Methods: 167 patients who underwent LT were retrospectively reviewed. Patients' BMI were categorized into underweight: < 18.5kg/m2, normal-overweight: 18.5-32.5kg/m2 and morbidly obese:>32.5kg/m2. Demographic and clinical data were analyzed using SPSS v20.
Results: Of 167 LT patients, 55.7% underwent deceased donor living transplant and 44.3% underwent living donor liver transplant. There was no difference in median age, ethnicity or gender between the three groups. The proportion of patients undergoing LT for acute liver failure, alcoholic liver disease, and hepatocellular carcinoma were comparable. Morbidly obese patients also did not have a higher rate of non-alcoholic steatohepatitis (NASH) compared to underweight and normal-overweight patients. (% NASH, Underweight 0%, normal-overweight 8.3%, morbidly obese 17.6%, p=0.389). Underweight patients appeared to have greater blood loss during LT, although this did not reach statistical significance. (Blood loss, ml (IQR), Underweight 8000 (1500-21000), normal-overweight 3100 (1800-5000), morbid obesity 3500 (2175-4500). Operative duration, length of ICU stay and length of stay were similar between the three groups. All cases of inpatient mortality (4.1%, n=6) occurred in the normal-overweight BMI group and not in underweight or morbid obesity groups. BMI measured at one year after LT was largely similar when compared to pre-transplantation.
Conclusion: Extremes of BMI as defined by local Asian cutoffs do not appear to have an impact on intra-operative outcomes and in-hospital mortality. BMI cutoffs alone should not be a contraindication to LT.

P-589

Outcome of living donor liver transplantation for secondary biliary cirrhosis in adult: single center experience

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Introduction: Although liver transplantation is a definitive cure for secondary biliary cirrhosis (SBC), there is limited data about results of living donor liver transplantation (LDLT) in adults.
Material and methods: This retrospective study assessed data from 29 SBC patients who had LDLT between December 1994 and July 2018.
Results: The study cohort comprised of 10 males and 19 females, aged 50.0 ± 8.6 years. Except for 3 patients, the rest were diagnosed with secondary biliary cirrhosis from hepatolithiasis, and 25 out of 29 (86.2%) had a history of receiving the hepatobiliary surgery. Model for end-stage liver disease (MELD) score was 18.8 ± 9.4. The major complication rate was 62.1%, and the most common complication was bleeding. The ICU and hospital stay were 24.4 ± 13.8 and 40.9 ± 24.8 days. Four patients died in first month after LDLT; Tow died of rupture of hepatic artery rupture, one died of Intra-cranial hemorrhage, and the other one died of sepsis.
Conclusion: LDLT for patients with SBC is very difficult, and there's a big danger of massive bleeding. Even though operation time is long and there's a lot of bleeding, thorough planning and a meticulous surgical technique that does not cause complications can reduce the mortality rate in LDLT for patients with SBC.

P-590

In-hospital survival after living donor liver transplantation: A large single center study

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Background: Complications following liver transplantation may be serious and potentially life threatening. However, most reports on outcomes have been about long-term survival. We aimed to

determine the risk factors and causes of in-hospital mortality after living donor liver transplantation (LDLT) in the index admission.
Methods: Medical records of 855 consecutive patients who underwent LDLT (12/2011 - 9/2018) at our center were reviewed. Fifty-eight pediatric recipients and retransplantation (n=2) were excluded from the analyses. Transplant- and non-transplant-related factors were collected during the index admission.
Results: Thirty patients (30/795; 3.8%) died during the index admission after LDLT. The average hospital stay was 14 days. The most common reasons for death were infection (63.5%), vascular complications (19%), and graft dysfunction (11%). The most common site of infections were blood-stream, intraabdominal collection, and pneumonia. Risk factors for mortality included preoperative renal dysfunction, intraoperative bleeding, high MELD score, and patients with acute-on-chronic liver failure.
Conclusion: Our experience suggests the in-hospital survival of > 95% after LDLT. These data confirm that continued efforts are needed for better patient selection, preoperative optimization, and identification of preventable complications to aim towards further improvement in the short-term survival after LDLT.

P-591

Long-term outcomes of combined liver and kidney transplantation: a single center experience

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Background: Combined liver and kidney transplantation (CLKT) is a therapeutic option for patients at end-stage liver and kidney disease but factors impacting patients and grafts survival are unclear. The aim of this retrospective study was to identify the immunological and non-immunological risk factors in CLKT recipients.
Methods: In our center, from 1999 to 2016, 69 adult patients, underwent CLKT, were included in the study. A survival analysis was performed by Kaplan Mayer method with log rank test and Cox's regression model.
Results: 69 CLKT recipients were included (66.7% male, mean age of 52.5±11.7yrs), liver cirrhosis was reported in 79.7% (n=55) with a median MELD-score of 21±6.6, and polycystic liver disease in 21.2% (n=14). Chronic renal failure was due to: anticalcineurin inhibitors toxicity 22.7%(n=15), unknown end-stage renal disease 36.9%(n=24); dialysis was performed in 43.6% (n=32) of patients before transplantation and 23.2% (n=16) have been previously liver-transplanted. Sensitized patients with the presence of anti-HLA antibodies were 43.5% (n=30): HLA-class I antibodies 37.7% (n=26), HLA-class II antibodies 32.8% (n=21), 54.5% (n=18) of them were preformed-DSA. The median follow-up was 37 months. A 1 and 5 years patients survival was of 79.5% and 64.7%, liver graft survival censored for death was 92.0% and 76.7% at 1 and 5 years and kidney graft survival censored for death was 92.0% at 1 year and 83.0% at 5 years. Kidney but not liver graft survival seems to be influenced by immunization status (HLA-class I antibodies p= 0.036, DSA p=0.07) but only at univariate analysis.
Conclusion: This retrospective and unicentric study, revealed a good 1 and 5 years patients and grafts survival in a cohort of 69 CLKT. The immunization status was not a risk factor for patients and grafts survival. Future investigations, with more patients, are needed to explore risk factors and immunosuppression strategy in this context.

P-592

Single aortic- or dual-perfusion during the liver retrieval: does it really matter?

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Background: In the era of the marginal grafts, it is really important optimizing every single surgical technique from the retrieval to the implantation to discard less grafts. The standard perfusion technique consists of cannulation of the aortic circulation, otherwise a second cannula can be placed through one of the portal branches for the dual perfusion (DP) and running both circuits contemporary.
A matched pair analysis was performed comparing grafts perfused through the aorta only (SP)and livers retrieved with the dual perfusion (DP).
Methods: Using a prospectively held database of three different centers, all DP grafts were matched against SP cohort. Matching was based on donor DRI and recipient MELD, blinded to outcome.

A comparative analysis of the donor and recipient characteristics and immediate post-operative outcomes between the groups was performed. Similar sub-analysis was performed considering only the sub-group of the marginal grafts.All livers were perfused with the same fluid in all centers.
Results: From January 2017 to September 2018, 49 DP grafts were paired with 49 SP, with comparable donor and recipient characteristics.
There was no significant difference in patient and graft survival. However, there was a significantly lower transaminase peak in DP patients compared with SP cohort (respectively ALT:694vs.1621;AST:482vs.1066, p< 0.05). DP patients experienced of significantly lower AKI incidence (38%vs.62%,p< 0.05)and shorter hospital stay. There was a trend of less PNF rate in the DP patients. Similar benefit was found for the marginal DP grafts compared with SP marginal livers (DGFrate:50% vs. 70%, p< 0.05).
Conclusion: Perfusing the liver graft contemporary with aortic and portal cannulation might be a promising technique to reduce the ischemia reperfusion injury consequences. Randomization study would be useful to validate these results.

P-593

Long-term survival (> 10 years) after liver transplantation at a university hospital

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The long-term survival of patients undergoing liver transplantation has most recently appeared in the literature given the higher survival rate obtained in the first months of follow-up and has been reported as above 50% in European centers. The aim of this work was to present the survival rate after 20 years of transplantation performed sequentially at a Brazilian University Center.
Method: Liver transplantations were performed from 1995 to 2007. The inclusion of cases was sequential mode, using a prospective data collection: the day before the transplant, the end of the sixth month and the end of at least 10 years after transplantation. Patients were excluded under the age of 18, and those who did not survive up to six months of the postoperative period. The variables collected were: age, sex, BMI, cold ischemia time, time of surgery, survival time, amount of RBCs received intraoperative and mean arterial pressure in the induction of the surgery. Receiver and donor variables were also noted. Kaplan-Meier method and non-parametric test were used.
Results: 174 cases were analyzed: 76 (43.7%) died in that period and 98 (56.32%) survived. It was found that younger patients had a higher survival time (alive = 40.1 years x death = 45.6 years; P= 0.00007), the average survival time was 223 against 112 months who died (P = 0.0001). The most common disease that led to death was viral hepatitis. The cumulative causes for death were cardiovascular effects (36.4%), relapse diseases (22.1%), cancer *de novo*(15.6%), infectious (14.3%), and others (10.4%).
Conclusion: Liver transplantation offers an excellent survival index of up to almost 20 years. This should be longer in future analysis due to better sustained viral response with new drugs and better monitoring for the detection of hepatocellular carcinoma.

P-594

The survey of QOL of pediatric patients who receiving liver transplantation for 5 years

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Objective: This research aimed to survey the quality of life (QOL) of the pediatric patients of liver transplantation for 5 years.
Methods: The Pediatric Quality of Life™ 3.0 Transplant Module was adapted to develop the questionnaire of the survey. The patients those who have received liver transplantation for 5 years were investigated.
Results: The median age when transplantation was 11 month, and the median age when investigation was 97.5 month. The mean height was 132.0±15.0 cm, while the mean weight was 28.9±12.9 kg respectively. The mean of BMI Z score was 0.3±1.49. The mean score of QOL was 73.2±13.8. The domain of “how I look” was median positive correlated with the year of follow-up, and the domain of “pain and hurt” was median positive correlate with weight Z score, and the correlation index was 0.357, 0.495 (P＜0.05). The domain of “my transplant and others” was median negative correlated with BMI and BMI Z score, and the correlation index was -0.317, -0.384 (P＜0.05). The domain of “worry” was median negative correlated with weight Z score, and the correlation index was -0.319 (P＜0.05).
Conclusions: The QOL of pediatric patients who have received liver transplantation is normal. The year of follow-up, weight Z score, BMI, BMI Z score, and weight Z score may be impact factors of QOL after liver transplantation.
Keywords: Liver transplantation; pediatric; QOL; survey

P-595

Effect and analysis of comprehensive nursing methods on early complications and quality of life in patients with ischemia-free liver transplantation

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Objective: To investigate the effect of comprehensive nursing methods on early complications and quality of life in patients with ischemia-free liver transplantation and cold-preserved liver transplantation.
Methods: The clinical data of 28 recipients after ischemia-free liver transplantation from July 1st 2017 to October 1st 2018, 45 patients received cold-preserved liver transplantation with comprehensive nursing and 42 patients received cold-preserved liver transplantation with general nursing in our hospital were retrospectively analyzed. The comprehensive nursing group adopted basic nursing, body position nursing, drainage pipe nursing, psychological evaluation, health education and other nursing methods. The control group adopted routine nursing methods of liver transplantation. The early complications, scores of birth rate and quality of life in the different groups were analyzed and compared.
Results: The overall incidence of complications (bleeding, biliary tract infection, pulmonary infection, hepatic artery thrombosis, etc.) in patients undergoing ischemia-free liver transplantation with comprehensive nursing was lower than that of patients receiving cold-preserved liver transplantation with comprehensive nursing, and the quality of life score of the former was significantly higher. Besides, the complications of patients receiving cold-preserved liver transplantation with comprehensive nursing were lower than that of general nursing, and the complications after cold-preserved liver transplantation were better in the former.
Conclusion: Comprehensive nursing can significantly reduce the early complications and improve the quality of life of patients after ischemia-free liver transplantation.

P-596

Successful deceased donor liver transplant with schistosomiasis positive donor graf

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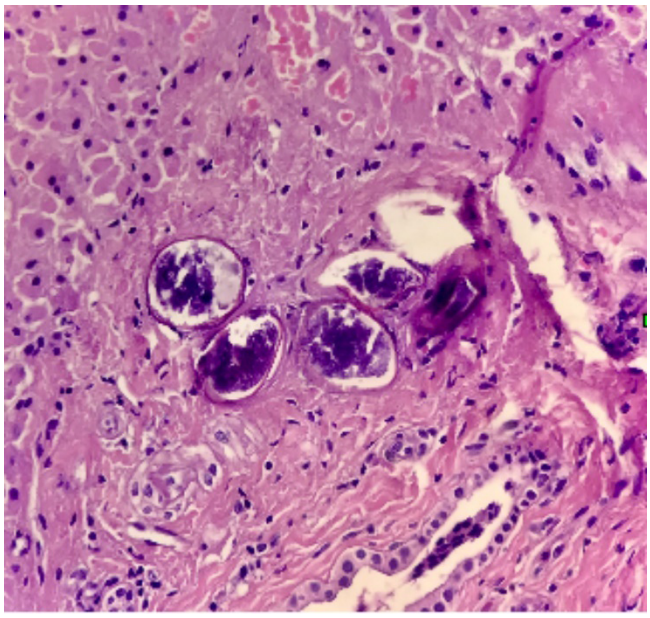
Introduction: Disease transmission in the liver donor graft during deceased donor liver transplantation (DDLT) must be avoided through meticulous screening. We report a successful management of a DDLT where the donor graft showed positive for schistosomiasis on final histopathology.
Methodology: Case report
Result: Recipient:52-year-old-male, Filipino (height: 168 cm;weight:105.1 kg), blood type O+ with end-stage liver disease due to non-alcoholic fatty live disease was referred for possible liver transplantation. He had a Child B classification and MELD score of 22. The indications for transplant were refractory ascites (> 10 sessions of therapeutic paracentesis), hypersplenism with thrombocytopenia. Donor:42-year-old-male, Filipino (height:157.5 cm;weight 52 kg), blood type O+, construction worker. He was declared brain dead 48 hours after suffering severe cerebral hemorrhage following a motor vehicle injury. Hepatitis work-ups were all non-reactive. CMV IgG and EBV IgG were both positive. VDRL/RPR and malaria tests were negative. Ultrasound of the liver showed mild fatty change. Standard whole liver graft procurement technique was employed using Custodiol.Graft weight was 1.1 kg. Operation:The recipient underwent total hepatectomy with IVC preservation. Standard DDLT operation with IVC piggy-back technique (cavo-cavostomy) was done. Total operative time was 9 hours 15 minutes. Total cold ischemia time was 6 hours.
Outcome: The recipient recovery was unremarkable. On 7th post-transplant day, histopathology report of the donor liver showed schistosomiasis with focal mild peri-portal fibrosis (on trichrome stain). Treatment with praziquantel 60 mg/kg/day orally in 3 divided doses x 1 day was given because S. japonicum is the most prevalent specie in the Philippines. The recipient remains asymptomatic for schistosomiasis infection 2 years after the operation.
Conclusion: In extreme unavoidable circumstance, the disease transmitted can only be known after the transplant operation. Vigilance must be observed. Appropriate treatment may ensure long-term graft and recipient survivals.



[Figure 1. Schistosomiasis ova in liver graft]

P-597

Graft-recipient-weight ratio shows no impact on renal function improvement one year after living donor liver transplantation

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Background: Liver transplantation (LT) is the ultimate curative treatment for end-stage liver disease. Our previous study showed that small-for-size graft was related to massive ascites after transplant which may deteriorate renal insufficiency. This study aimed to investigate the relationship between graft size and post-transplant renal insufficiency in living donor liver transplantation (LDLT).
Patients and methods: This retrospective study reviewed medical records of adult patients receiving LDLT at Kaohsiung Chang Gung Memorial Hospital from July 2008 to September 2017. 44 patients with chronic renal insufficiency (CRI), defined as serum Cr > 1.5mg/dL, before LT were enrolled. According to renal function one year after LT, the patients were divided into mild CKD (chronic kidney disease) and severe CKD groups, defined as CKD stage 1-3, and CKD stage 4-5, respectively.
Results: The mean graft-recipient-weight ratio (GRWR) was 0.98% among the 44 patients. There were 6 (13.6%) mortalities of the 44 patients within 1 year after LDLT. At initial presentation, all patients were at least CKD stage III. One year after LDLT, renal function in 25 (65.8%) of the 38 survived patients improved to mild CKD. The mean GRWR was 0.97% in the improved group, comparing 0.99% in the poorer group (p=0.738).
Conclusion: The current data revealed that GRWR didn't correlate to improvement of renal function. Larger sample size and longer follow-up may be warranted.

P-598

Progressive multifocal leukoencephalopathy caused by JC-virus infection after orthotopic liver transplantation: a case report and review of the literature

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Introduction: A 65-year-old male was admitted because of muscle weakness, physical and mental deterioration, 30 weeks after orthotopic liver transplantation (OLT) for NASH end-stage liver disease. MRI of the brain revealed bilateral white matter changes both parieto-occipital as cerebellar suggestive for progressive multifocal leukoencephalopathy (PML) proven by liquor analysis revealing a positive JC-virus PCR.
Method: a critical literature search on PML after OLT was performed in PubMed and Web of science.
Results: PML is seen in the immunocompromised patient, but is less common in liver transplant recipients with only 11 cases reported. PML probably develops independently to the etiology of liver cirrhosis leading to liver transplantation. The mean time from OLT to development of neurological symptoms in the published cases varies between 2 and 113 months. Transmission of the JC-virus from donor to organ receiver cannot be ruled out, but is doubtful in light of the high prevalence of this latent virus amongst the general population and the low incidence of PML in liver transplant recipients. Brain biopsy has long been seen as the gold standard for diagnosis, although a positive liquor PCR for JC virus in combination

with white matter changes on MRI and neurological symptoms is highly convincing. Therapy of PML is directed at tapering or quitting the immunosuppressive medication. Several other agents, including cytarabin, cidofovir and mirtazapine have been suggested for treating or stabilizing PML, but experience is mainly obtained in patients with AIDS, auto-immune and hematological diseases. Since therapeutic options are limited the prognosis remains poor showing only one case with initial clinical and radiological improvement. Interestingly, our patient's condition stabilized and even improved on mefloquine and mirtazapine, now eight months after diagnosis.
Conclusion: PML due to JC viral infection after liver transplantation is rare, hindered with limited therapeutic options and therefore a dismal prognosis.

P-599

The addition of deceased brain donor oral Simvastatin administration to cold storage solution of explanted whole liver grafts: a randomized double-blinded phase 2 preliminiary results

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Background: Liver transplantation is the best treatment for end-stage liver disease. The interruptionof the blood supply to the donor liver during cold storage damages the liver, affectinghow well the liver will function after transplant. The drug Simvastatin may help to protect donor livers against this damage and improve outcomes for transplant recipients. The aim of this study is to evaluate the benefits of treating the donor liverwith Simvastatin compared with the standard transplant procedure.
Patient and methods: We propose a prospective, double-blinded, randomized phase 2 study of 2 parallelgroups of eligible adult patients. We will compare 3-month, 6-month, and 12-month graft survival after LT, in order to identify a significant relation between the twohomogenous groups of LT patients. The two groups only differ by the Simvastatin or placebo administration regimen while following the same procedure, with identicalsurgical instruments, and medical and nursing skilled staff. To reach these goals, wedetermined that we needed to recruit 106 patients. This sample size achieves 90%power to detect a difference of 14.6% between the two groups survival using a one-sided binomial test.
Results: The blinded preliminary results will be discussed regarding the enrolled half of the amount patients (n= 53) required to reach the study population.
Discussion: This trial is designed to confirm the effectiveness of Simvastatin to protect healthy andsteatotic livers undergoing cold storage and warm reperfusion before transplantationand to evaluate if the addition of Simvastatin translates into improved graft outcomes. International Standard Randomized Controlled Trial Registry number: ISRCTN27083228.
The proposed trial has been validated and accepted for financial support by the Italian National Health Ministry (Programme of "Ricerca Finalizzata 2013" - Clinical health care research - GR-2013-02357764).

P-600

Delayed kidney transplantation after 83 hours of cold ischemia time in combined liver-kidney transplant

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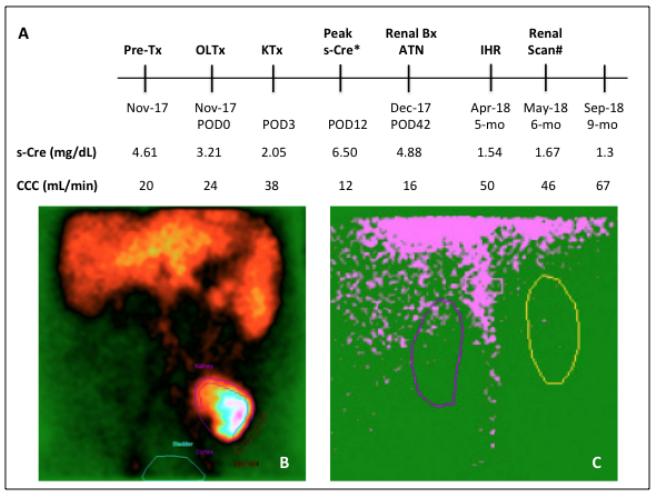
Background: Combined liver-kidney transplantation (CLKT) involves the sickest patient population and has expected lower outcomes compared to kidney transplant (KT) and liver transplant (LT). We showed the positive impact of delayed KT in CLKT on patient survival compared to simultaneous liver-KT. Here, we report a case where we delayed the kidney portion of CLKT up to 83h.
Methods: The rationale behind performing delayed KT was to offer less hostile environment with hemodynamically more stable LT recipient at the time of KT. We support all kidneys with continuous hypothermic pulsatile machine perfusion (HMP) until KT, which was performed at a later time as a second operation. Recipients are also supported with CVVH until KT after LT.
Results: Recipient was a 54 year-old male with alphal-antitrypsin deficiency-related cirrhosis and CKD on hemodialysis for >3 months. His MELD was 33 and he was very frail and sarcopenic. He underwent a LT from a 47-year-old donor who died of stroke in November 2017. Donor kidney was supported with HMP for >3 days due to hemodynamic instability of the recipient. Kidney CIT was 83.3 hours. KDPI was 71%. The recipient developed a DGF. He was supported with CVVH and hemodialysis for 5 months post-CLKT. At 6-month post-CLKT, he gained his kidney function. Renal scan confirmed no activity in native kidneys (Figure 1). Timeline of important events is summarized in Figure 1.
Conclusion: This case reports the longest CIT of a renal allograft in a complex case. It also demonstrates the amazing capacity of renal allograft to recover its function despite multiple insults in a hostile environment, even 6 months after CLKT.



Legend: (A) Description of important events in pre-, peri-, and post-transplant. Liver transplant surgery (POD0) was very difficult due to adhesions, scarring of the cirrhotic liver, and thrombocytopenia, requiring 30 units packed red blood cells, 16 units fresh frozen plasma, and 3 units platelets. His immediate postoperative course was complicated requiring multiple pressor support and reintubations for pulmonary edema and altered mentation. The patient started on CVVH on POD12. A kidney biopsy on POD42 confirmed the ATN. Post-biopsy, he developed a perinephric intraperitoneal hematoma requiring transfusion and operative exploration. In April 2018, his right inguinal hernia was repaired – by this time, he had improving urine output and creatinine and was trialed off of hemodialysis after surgery. (B) Renal scan 6-month after the transplant showing activity on the transplanted kidney in the left iliac fossa. (C) Native kidneys showed no uptake of radioactive material indicating no function of native kidneys, and confirming that renal function and creatinine clearance only depend on the transplanted kidney.

[Figure 1]

P-601

Management of portal vein thrombosis during liver transplantation: a single-center experience

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Introduction: Portal vein thrombosis (PVT) is not uncommon in liver cirrhosis patients. In past, PVT had been considered as contraindication to liver transplantation (LT) because of technical challenges for adequate restoration of portal inflow followed by high morbidity and mortality. However, alternative options for PVT during LT have been introduced, and nowadays, PVT is no longer considered as absolute contraindication for LT. Herein, we introduce our experiences and outcomes of LT for patients with PVT.
Patients and methods: Between Mar 2014 and June 2018, 65 patients underwent LT at out institution, and 13 (20%) of whom had PVT preoperatively. The characteristics and management of these patients were reviewed retrospectively and the outcomes were compared with that of non-PVT group.
Results: The type of PVT included Yerdel grade 1 in 7 patients (53.8%), grade 2 in 4 patients (30.8%), grade 3 in 1 patient (7.7%) and grade 4 in 1 patient (7.7%). For restoration of portal inflow, eversion thrombectomy was performed in 11 patients (84.6%), reno-portal bypass in 1 patient (7.7%) with grade 4 PVT, and SMV jump graft in 1 patient (7.7%) with grade 2 PVT. There was no portal vein-related morbidity except one patient who need portal vein stent because of stricture. The outcome after LT was comparable with that of patients without PVT.
Conclusion: Although it has a technical complexity in surgical procedure, LT is no longer contraindication for patient with PVT because of various alternative options and the outcome is comparable with the patient without PVT.

P-602

Modified technique in liver procurement for deceased donor - comparing outcomes and survival with conventional method

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Background: Techniques in liver procurement for deceased donor has been standardized since 1980s. Modifications have been made after 3 decades of experience but there are few studies about the efficacy and safety of such changes. This study aims to compare the outcomes between in-situ mobilization (modified technique), and dissection at back table (conventional technique).
Method: All patients who underwent deceased donor liver transplantation from 2010-2017 in this centre were included for retrospective analysis. Paediatric recipients, re-transplantations, reduced size grafts and split grafts were excluded. In modified technique, diaphragm and retroperitoneal attachment to inferior vena cava were divided prior to exsanguination as in total hepatectomy. After delivery of graft, brief trimming was done and integrity of vessels was checked immediately on-table. Graft would be stored for implantation directly. In conventional technique, diaphragm and retroperitoneal attachments were delivered en bloc and trimmed at back table.
Graft survival was compared. Recipient deaths with functioning graft were censored. Other parameters such as procurement duration (time from donor skin incision to graft delivered) and cold ischaemic time (time from cross clamping to implantation) were also compared.

Results: 271 transplantations were included for analysis, where 123 procurements using the conventional method and 148 using the modified method. There was no significant difference in demographics of both groups (Table 1). Graft survivals were similar between both groups (5-year survival of modified and conventional methods 99% and 96% respectively), p=0.201 (Figure 1). Procurement duration was significantly shorter in conventional group (170 minutes) than modified group (232 minutes), p< 0.001. However, cold ischaemic time was significantly shorter in modified group (338 minutes) than in conventional group (386 minutes), p< 0.001.
Conclusion: The modified technique did not significantly affect the graft survival. For surgeons who are experienced in mobilizing the liver, this technique is safe and feasible.

P-603

Effect and analysis about clinical application of rapid rehabilitation surgery nursing in perioperative period of ischemia-free liver transplantation

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Objective: To investigate the effect of clinical application of rapid rehabilitation surgery nursing in perioperative period of ischemia-free liver transplantation.
Methods: The clinical data of 28 recipients after ischemia-free liver transplantation from July 1st 2017 to October 1st 2018 in our hospital were retrospectively analyzed. According to different nursing methods, the patients were divided into rapid rehabilitation surgery nursing group (16 cases) and control group (12 cases), and compared the satisfaction degree, cooperation degree, nerve function, pain level, self-care ability and average length of stay between the two groups.
Results: The satisfaction of patients in the rapid rehabilitation surgery nursing group was better than that in the control group (P < 0.05). The neurological function, pain level and self-care ability of the patients in the observation group were better than those in the control group (P < 0.05). The average length of stay in the observation group was lower than that in the control group (P < 0.05).
Conclusion: The clinical effect of fast rehabilitation surgical nursing in perioperative period of ischemia-free liver transplantation is remarkable. It can effectively improve patients´ satisfaction, relieve pain, shorten hospitalization days and promote post-operative rehabilitation.

P-604

Simplifying medications in liver or kidney transplant patients

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Background: Many medications including immunosuppressants are needed for long-term use to prevent rejection and complications after transplantation. Patient survival and graft survival are dependent on the compliance of these immunosuppressants. However, the increased frequency of medications results in poor compliance. Therefore, the frequency of medication affects re-admission rates and treatment costs. The aim of the present study is to identify the decreasing frequency of dosing by simplifying or standardizing the medication schedule.
Methods: We monitored potential side effects from reducing the number of doses and instructed patients to increase number of doses when necessary. The pre and post-application prescriptions were monitored by setting the rate of decreased number of doses within six months of transplantation from March 2018 to October 2018 as an indicator. Calcineurin inhibitors and mycophenolate were taken twice a day on an empty stomach. Steroids and preventive medications such as antibiotics, ursodeoxycholic acid and protectants were prescribed after a meal once or twice a day. Other medications were prescribed consistently based on pharmacokinetic parameters to be taken on an empty stomach or after a meal.
Results: The number of doses decreased by 33.72 percent from 8 to 5.13 times a day in liver transplant recipients and decreased by 10.92 percent from 6.17 to 5.5 times a day in kidney transplant recipients.
Conclusion: We suggest increasing compliance, ease of use of medications and satisfaction for patients by simplifying medication schedules.

P-605

Nursing care of complications after liver transplantation in a child donor and adult recipient

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Objective: To investigate the nursing methods of hepatic artery thrombosis and bile leakage after liver transplantation in a child donor and adult recipient.
Methods: Retrospective analysis of a case of hepatic artery thrombosis and bile leakage after 2018 liver transplantation in our center Clinical treatment and nursing data. To summarize the clinical treatment and nursing experience of patients with hepatic artery thrombosis and bile leakage.
Results: After hepatic artery thrombolysis, abdominal cavity drainage, somatostatin anti-infection therapy, and all kinds of nursing methods during the treatment, finally the hepatic artery was unobstructed, bile leakage was cured, liver function was normal, and the patient was discharged from hospital smoothly. The follow-up has been good so far.
Conclusion: For the occurrence of hepatic artery thrombosis and bile leakage after liver transplantation, early detection and early treatment, effective treatment and targeted nursing can promote the prognosis of the disease and improve the quality of life of the patients.

P-606

The reason of death for the liver transplantation recipients at a single center in China

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Background: Liver transplantation with organ donation after the citizen's death was increasing rapidly in the past few years in China. The outcome of the liver transplant recipients needs more attention.
Method: The clinical data of the liver transplant at the Affiliated Foshan Hospital of Sun Yat-Sen University between November 2011 and September 2018 was retrospectively analyzed.
Results: Liver transplantation with donation after citizen's death program of the Affiliated Foshan Hospital of Sun Yat-Sen University was started from November 2011. 106 cases underwent liver transplantation with donation after citizen's death at the Affiliated Foshan Hospital of Sun Yat-Sen University between November 2011 and September 2018. The 1 and 3 years survival rate after liver transplantation was 88% and 77% respectively. The primary disease of the liver transplant recipients was as following, 41 cases with hepatocellular carcinoma, 20 patients with acute liver failure, 95 cases with hepatitis B virus(HBV) infection associated end stage liver disease. Until now, 15 liver transplant recipients died of different reason after liver transplant. Among them, 8 cases died of hepatocellular carcinoma recurrence, 2 cases died of severe lung infection, the other five cases died of liver failure of HBV recurrence, graft versus host disease, massive hemorrhage of the upper alimentary tract, primary nonfunction, and multiple organ dysfunction syndrome respectively. Among the recipients with hepatocellular carcinoma recurrence, 7 cases were beyond Milan Criteria before liver transplantation.
Conclusion: Hepatocellular carcinoma recurrence was the key reason for the liver transplant recipients' death. The indication of liver transplant for hepatocellular carcinoma should be strictly under the international criteria such as Milan Criteria.

P-607

Ischaemia reperfusion related ontable primary graft non function of the liver

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Background: Primary graft non-function is the most severe form of graft dysfunction and is associated with high morbidity, mortality and graft loss. Ischemia Reperfusion is the main mediator of graft injury. This is a case report of a 60 year-old male with hepatitis B related end-stage liver disease who underwent liver transplant receiving a DCD graft and developed immediate primary non-function after reperfusion.
Method: Functional warm ischaemia was 27 minutes, cold preservation 11 hours and donor hepatectomy time was 60 minutes. Frozen biopsy of the DCD graft, taken during bench preparation, showed focal minimal hypoxic/ischaemic changes with no evidence of ischaemic necrosis. The patient was stable throughout the hepatectomy and following arterial reperfusion. However, immediately after portal reperfusion, the patient developed ventricular fibrillation and arrested. 15 minutes CPR was carried on and high doses of adrenaline infusion were required. The patient developed high lactic acidosis and coagulopathy with cardiovascular compromise. ECMO attempt failed due to significant hematoma formation during cannulation of femoral artery. Therefore the graft was removed and a temporary porto-caval shunt was performed. The patient was relisted for super urgent liver transplant and received a DBD graft few hours later followed by stable recovery.
Results: The post-reperfusion biopsy of the first graft showed diffuse hepatocellular apoptosis and the histology report of the hepatectomy specimen revealed submassive ischaemic necrosis of hepatic parenchyma. Patient recovered well on Liver ITU with good graft function but unfortunately developed critical limb ischemia on the leg where ECMO was attempted and had knee amputation.
Conclusion: Currently the patient is 12 months post transplant with good graft function. This is a rare case of on table primary nonfiction of severe ischemia / reperfusion damage with immediate graft loss despite the fact the pre-reperfusion biopsy was quite reassuring.

P-608

The course of renal disease liver transplant recipient who requiring perioperative dialysis in liver transplantation

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Introduction: Renal dysfunction is a common complication in patients with end-stage liver disease and post liver transplantation. In addition, it is one of the factor affects the outcomes of liver transplantation. The aim of this study is to review the courses of LT recipients who needed dialysis peri-transplantly at our center.
Methods: We reviewed the medical records of 26 LT recipient from May 2015 to February 2018 at our center. We compared their clinical demographic, morbidity, and motality between peri-transplant dialysis patients and those not needed.
Results: We have performed 26 liver transplants from May 2015 to February 2018. Among them, 9 patients had pre or post transplant dialysis and 17 patients did not. Dialysis was performed with continuous renal replacement therapy in the intensive care unit and conventional dialysis on general ward Patients who underwent dialysis had a higher preoperative MELD (42 vs 13, $p < 0.001$), older donor age (41 vs 24, $p< 0.001$) and longer post LT hospital sta (37 vs 20, $p< 0.001$) However, there was no significant difference between the two groups in terms of serum creatinine (1.36 vs 0.93 mg/dl, p=0.187) at post LT 2 week, (1.10 vs 0.96 mg/dl, p=0.341) at first month (1.06 vs 0.86 mg/dl p=0.105) at third month and (0.92 vs 0.94 vs 0.89 mg/dl p=0.825). Mortality was higher in peri-transplant dialysis group ($p = 0.043$). Duration of pre-LT dialysis was significalty related to durtiaon of post-LT dialysis (p=0.028) and post LT motality (p=0.011).
Conclusion: The pre-transplant dialysis period is considered to be an important factor in survival and recovery of kidney function after LT. Therefore, if the patient has started dialysis, it may be better to proceed the transplant as soon as possible.

Poster Round II, Session 1, 2, 3: Viral Hepatitis/Alcoholic Liver Diseases/NASH/NAFLD

P-609

Response-guided ribavirin therapy for chronic hepatitis E virus infection

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Background: Previously we presented an Asian case series of chronic hepatitis E (HEV) infection treated with ribavirin for 12 weeks, which had high relapse rate (50%), particularly for kidney transplant recipients, due to higher immunosuppression requirement and adverse effects. We aim to study the feasibility of a response-guided therapy for chronic HEV in a new case series and re-treatment of the relapsed/persistent cases from the previous series.
Methods: All immunosuppressed patients from a single tertiary hospital with HEV viremia from 2014 to 2017 were included. Patients received ribavirin 800 mg/day and subsequently titrated down if adverse effects occur. Patients with renal impairment received half of standard doses. Treatment duration was individualized on the basis of virologic response, measured 4-weekly. HEV RNA was quantified with real-time PCR assay (RealStar® HEV RT-PCR Kit 2.0, Altona Diagnostics, Hamburg). The limit of detection was 100 IU/mL. Once HEV RNA became undetectable, patients continued taking ribavirin for additional 8 weeks for consolidation. Liver function and HEV RNA were monitored 12-weekly for 1 year after completing therapy.
Results: Eleven new cases and four patients with relapsed/persistent HEV infection were diagnosed and treated with ribavirin therapy. Ten were kidney transplant recipients, and the rest had liver and bone marrow transplantation, or were taking corticosteroid. Sequencing confirmed that all had HEV genotype 3. Both groups achieved 100% SVR with no relapse after 1 year. Treatment duration varied (median=20 weeks, range: 12-32 weeks for new cases; median=46.5 weeks, range: 12-192 weeks for re-treatment group). Approximately 25% achieved rapid virologic response at week 4. Anemia occurred in all patients, but dose reduction or erythropoietin therapy was needed only in renal transplant recipients.
Conclusion: Response-guide therapy is feasible and may be useful to optimize the individual outcome of HEV patients, particularly for the kidney transplant recipients.

P-610

Heterozygous α 1 antitrypsin deficiency Z allele is enriched in patients with NASH, alcoholic liver disease and cryptogenic cirrhosis awaiting liver transplantation

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Background: The role of alpha 1 antitrypsin (A1AT)deficiency *Z phenotype as a potential cofactor in advanced liver disease arising from other primary etiologies is contentious. The aim of this study was to determine the prevalence of the A1AT *Z phenotype among various etiologic subgroups of cirrhosis in patients awaiting liver transplantation (LT) in the modern era.
Methods: This retrospective cohort study included adult patients with end stage liver disease considered for LT between February 2002 and December 2017 at Mayo clinic, Rochester MN. Data for the study population including etiology of liver cirrhosis, MELD-Na score, A1AT phenotype, graft survival and pulmonary outcomes was determined by retrospective review of the LT database.
Results: The 1252 adult patients with chronic liver disease in this study were classified into 7 etiologic subgroups: 172 patients with NASH, 188 with alcoholic liver disease (ALD), 39 with cryptogenic cirrhosis, 326with viral hepatitis, 328 with cholestatic liver disease(PBC, PSC), 72 with de novo cholangiocarcinoma, 40 with autoimmune cirrhosis and 87 with other chronic liver diseases. Overall, 128/1252 patients (10.2%) were heterozygous carriers of single PI*Z allele for α 1 A1AT.When comparing the distribution of heterozygous α 1AT carrier among different subgroups, the prevalence of heterozygous α 1ATD was significantly increased in NASH, ALD and cryptogenic cirrhosis subgroups compared to other etiologies. 37 of 172 with NASH (21.5%), 37 of 188 with ALD (19.7%), and 9 of 39 with cryptogenic cirrhosis (23.1%) were identified as PI*Z allele carriers, while in other subgroups, we detected 18 patients with viral hepatitis (5.5 %), 11 patients with cholestatic disease (3.3%), 3 with de novo cholangiocarcinoma (4.2%), and 4 with autoimmune cirrhosis (10.0%).
Conclusion: The prevalence of heterozygosity for the Z allele is significantly enriched in NASH, ALD and cryptogenic cirrhosis subgroups compared to other etiologies.

P-611

Decline in HCV as an etiology for liver transplantation in direct acting antivirals era

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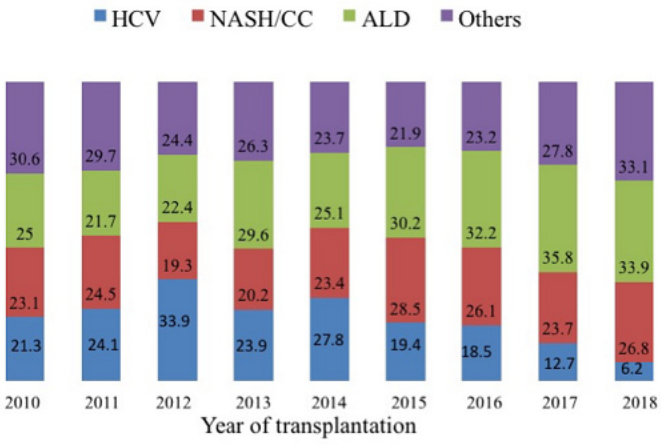
Background: Hepatitis C (HCV) has become an easily treatable disease after introduction of Sofosbuvir based direct acting antivirals (DAA) regimens. HCV as an indication for liver transplantation is declining. We present a large single center experience of change in etiological profile of liver transplant after availability of DAAs.
Methods: A retrospective analysis of prospectively collected liver transplantation database of adults was performed from June 2010 to July 2018. A total of 1754 adults underwent liver transplantation in the defined period and year wise break up as: 108 from June to December 2010, 212 in 2011, 192 in 2012, 213 in 2013, 291 in 2014, 242 in 2015, 211 in 2016, 173 in 2017 and 112 from Jan to July 2018.
Results: While percentage of transplants for hepatitis C remained almost consistent up to 2014 (before availability of DAAs), there was progressive decline from 2015 to 2018 as seen in figure 1, p=0.000. Hepatitis C as indication of LT was present in 271/1016 (26.6%) in 2010-2014 period, which decreased to 115/738 (15.5%) in 2015-2018 period, in fact HCV was indication for 6.2% transplants only in 2018. The liver transplantation recipients for hepatitis C related cirrhosis had significantly lower Child's and model for end-stage liver disease (MELD) score in 2015-18 period as compared to 2010-2014 period; Child's score was 8.0±2.2 versus 8.6±2.1,p=0.007, MELD 14.2±5.3 versus 17.3±5.8, p=0.000 respectively. There was trend towards better survival in hepatitis C patients in 2015-2018 period as compared to 2010-2014 period.



[Etiology profile of liver transplant recipients show decline of HCV after introduction of DAAs]

Conclusion: Hepatitis C as an indication for liver transplantation has decreased significantly; also pre-transplant disease severity is less in HCV patients in DAA era.

P-612

Incidence of AKI in various etiological conditions in LDLT - experience with 1450 cases for a single centre

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Objective:
Primary: To analyze retro-aspectively the incidence of acute kidney injury in LDLT in various etiological conditions in 1450 cases done from november 2010 to june 2018 in a single centre.
Secondary: Staging of AKI done as per AKIN criteria for 7 days post-operatively.
Methods: All LDLTs done at our center between November 2010 to June 2018 were considered in this retrospective analysis. 5 major groups were formed as per main etiology of LDLT - 1. NASH & NAFLD, 2. Cryptogenic, 3. Ethanol, 4. HBV & HCV, 5. Autoimmune.
Combined Liver + Kidney transplant, Paediatric, ALF & ACLF were excluded from this study.
Baseline creatinine, creatinine post-operatively were evaluated for 14 days, as per AKIN criteria and staging of AKI was done accordingly. Statistical analysis was done by using two propotion Z test.
Results: Greater Incidence of AKI was seen in NASH & NAFLD group followed by Cryptogenic group.
Creatinine levels peaked on 5th post-operative day in all the groups.
Conclusion: The critical period to monitor renal dysfunction is upto 5 days post liver transplant. This has greater relevence in the etiology of NASH & NAFLD as well as Cryptogenic liver disease.

P-613

Sofosbuvir, Velpratasvir, Veloxpravir Efficacy in 12-week treatment in triple infected (Chronic Hepatitis C, Chronic Hepatitis B, and HIV} Geno 3 naive population SOLVVE-C

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Objectives: Chronic Hepatitis C treatment is no longer challenging in the era of DAAs with an SVR of up to 97%. Triple infection treatment with HCV, HIV and Hepatitis B has not been explored in real life situations. HCV Genotype 3 is still the most challenging clinical state in Hepatitis C treatment. Regardless of concomitant triple infection, shorter duration of therapy revealed favorable outcome with the highest retention, fewer side events, and cost containment. This study evaluates the efficacy and safety of Sofosbuvir, Velpratasvir and Veloxpravir in the treatment of triple infection with HBV, HIV and HCV (Genotype 3).
Methods: Twenty-two (n = 22) HCV treatment naive patients with Triple Infection (HIV HBV HCV Genotype 3) were recruited for the study.
Patients with HIV were on Atripla for over three years with HIV with Undetectable Viral load and HBV Viral load Undetectable.
HCV infected patients had a Median Viral load of 3 million IU and Genotype 3 prior to treatment.
Results:
Duration of treatment HCV Viral load
Viral load - Undetectable Viral load detectable
Fourth week 18/21 3/21 detectable
Eighth week 18/21 3/21 detectable
Twelfth week 18/21
Twenty fourth week 18/21
One patient dropped out of study due to severe bilateral Pneumonia.
One patient stopped therapy due to Rectal Bleed after three weeks of treatment.
One patient stopped therapy due to Virological Failure with RAS y93.
One patient developed Herpes Zoster in the 10th week of treatment.
Intention to Treat (ITT): 18/21
Resistance-associated substitution Pre therapy Post therapy:
RAS 31 1 3
RAS 36 0 1
RAS 93 1 1
Conclusion: The study demonstrates the efficacy of DAAs in 12-week treatment with an SVR of 87% in a very challenging triple infected cohort, with significant efficacy, tolerability, and safety. A larger trial is needed to validate the results.

P-614

Fibrosis-related miRNA expression profiles in end-stage liver disease candidates to liver transplantation: comparative study between Western and Eastern patients

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Background: Interaction of HCV and HIV with the miRNA pathways of host hepatocytes represents an important pathogenic mechanism in liver damage with potential pro-fibrotic, pro-inflammatory and pro-oncogenic effects. No data are available on the impact of different patient´s ethnicities on the host-cell susceptibility to such viral interference.
Methods: Liver biopsies of HCV-mono and HIV/HCV co-infected patients who underwent liver transplantation (LT) at the Nagasaki University Hospital (Japan) and Udine University Hospital (Italy) were analyzed. Udine: U-mono(n=10pts), U-co(n=15), Nagasaki: N-mono (n=14), N-co (n=1). The targeted miRNA were miR- 122 (active in lipid metabolism control) 29a and 101 (controlling stellate cell function). The analysis was performed by real-time PCR on formalin-fixed paraffin-embedded tissue. Severity of liver fibrosis was assessed by HE, Azan staining. The median age/MELD score at LT were: 57/17 (N-mono), 41/18(N-co), 57.5/21(U-mono) and 45/15(U-co). Normal liver biopsies from patients submitted to hepatic resection for liver metastasis were used as control (n=4)
Results: The study groups were comparable in terms of degree of fibrosis. miR29a,122,101 expressions were downregulated in each group as compared to control. However in N-co and U-co groups the miR29a levels were markedly more suppressed compared to mono groups. No ethnicity-related differences (U vs N) between any group were recorded.
Conclusion: HIV infection may cause progressive fibrosis by downregulating miR29a pathway which is correlated with inactivation of stellate cells. No ethnicity related differences were recorded in mono and co-infected patients in terms of viral miR- 122, 29a, 101 dysregulation and pro-fibrotic effect.

P-615

Outcome of hepatitis C related liver transplantation in direct acting antivirals era

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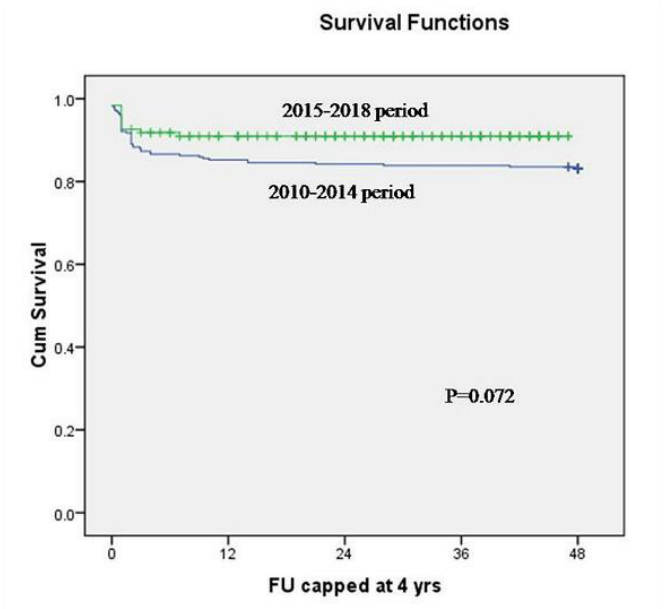
Background: hepatitis C has become easily treatable disease after introduction of Sofosbuvir based direct acting antivirals (DAA) regimens. We present a large single center experience of changed severity and outcome profile of hepatitis C patients after availability of DAAs.
Methods: A retrospective analysis of prospectively collected liver transplantation database of adults was performed from June 2010 to July 2018. A total of 410 patients (including 26 coinfection with hepatitis B) underwent liver transplantation (LT) for hepatitis C out of 1754 adult transplantation in the defined period.
Results: The study group comprised of 296 males and 114 females, aged 52.1±7.9 years. Hepatitis C as indication of LT was present in 289/1016 (28.4%) in 2010-2014 period, which decreased to 121/738 (16.3%) in 2015-2018 period. The liver transplantation recipients for hepatitis C related cirrhosis had significantly lower Child's and model for end-stage liver disease (MELD) score in 2015-18 period as compared to 2010-2014 period; Child's score was 7.9±2.2 versus 8.6±2.1,p=0.003, MELD 13.9±5.3 versus 17.1±5.8, p=0.000 respectively. There was trend towards better survival in hepatitis C patients in 2015-2018 period as compared to 2010-2014 period as shown in figure 1. Significantly more patients had HCV RNA negative status before liver transplantation in 2015-2018 period (38.8% versus 13%, p=0.000), also proportion of liver transplantation for decompensated cirrhosis (without hepatocellular carcinoma) decreased significantly in later period, 64.0% in 2010-2014 versus 42.1% in 2015-2018, p=0.000. MELD score remained significantly low in 2015-2018 period even after adjustment for patients having hepatocellular carcinoma.



[Survival of hepatitis C liver transplant recipients in 2010-2014 and 2015-2018 periods]

Conclusion: In the DAA era, HCV patients have less severe disease at transplantation and a trend towards better outcome.

P-616

Short and long-term outcomes of intentional allocation of hepatitis C positive livers (even viremic donors) into hepatitis C negative recipients

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Background: The current discrepancy between supply and demand of liver grafts has dramatically increased the waiting time and mortality on the waiting list. The recent approval of direct-acting-antivirals (DAA) dramatically changed the landscape of hepatitis C (HCV) treatment with pangenotypic efficiency superior to 95%. This success opened an opportunity to use Hep C positive livers into hep c negative recipients.

Methods: We reviewed the electronic records of all patients that received a liver from a hepatitis C positive donor (either HCV Ab positive or hepatitis C NAT positive). We recorded donor and recipients demographics, complications and response to treatment at 12 weeks.
Results: Between 04/30/2016 (first intentional allocation of hep c positive liver into hep c neg recipient to our knowledge) and 11/30/2018 we transplanted 9 recipients with HCV positive livers (Five of these donors were viremic-RNA+). The median MELD score of recipients was 29 (range 20-37). The median follow-up was 491 days (range 37-945 days). As expected, there was transmission in all five patients that received NAT positive livers (viremic donors) and in none that received NAT- livers (nonviremic donors). There was no problem to obtain insurance approval for DAA therapy. Therapy with DAA started as early as 2 weeks. SVR at 12 week occurred in two patients (the other three are still under treatment). There was no transmission of HIV and Hep B.
Conclusions: Here, we report our case-series of intentional allocation of hep c positive livers into hep c negative recipients, describe their short and long-term outcomes. The intentional use of hep c positive donors into hep c negative patients has the potential to expand the donor pool and may decrease mortality on the wait list.

P-617

Individualized optimization of posttransplant hepatitis B prophylaxis with hepatitis B immunoglobulin using pharmacokinetic half-life simulation

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Background: Prophylaxis for hepatitis B virus (HBV) recurrence is essential after liver transplantation (LT) in HBV-associated recipients. This study established an individualized HBV prophylaxis protocol, through optimization of hepatitis B immunoglobulin (HBIG) administration, with the application of simulative half-life (SHL).
Methods: This study involved five parts:
Part 1 developed the SHL estimation method with 20 patients;
Parts 2 and 3 assessed the SHL variability and developed a simulation model to apply SHL in 100 patients;
Part 4 validated the simulation model in 114 patients, and Part 5 was a cross-sectional study on the current status of HBIG infusion intervals in 660 patients.
Results: In Part 1, infusion of 10,000 IU HBIG induced add-on rise anti-HBs titer of 5252.5±873.7 IU/L, and mean SHL of 20.0±3.7 days were 4.4% lower and 2.2% longer than the actual measurements, respectively. In Part 2, the medians of the intra- and inter-individual coefficient of variation in SHL were 13.5% and 18.5%, respectively. Pretransplant HBV DNA load and posttransplant antiviral therapy did not affect SHL. In Part 3, a simulation model was developed to determine the interval of HBIG infusion, by using SHL. In Part 4, all 114 patients were successfully managed with regular HBIG infusion intervals of ≥8 weeks, and the interval was prolonged to ≥12 weeks in 89.4%, with a target trough anti-HBs titer ≥200 IU/L. In Part 5, 47.4% of our patients received HBIG excessively, at a target trough titer of 500 IU/L.
Conclusion: SHL estimation using only clinically available parameters seems to be reliably accurate when compared with actual measurements. We believe that SHL estimation is helpful to establish a personalized HBV prophylaxis protocol for optimizing HBIG administration.

P-618

Postoperative management rather than preoperative prediction may be more helpful in preventing harmful drinking after liver transplantation for alcoholic liver disease

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Introduction: In Korea, since the adoption of MELD-based allocation system in June 2016, there happened an issue that too many livers were allocated to alcoholic patients. It's because alcoholic hepatitis patients whose MELD score were very high outnumbered the deceased donor. Some insisted that a liver graft from a deceased donor, which is a valuable social resources should not be allocated to the alcoholic patients. We studied rates and timing of alcohol relapse including harmful drinking and preoperative factors that could predict alcohol relapse.
Methods: Alcohol relapse among 42 patients who underwent liver transplantation for alcoholic liver disease was investigated. Follow periods were from 3 to 85 months. Alcohol relapse was diagnosed by interviewing the patients. Time to alcohol relapse after LT was recorded. Preoperative factors including 6 month sobriety, history of major psychiatric disease, history of drug addiction, marital state and type of transplantation (living donor or deceased donor) were analysed in relation to alcohol relapse.

Results: Alcohol relapse occurred in 10 (25%) patients including harmful drinking in 4 (10%). Any preoperative factors including 6 month sobriety could not predict alcohol relapse or relapse into harmful drinking. There was no patient with history of drug addiction. Alcohol relapse rates were not different significantly between LDLT and DDLT groups. All the relapses into harmful drinking occurred within 3 months after LT. One patient who was getting into harmful drinking 2 months after LT stopped drinking for the next 6 months until now by aggressive education that let him know himself in trouble by drinking.
Conclusion: Pre-transplant prediction of alcohol relapse is barely feasible in patients with alcoholic liver disease. Aggressive monitoring and managing alcohol relapse in the very early postoperative period may be more helpful in preventing the patient go into harmful drinking.

P-619

Successfully blocking HBV transmission from an infected native liver to a graft in auxiliary liver transplantation

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Auxiliary grafts have a high risk of Hepatitis B virus (HBV) infection in patients with chronic HBV-related diseases. HBV-related auxiliary partial orthotopic liver transplantation (APOLT) cases were reviewed to show the results of current methods to block native-to-graft HBV transmission. Three patients received APOLT for HBV-related liver cirrhosis and a recurrent upper gastrointestinal hemorrhage between April 2015 and January 2017 by the liver transplant team of Beijing Friendship Hospital affiliated with Capital Medical University. All 3 patients were positive for HBV surface antigen (HBsAg) and had a negative HBV DNA test result before transplantation. After auxiliary transplantations, HBsAg was found to be positive in 2 patients and negative in 1 patient. To avoid graft infection of HBV, entecavir-based therapy was employed and the remnant native livers of the recipients were removed 51-878 days after liver transplantation. Then, serum conversions of HBsAg were found in all 3 cases. For the first time, this case series shows the possibility of blocking the transmission of HBV from a native liver to a graft in auxiliary transplantation by entecavir-based therapy. Among the cases, a left lobe graft was successfully implanted as a replacement of the right lobe of the recipient, which is also discussed.

P-620

Liver recipient characteristic (still) reflects general epidemiological data on HCV and HCC morbidity. Poland - country data

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Introduction: Hepatitis C viruses has been recognized carcinogenic to human. In Polish population currently persistent HCV infection (HCV cirrhosis) and its complication HCC affect meaningly the requisition on liver transplantation.
Aim and methods:
1. To identify indicators and trends of HCV and HCC as indications for liver transplantations in the years 2001-17. Data from transplant registries administered by Poltransplant (competent authority in organs).
2. To identify indicators and trends of HCV and HCC morbidity. Data from National Cancer Registry and National Institute of Public Health - National Institute of Hygiene and Chief Sanitary Inspectorate.
3. To compare collected data and establish, whether indications for primary deceased liver transplantation reflect country epidemiological data on HCV and HCC.
Results:
1. In analyzed period 3728 primary liver transplantations have been performed. About 16% (581) of cases were caused by HCV and 7% (266) by coexisted HCV/HCC. Among all indications coexisting HCV/HCC shows the greatest dynamics - in 2001 no cases and in 2017 - 12%.
2. The numbers of HCV and HCC cases has been significantly increased; HCV from 2000 to 4000 and HCC from 250 to 750.
3. Comparative analysis showed that diseases being an indication for liver transplantation correspond to epidemiological trends of HCV and HCC.
Conclusions:
1. Data suggest that HCV infections (and resulting a greater number of HCC) are constantly significant problem. This phenomenon is in parallel reflected by growing number of LTx for HCV and HCC.
2. Graft deficiency remains the main problem in liver transplantation. In an era when HCV and indirectly HCC are treatable illnesses due to DAA, there is a possibility of reducing the need for transplantation in these diseases. This will increase the chance for recipients with other indications. To realize this idea sufficient national programs for detecting and treatment of HCC with DAA is needed.

P-621

Is it possible to improve the liver dysfunction associated with the recurrence of HCV post-Liver Transplantation, with the new DAA treatment?

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Liver fibrosis regression is possible even in cirrhotic stage in Hepatitis C(HCV) patients after antiviral treatment, also in liver transplant(OLT) patients. The new direct-acting antivirals (DAA) have made possible to treat OLT patients in advanced stages fibrosis, previously not candidates for interferon-based treatments.
The aim of our study was to determine whether the sustained viral response(SVR) after DAA-treatment in OLT resulted in improved liver function, from an analytical and clinical point of view.
Material and methods: 42 OLT patients were treated with DAA from June 2014 to December 2015. We excluded 2 patients who died during the treatment due to complications associated with HCV disease. Finally, we study 40 OLT patients with HCV and who achieved SVR after treatment with DAA, followed for at least one year. Liver function data (Transaminases, MELD and Child) and clinical data (ascitis, hepatic encephalopathy and upper gastrointestinal bleeding due to VE) were collected at the start of treatment, at 6 and 12 months after SVR.
Results: Three out 40 patients were relapsed to previous treatment with DDA. The treatments used were Sofosbuvir+Daclatasvir 45.0%, Simeprevir+Sofosbuvir 42.5%, Sofosbuvir+Ledipasvir 7.5% and 3D/2D combo in 5%. 8(20%) patients had a hepatocellular carcinoma(HCC). The mean of pre-treatment MELD was 10.78, and 8.74 and 8.46 at six and 12 months postOLT($p< 0.001$). GOT/GPT before and after treatment were also significant($p< 0.001$). In 12 patients there were pretreatment ascitis(3 refractory). At one post-SVR, three patients remained with controllable ascites. The two patients with chronic encephalopathy pretreatment were controlled. No patient died in the follow-up. One patient developed a recurrence of HCC 5 years POST-OLT.
Conclusions: The treatment of hepatitis C post-OLT is very effective and achieves in the medium term a significant improvement in liver function measured by MELD, and clinical complications and control even patients with very advanced disease.

P-622

Cytoplasmic Miz1 suppresses nonalcoholic steatohepatitis by promoting mitophagy through its interaction with Peroxiredoxin 6

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Mitochondria play a crucial role in the progression of nonalcoholic steatohepatitis (NASH). Myc-interacting zinc-finger protein 1 (Miz1) was recently identified as a Pox virus and zinc finger (POZ) protein which has transcriptional activity. Here, we study the function of Miz1 in NASH progression. We found that Miz1 expression was decreased in human steatohepatitis and negatively correlated with the degree of NASH. During NASH progression, only cytoplasmic Miz1 is degraded by polyubiquitination which was induced by aberrantly increased TNF-alpha. Subsequently, a part of Peroxiredoxin 6 is getting dissociated from its partner Miz1 and translocate into the mitochondrial outer membrane, thereby inhibits the PINK1/Parkin-mediated mitophagy in hepatocytes. This inhibition of mitophagy triggers NLRP3/IL-1β signaling pathway which can aggravate NASH progression. Notably, Miz1 function is independent of its transcriptional activity in hepatocytes. These results strongly suggest that Miz1 and its partner PRDX6 could be a novel molecular pathogenesis of NASH and may attributed to explore the potential prevention and therapeutic strategies for this common liver disease.

P-623

Ophthalmic complications of non-alcoholic fatty liver disease: a cross-sectional observational clinical study

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Objective: Non Alcoholic Fatty Liver disease (NAFLD) is a global epidemic with a multifactorial heterogeneous etiology. This study reveals a unique ocular complication of NAFLD - Premature Cataract formation in a Non-Diabetic cohort of NAFLD.
Method: Four Hundred (n= 400) NAFLD patients were initially recruited from age group 50 to 60 with BMI > 30%.
The mean HbAlc was less than 7.1. The mean weekly Alcohol consumption was less than 30 grams.
Patients underwent Serum NAFLD score analysis, abdomen sonogram, ECHO, Carotid Doppler for atheroma Volume, Fibroscan for Base Line fibrosis and Ophthalmic Evaluations. All patients were placed on strict regulated Weight loss and exercise for 6 months. All patients had measurement of Leptin, Adiponectin, Retinol Binding Protein 4, Triglyceride, HOMA score, TNF Alfa levels prior to the study. Patients also underwent sleep study to look for sleep apnea.
Patient Characteristics:
Baseline Serum Triglyceride (Median) 273
HbAlc 6.5 - 7.1 (Median - 6.7)
HOMA Score (Median) 2.9
Leptin (Median) 7.3
TNF Alfa (Median) 2.9
Liver/Spleen Ratio 1.33
Genetic Assay
PLPAL P 3 Homozygotes 51%
NCAN Homozygotes 26%
APOC3 Homozygotes 54%
Results: Characteristics of patients with Premature cataract
No of Patients with premature cataract formation 278/400 (69.5%)
BMI (Mean) Greater than 32%
HOMA score (Median) 3.6 (High)
Leptin (Median) 7.3 (High)
TNF Alpha (Median) 2.8 (high)
Adiponectin levels (Median) 0.7 (Low)
Sleep Apnea Score Moderate (3 times per sleep in 8 hours)
Serum Triglyceride (Median) 273 mg/dl (Elevated)
Conclusion: Our study showed that NAFLD is associated with early development of Cataract formation in NAFLD, especially in the subgroup of high Inflammatory markers (High levels of TNF Alfa and Leptin, Sleep apnea, High Triglyceride levels, Elevated HOMA score and Moderate Atheroma load with normal Glucose Homeostasis). Patients with NAFLD will benefit with regular ophthalmologic evaluations to screen for premature cataract development.

P-624

Liver steatosis after living donor liver transplantation

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Background: Prevalence of fatty liver disease trend to continuous increase. The aim of this study to find prevalence of liver steatosis after living donor liver transplantation (LDLT), association of liver steatosis from donor, other risk factor in LDLT condition.
Material and method: 701 LDLT, including adult and pediatric, were performed in Kaohsiung Chang Gung Memorial Hospital between January 2012 to December 2017. We analyzedthe data from the patient who made post-transplant liver biopsy and donor liver biopsy from pre or intraoperation, graft type. To define risk factor for post transplant liver steatosis when histologic result macrovesicular steatosis more than 5% in univariate and multivariate analysis.
Result: 431 of 701 LDLT cases were performed post LDLT liver biopsy. 48 of 431 patients were excludeddue to pathologic liver disease. The majority of liver transplant indicationsis HCC (43.9%). Liver steatosis was found 61 in 383 patients (16%) can divided by degree liver steatosis: grade 1(less than 30%)(54.1%), grade 2 (more than 30% and up to 60%)(34.4%), grade 3(more than 60%) (11.5%).When post transplant liver steatosis developed, 40% of these group are de novo NAFLD.Multivariate analysis shown significant in pre-transplantrecipient BMI, donor liver graft steatosis and time from liver transplant to liver biopsy.
Conclusion: In LDLT condition, pre-transplantrecipient BMI, donor liver graft steatosis and longer time follow up per month are risk for post-transplant liver steatosis but not associate with graft type. Monitoring post transplant liver steatosis is important in thelong term.

P-625

The final effort of the hepatitis C virus (HCV) in the world of organ transplant

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Introduction: Until recently, chronic infection with HCV in solid organ transplant patients was involved with increase mortality and graft loss. One of the problems was that the treatment (INF based) was toxic, increased ACR episode of the allografts and relatively ineffective .Therefore, the international guidelines for organ allocation for kidneys, lungs, heart and liver restricted organs from HCV+ donors to recipients with chronic HCV infection. In the recent years, new treatments with interferon free Direct Acting Antiviral (DAA) medications, highly effective with only few minor AE, became available These treatments raised the possibility to change the policy of the allocation of organs from HCV+ donors.
Aim: To summarize our experience of treatment with DAA in chronic HCV infected solid organ recipient.
Methods: Retrospective, Single center, study using the data of all organ transplant patients who were treated with DAA for chronic HCV.
Results: 56 organ transplant patients were treated with DAA in Rabin Medical Center in Israel since 2015. 38 livers, 2 combined liver and kidney, 14 kidneys and 2 lung transplant patients. One of the lung transplant patient got the organ from HCV+ donor. The treatment protocols were varies, based on the reimbursement availability. The SVR rate was 96.2%, 2 liver transplant patient had relapse of the virus, 2 patients died during the treatment (from sepsis or CHF that were not related to the treatment) and 4 died post treatment. The lung transplant patient that got the organ from HCV+ donor had SVR with no complications during the treatment. No major DDI were seen during DAA treatment.
Conclusion: Our experience shows that any protocols of DAA treatment is safe and effective in solid organ transplant patients and can support the change of allocation policy of using HCV+ donors.

P-626

Prevalence of hepatitis C viral infection in a surgical population of Southeast China: a large-scaled multicenter study

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Background: Hepatitis C virus (HCV) infection is a disease that affects 80 million people globally. The majority of HCV infected patients become chronic and develop advanced liver disease. This study aims to investigate the current epidemiology of HCV infection in a Southeastern Chinese surgical patient cohort.
Methods: Blood samples from 78,484 surgical patients from 18 different city and county hospitals were enrolled. Incidence of serum HCV antibody positivity, HCV RNA load and HCV genotyping, as well as incidence of HBV infection were investigated. The data were stratified using multi-stage cluster random sampling method and further analyzed by SPSS-20 package.
Results: HCV antibody positivity was detected in 0.15% of the population (95% CI: 0.12%-0.18%), 0.17% after standardization. Genotype 1b (55.74%) was the dominant type. HCV infection peaked in the age groups 16-20, 41-50 and 61-65 years old and was higher in males than in females (0.19% *vs.* 0.13%, $P< 0.05$). The geographical distribution of the infection rates was different: 0.19% (95% CI: 0.14%-0.24%), 0.18% (95% CI: 0.13%-0.23%) and 0.06% (95% CI: 0.03-0.09%) in plain areas, islands, and valley regions. HBV co-infection was present in patients with high HCV RNA level (aOR=5.88, $P=0.01$).
Conclusion: The prevalence of HCV infection in this Southeast Chinese cohort was 0.17%, a number lower than the reported 0.43% infection rate in China in 2006. This result can be (partially) explained by the improvement of blood donor screening and raised general awareness about proper use of disposables.

P-627

Management of de novo hepatitis B infection from hepatitis B core antibody-positive donors

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De novo hepatitis B infection from HBcAb-positive donor in liver transplants is well known, but effective prevention or standard management strategy is not well established. In our hospital, we do prophylaxis with HBIG monotherapy for recipients, who are HBsAg negative at the time of transplantation and receive a liver from an HBcAb positive donor. We had 4 recipients who are naïve to HBV and receive an HBcAb-positive graft since Aug. 2006. Two had died of other causes. Two patients have developed de novo hepatitis B. One received liver transplantation in October 2006, and another received transplantation October 2009. We checked the patient's serum every year for HBsAg routinely as a protocol and all tests showed negative, but one in January 2014 and another in September 2013, the result of these tests showed HBsAg positive. There was no unusual laboratory findings including liver function test except undetectable HBsAb titer even though HBIG had been administrated two months ago in both patients. HBV DNA quantification test showed 3.07E+08 Copies/mL and 1.51E+08 Copies/mL for each patient. After de novo infection, we stopped HBIG infusion and added radiologic exam every 6 months on the regular follow up exams. One showed AST/ALT 191/252 IU/L in the next test, so we started tenofovir and then the level of AST/ALT and HBV DNA quantification went down. Another showed no abnormality in liver function test till now, so we are following up with high HBV DNA quantification test (1.63E+08 Copies/mL) and without an antiviral agent. Until November 2018, they are doing well. We previously suggested more than HBIG monotherapy would be needed for these recipients, but also, we now suggest that the outcome of de novo hepatitis B infection is not that disastrous as we previously experienced in the era of no antiviral agents.

P-628

IVC clamping first and rapid implanting technique applied in liver transplantation treating complicated polycystic liver

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Background: Liver transplantation is the final and most effective approach to cure end-stage hepatic diseases. However, when facing some complicated cases, more blood product consumption, longer ICU monitoring, substitute treatment, higher level of antibiotic are needed, and patients might face poor outcome of liver transplantation. Here, we introduce a difficult and complicated polycystic liver case accepting liver transplantation with new liver transplantation technique: IVC clamping first and rapid implanting technique.
Methods: A 50-year old male teacher, who suffering from huge polycystic liver and polycystic kidney for over 40 years. He came to our hospital ask for treatment. After analyzing his condition, we concluded liver transplantation was the only way to help him. In the surgery, IVC was dissociated and clamped firstly. Then we controlled the first hepatic hilum rapidly. After these steps has finished, we started to remove the abnormal liver. Lastly, we performed rapid liver implantation. The total blood loss, transfusion, approach of reconstruction, implantation time,postoperative blood tests, imaging examinations, postoperative complications and immunosuppression protocol were recorded. The follow-up time is 11 months.
Results: After surgery, the patient stayed in ICU 14 days without any severe complications. The patient discharged from hospital on the POD 49 days. He is alive now after surgery nearly a year.
Conclusion:
1. Dissociating the IVC and hepatic hilum first, then clamping these conduit quickly, which could reduce blood loss effectively.
2. Precise assessment of hepatic artery and portal vein is helpful for the reconstruction of hepatic inflow conduicts
3. Implanting a health liver and reconstruction of conduit precisely and quickly is key to recovering and reducing postoperative complications.

Surgical Video ePosters 1

eP-001

Right anterior section graft for living donor liver transplantation

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In living donor liver transplantation, the right lobe graft is commonly utilized to prevent the small-for-size syndrome, albeit with a considerable morbidity to the donor. Conversely, the feasibility of the left lobe graft and the right posterior sector graft in small size recipients is now commonly employed with comparable outcomes as the right lobe graft. However, the efficacy of the right anterior sector graft has rarely reported in the literature. Thus, we present a case of a 56-year-old man, with alcoholic liver cirrhosis, who successfully underwent living donor liver transplantation using the right anterior sector graft. Preoperatively, it was observed that the right lobe of the donor occupied 76.2% of the total liver volume exposing the donor to a small residual liver volume. The volume of the right posterior sector and the left lobe were insufficient, providing a graft-to-recipient weight ratio of 0.42% and 0.38%, respectively. It was noted, however, that the right anterior sector could comply an acceptable GRWR of 0.83%. The clinical signs and symptoms, and liver function improved after the anterior section graft transplantation with no reported complications. The procurement of anterior sector graft is technically feasible in selected patients, especially in high volume liver center.

eP-002

Robotic donor hepatectomy

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Introduction: We demonstrate our technique of Robotic Donor Hepatectomy using Da Vinci Xi System.
Materials and methods: We have performed 22 Robotic Right Donor hepatectomies since June 2018. Decision for robotic surgery is based on patient consent and availability of robotic slots. Donors with Type III portal venous anatomy and when recipient had Acute Liver Failure/ Acute on Chronic Liver Failure were excluded.
Patient in Reverse Trendelenburg position (25 degree) and ports are placed in a straight line just above the umbilicus. After docking from the head end, the liver is mobilized off the diaphragm till the right hepatic vein is seen. Hilar dissection is then performed to expose the right hepatic artery and right portal vein after removing the gall bladder followed by division of caudate process. The transection plane is marked using indo cyanine green visualization by temporarily clamping the right pedicle. Parenchymal transection is done by rubber band retraction technique.
Robotoclasia, Our technique of Parenchymal transection performed using a combination of bipolar Maryland and Monopolar hot shear. Middle Hepatic Vein is harvested up to the joining of segment IV B and V vein. Hilar plate is divided using Hem O Lock clips. Bile duct division is then performed after Indo cyanine green visualization and remnant side is closed by intra-corporeal suturing using 6,0 polydioxanone continuous sutures. Completion of parenchymal transection is done till complete caval visualisation.
Hepatic artery division and portal vein division is done with Hem-o-Lok. Hepato-caval ligament and Right hepatic vein is divided with powered stapler.
Specimen retrieval by pfannenstiel incision. Remnant liver sutured to falciform.
Conclusion: Robotic Donor Hepatectomy is safe and feasible option for LDLT program with donor safety being the epitome of all innovations. However, large trials are required to comment on the efficacy of robotic donor program.

eP-003

in situ liver splitting for pediatric and adult liver transplantation

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We present the technique of *in situ* liver splitting, with all the dissection and section of the pedicles. Tips and tricks are presented: how to deal with segments 1 and 4, how to be sure of the correct place to cut the bile duct.
At the end we show the adult implantation technique with a piggy back option. There is no bleeding on the cut surface of the liver.

eP-004

Dual lobe liver transplantation in a patient with renal dysfunction using a novel technique of without cross-clamping the inferior vena cava

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Background: Conventionally Dual Lobe Liver Transplantation (DLLT) involves IVC clamping and implantation of the right lobe (RL) & left lobe (LL) together, with venous outflow and portal inflow anastomosis of both lobes, followed by simultaneous perfusion. We present our technique of DLLT (right + left lobes) without IVC cross-clamping and sequential perfusion. The patient was a 47-year male, 110 kg (Child's- 12 & MELD-31) with recent AKI. The patient's wife and daughter were donors. The estimated GRWR with their right lobe grafts were 0.65 and 0.57 respectively. Hence the right and left lobes (696+274g -GRWR 0.9) were planned from wife and daughter respectively.
Method: *Recipient hepatectomy* was performed keeping the portal structures long. RL benching was complex, 2 inferior hepatic veins were reconstructed with PTFE boat graft, and anterior sector outflow with Neo-MHV.
Implantation- RL was implanted first by side-clamping the IVC with successive, appropriately sized Satansky vascular clamps for the RHV, the boat graft and then the MHV anastomoses. Then these anastomoses were clamped together with our indigenously designed side-biting vascular clamp with 10 cm long blades. This was followed by the donor to recipient RPV anastomosis. The RL graft was flushed with Ringer's Lactate & blood and then perfused with portal blood. Next, the MHV/LHV stump was side clamped, and the LL was implanted by anastomosing the venous outflow and then the LPV, flush and then portal perfusion. Post-perfusion of both lobes, arterial anastomoses were done. Biliary reconstruction was done with the recipient RHD was to spectacled (RASD + RPSD) RL donor ducts and LHD-LHD with Glissonian sheath & parachuting technique. Recipient and both donors are well 6-month post DLLT.
Conclusion: DLLT is feasible in heavy/morbidly obese, high MELD recipients with renal dysfunction, without clamping the IVC, using a specially designed side vascular clamp, and sequential implantation technique.

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eP-006

Standardized extrahepatic glissonean pedicle approach and liver hanging maneuverfor living donor hepatectomy

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Introduction: Bile duct injuries after living donor hepatectomy has yet to be eradicated. Two major advantages of glissonean approach and liver hanging maneuver (LHM) are: (i) To minimize dissection and preserve blood supply around the hilar plate by determining the point of bile duct division and the goal of hepatectomy preceding liver parenchymal dissection (safety), and (ii) To allow maximum length for each hilar structure (rationality).
How we do it: Step 1. After cholecystectomy, the right or the left glissonean pedicle is isolated with the corresponding caudate pedicle using intraoperative ultrasound for right or left-sided liver grafts, respectively. For left liver/left lateral section grafts, following the isolation of the Arantius plate and the confluence of the middle and left hepatic veins, the umbilical plate is encircled by dissecting the Arantius' plate to its origin. Step 2. Intraoperative cholangiography is performed to determine the point of bile duct division. The glissonean pedicle is then clamped with a tourniquet and the demarcation line is marked toward the aforementioned clip at the hilum. Step 3. For right liver and left liver with Spiegel´s lobe grafts, conventional LHM is applied. For left liver/left lateral section grafts, a tape is passed through the right and middle hepatic veins, along the Arantius' plate, and to the right of the umbilical portion (modified LHM). The tape for LHM guides the direction of liver parenchymal dissection. After completion of hepatectomy, the tape encircling the umbilical plate is repositioned to divide all caudate pedicles branching from the left glissonean pedicle for left liver/ left lateral section grafts. Step 4. The hepatic artery and portal vein are isolated dissected off sufficiently from the hilar plate. Step 5. Division of hilar structures and hepatic veins and graft retrieval.
Conclusion: Glissonean approach and LHM for living donor hepatectomy is safe and rational.

eP-007

A novel technique of portal vein reconstruction in pediatric LDLT using transversely tansposed PV autologous graft

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Background: The success of pediatric LDLT depends upon good inflow to the graft. Portal vein (PV) thrombosis rate of almost 2-10% has been described in literature. Variation in surgical techniques in form of porta dissection, level of graft implantation and use of venous grafts has been described to address this problem. The availability, procurement and its associated morbidity and the quality of autologous venous grafts in LDLT setting has been debatable.
Method: Keeping this background in mind, we describe a novel fool-proof technique of PV reconstruction in pediatric LDLT obviating the need of retrival of venous graft and PV stenting.
Technique: The native PV is dissected upto spleno-portal junction (SPJ). After ligating and dividing the right and left PV branches high up in the hilum, the main PV is divided at SPJ. The native PV is incised at logitudinal axis and transversely transposed to form a cylindrical graft to increase its diameter more than four-fold. Lateral venotomy is made at the SPJ to increase the diameter for anastomosis. The graft is joined to SPJ end-to-end. The graft is assessed for outflow and size. The graft is then joined to graft left PV end-to-end. The portal flow are assessed by intra-operative doppler and assessment is done twice daily in post-operative period for 1 week.
Conclusion: Transversely transposed autologous portal vein (TTAPV) graft technique is unique in PV reconstruction in pediatric LDLT with 100% success rate. Autologous graft from pediatric PV can be obtained and used successfully without morbidity. Use of TTAPV obviates the need of PV stent placement and its associated complications.

eP-008

Pure laparoscopic donor right hepatectomy in a living donor with anatomic variations of type 3 portal vein, type 3b bile duct, type 4b hepatic vein

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Laparoscopic donor right hepatectomy (LDRH) is an innovative procedure. We recently performed a pure LDRH in a living donor with type 3 portal vein, type 4b hepatic vein, and type 3b biliary anatomic variation. The operation began with full mobilization of the right hemi-liver from the attached ligament. After division of the cystic duct and artery, a hilar dissection was performed for identification of hepatic inflow. The right anterior portal vein (RAPV), right posterior portal vein (RPPV), and right hepatic artery (RHA) were identified, and then temporarily clamped with laparoscopic bulldog clamps to check the transection plane demarcated on the liver surface. The hepatic parenchymal transection was initially performed using an ultrasonic dissection device When transection was achieved to the level of the peri-hilar plate, a Cavitron Ultrasonic Surgical Aspirator was used to minimize injury of the hilar plate. The optimal level of bile duct division was determined by using intraoperative ultrasonography. The right anterior and posterior hepatic ducts were divided with scissors, and the remnant hepatic duct stumps were closed with metal clips. When the parenchymal transection was complete, the right hepatic vein (RHV) and inferior hepatic vein (IHV) were encircled, and then the right hemi-liver was placed into an endoscopic pouch. Next, a Pfannenstiel incision was made, and the string of the endoscopic pouch was placed on the extracorporeal side via an incision for prompt retrieval of the graft. The RHA, RAPV, and RPPV were ligated using a Hem-o-lok. The RHV and IHV were transected by unilateral linear staplers. The operation time to retrieval of the graft was 230 minutes. A follow-up Computed tomography three months postoperative did not detect any specific problems. Therefore, pure LDRH in an anatomically complex living donor was a safe and feasible approach for experienced surgeons.

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eP-009

Meso-rex revision using a collateral in a pediatric patient with portal perfusion steal syndrome

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A female with a past medical history of biliary atresia-polysplenia syndrome, ABO incompatible liver transplant, mesenteric to left portal vein bypass [meso-Rex bypass (MRB)] using an ABO compatible deceased donor iliac vein. At the of 3 years, she was taken to the operating room due to the failure of the MRB, it was confirmed that the MRB had no flow and a large splenorenal collateral vein that was identified during transplantation and MRB and at the time was decided not to ligate, was causing a portal perfusion steal syndrome. After ligating the splenorenal collateral vein, a 10-12 cm of the dissected vein was used as an autologous venous conduit. MRB has increased in popularity, this due to the possibility of redirect the mesenteric blood flow into the liver in a physiologic matter, this through a conduit that allows a low-resistance access into the intrahepatic portal system. In addition, this case shows that a redo meso-Rex bypass is a feasible option with good outcomes in pediatric patients, a collateral vein can be used as an autologous venous conduit in meso-Rex bypass, and collateral vein should be ligated during liver transplantation and meso-Rex bypass surgery to avoid portal perfusion steal syndrome.

eP-010

Living donor hepatectomy in left sided gallbladder donor with portal vein and bile duct variation (Right trisegmentectomy including S5,6,7)

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Donors with left sided gallbladder are often accompanied by anatomical variations such as portal vein and intrahepatic bile duct. Therefore, there are many perceptions that it is inappropriate as a donor of liver transplant. However, if the remnant liver volume and graft volume are sufficient, you can obtain appropriate graft through well-tailored dissection.
In this case we can observe variations in which segment 8 portal vein branches from the umbilical portion and segment 4 intrahepatic duct drains into the right hepatic duct. Assuming the use of segment 5,6,7 graft, the remnant liver volume was expected as 53.7% and the GRWR was 0.96.
First, we temporarily clamped the inflow into the graft and injected ICG dye to identify the demarcation line for dissection through the fluorescence image. After dissection of liver parenchyma, fluorescence image and intraoperative cholangiogram were used to confirm the drainage point of segment 4 hepatic duct. As a result, we were able to safely divide the hepatic artery, portal vein, bile duct, and hepatic vein and secure the graft.
Conclusion: In a donor with left sided gallbladder, we can safely proceed donor hepatectomy if the anatomy is well examined and supported by appropriate technique.

eP-011

Orthotopic piggyback liver transplantation by side-to-side caval anastomosis

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Liver transplantation with preservation of the recipient vena cava (piggyback technique) has been performed as an alternative method. Caval reconstruction in piggyback liver transplantation is generally performed by two end-to-end anastomoses. Here, we used a variant of the piggyback in 100 patients in whom both IVCs are anastomosed side-to-side which can be performed in a quick and safe manner.

The side-to-side caval anastomosis technique is as follows. During the backtable procedures, the upper end of the IVC is closed with 4-0 Prolene continuous sutures. The infrahepatic IVC is also sutured with 1 cm hole of the donor's IVC is left. 100 mL of cold bath solution is flushed into the IVC from the hole to check for leakage. All detected points of leakage are oversewn with Prolene.

Hepatectomy is performed after retrohepatic vena cava dissection with control of the three major hepatic veins and the short hepatic veins. After the recipient´s liver is removed, a vascular clamp is placed laterally on the anterior part of IVC, preserving IVC blood flow during the anhepatic phase. The graft was placed orthotopically into the hepatic fossa and the caval graft was pulled straight to adjust the distance between the vena cavas of graft and recipient. A longitudinal 4 cm cavotomy is performed in both the recipient and donor IVC. A side-to-side caval anastomosis is then performed by 4-0 prolene running sutures. The large side-to-side caval anastomosis achieved optimal hepatic outflow, avoiding vascular problems. Once portal vein anastomosis is completed, blood flow is restored by removing caval and portal clamps. The 1 cm hole of the donor's IVC is closed with 4-0 Prolene sutures before 100ml blood with perfusion fluid from donor liver were flushed away from the hole. The time for side-to-side cavocaval anastomosis was about 15 minutes.

eP-012

Pre-implantation splenectomy and triple vessel outflow technique in left-lobe living donor liver transplantation

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Left-lobe grafts are under-utilized for adult living donor liver transplantation (LDLT) in North America because of fear for the development of small-for-size syndrome (SFSS). Maximization of outflow and adequate inflow modulation are important to avoid SFSS. We herein report a novel triple-vessel outflow reconstruction to maximize the outflow of left-lobe grafts. This was combined with a change in the primary inflow modulation from hemi-portocaval shunt to splenectomy.

Splenectomy can be performed before or after liver implantation. Pre-implantation splenectomy for left-lobe LDLT is performed in patients who had one or more of the following risk factors for SFSS: GRWR $\leq$ 0.7, pre-operative hepatic pressure gradient $\geq$15 mmHg and MELD score $\geq$20. Indications of post-implantation splenectomy included portal hyper-perfusion (portal flow200ml/100gLW) and/or portal-hypertension (portal pressure $\geq$20 mmHg and/or hepatic pressure gradient $\geq$10 mmHg).

The case presented was a 55 year-old female with cryptogenic cirrhosis and a MELD score of 18. The donor was her 29 year-old son who donated his left-lobe. Estimated GRWR was 0.86. Because of pre-operative hepatic pressure gradient of 15 mmHg, pre-implantation splenectomy was performed using a vessel-sealing device.

At back table, a venoplasty was performed to fashion a single wide outflow orifice. For implantation, a large venous cuff was created by connecting the right, middle and left hepatic veins with the same technique used for a whole liver graft piggyback implantation in our program. The technique easily provided a wider diameter than that of the graft hepatic vein. Hepatic venous anastomosis is performed with partial horizontal clamping of vena cava.

Since the implementation of the strategy of splenectomy and triple vessel technique, SFSS has not occurred in the subsequent 33 left-lobe LDLTs. Surgical, thrombotic or infectious complications were comparable between LDLT alone and LDLT with splenectomy.

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eP-013

No touch isolation technique for the prevention of postoperative recurrence of hepatocellular carcinoma after liver transplantation-combined with trans-arterial radioembolization

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Recently, trans-arterial radioembolization (TARE) was done in the patients who had advanced stage hepatocellular carcinoma. Sometimes totally necrosis of tumor was reported after the operation. No touch isolation technique is concept of preventing tumor spread during tumor operation. We expected that if we can use this technique and control all viable tumors before transplantation. We could get better outcomes in the hepatocellular patients.
We performed living donor liver transplantation using no-touch isolation technique in the patients who had multinodular hepatocellular carcinoma and high AFP, PIVKA level after TARE and conventional TACE.
Case: 36-year-old female patient had liver cirrhosis with hepatitis B virus infection and multiple hepatocellular carcinomas in both lobe. Alpha-feto protein level was 850,000 PIVKA 136,000. At first, there were high chance of recurrence, we did not consider liver transplantation. Hepatologist decided to do TARE and additional conventional TACE. After that treatment, AFP and PIVKA level were dramatically decreased, and there was no viable tumor in follow up CT after 3 weeks.
Living donor liver transplantation was done, the donor was 32 years old her sister, there was no variation in the donor side. Total operative time was 4 hour 30 min and blood loss was 100cc. We did recipient hepatectomy using no-touch isolation technique, suprahepatic and infrahepatic IVC were isolated and clamped. Then we clamped hilum and resected using high hilar dissection technique. Immediate postoperative period there was no acute complication, patients transferred to general ward at postoperative 4 days then discharged postoperative 14 days. Postoperative 1 month, patients is alive, there is no recurrence, and AFP level is 11.5 and PIVKA level is 33.
TARE(trans-arterial radioembolization) is a good modality for pre-transplant treatment for far advanced stage case of hepatocellular carcinoma. No touch isolation technique during recipient hepatectomy might be helpful in advanced stage hepatocellular carcinoma patients.

eP-014

Liver transplantations from situs inversus donors

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Situs inversus is a rare congenital anatomical abnormality that results in dextrocardia and a mirror image of all normal abdominal organs. Deceased donors with this condition are often declined based on anatomical concerns. Here we present two such cases with contrasting liver graft implantation techniques.
The first is a modified retroversus piggyback technique with 180° ventral-dorsal (backwards) rotation of the liver graft along the axis of the vena cava. This orientation resulted in the retrohepatic vena cava facing anteriorly and the larger anatomic left liver in the right upper quadrant. In 2006, the recipient was a 49-year-old male with end-stage liver disease secondary to hepatitis C and alcohol-related cirrhosis complicated by a 4.2 cm hepatocellular carcinoma (HCC). His tumor-adjusted and unadjusted model for end-stage liver disease (MELD) scores were 25 and 10, respectively. Total operative time was 5.5 hours. His hospital course remained uneventful with excellent immediate graft function; he was discharged home in good condition on postoperative day 9. The patient remains well with normal liver function and without HCC recurrence to this day.
The second liver implantation technique is direct placement of the graft into the recipient's right upper quadrant, without rotational adjustment. In 2017, the recipient was a 67-year-old male with alcohol-related cirrhosis and a MELD score of 18. The transplant was uncomplicated with a cold ischemic time of 7hours. There was excellent immediate graft function and the patient was discharged home in good condition on postoperative day 5. The patient continues to do well with normal liver function to this day.
Livers from deceased donors with situs inversus totalis may be used successfully in liver transplantation with excellent short- and long-term outcomes; technical modification(s) at implantation may be required.

eP-015

No touch left approach technique in LDLT for right advanced HCC

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No touch technique approaching left side for right lobe advanced HCC decreases HCC recurrence. The patient was 49 year old male, he had HBV related LC and HCC in right lobe with PV tumor thrombosis invading into the main PV.
So, he underwent two time TACEs and reduced dosage radiation therapy to PVTT before liver transplantation. On the pre-TACE dynamic CT scan, large tumor was located in right lobe and it invaded into the main portal vein.
Celiac angiography showed well stained large tumor in right lobe. And successful TACE was done by superselection through RHA.
Locoregional treatments made tumor regression a lot.
In this preoperation CT scan, we could see that large tumor containing lipiodol had shrunk and PV tumor thrombus was retracted from the main portal vein.
However, as you can see on right side CT scan, pericholedochal cavernous formation caused by PVT was seen.
Taking these findings into consideration, we decided to perform LDLT by no touch left approach technique with consent of the patient and his family. Pre-operation laboratory findings showed that Child Turcotte Pugh score was 6 in class A, and MELD score was 6.
Tumor markers, that is, AFP and PIVKA II, had decreased to nearly one in twenty after locoregional treatments.
Donor was his 20 year old, ABO compatible daughter.
Estimated GRWR was 0.82 and SLV was 43.8%. Core needle biopsy showed no steatosis. The patient underwent LDLT using by modified RL graft on 18th Feb. 2016.
Left approach for right side advanced Hcc is essential for less intraoperative tumor spread. First, we perform early hilar division, and make temporary portocaval shunt. After that, we divide LHV & MHV, and then clamp RHV at left side. Finally, right lobe mobilization and total hepatectomy are going to be done.

eP-016

Ex-vivo organ perfusion technique for deceased brain death (DBD) donor

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Background: We describe our technique of ex-vivo organ perfusion in deceased brain death (DBD) donors.
Methods: This technique comprises of warm dissection of liver, kidneys and heart, in hemodynamically stable DBD donors and perfusing them ex-vivo. The cardiac and abdominal dissection can take place simultaneously. As a precaution, the iliac arteries and abdominal aorta are dissected and kept ready for rapid cannulation and perfusion, should the donor become unstable at any stage.
The liver dissection is in principal similar to living donor hepatectomy, where portal dissection is combined with supra and infrahepatic caval dissection to completely mobilize liver to allow it to be removed and perfused ex-vivo. The renal dissection is done after hepatic dissection is complete and involves exposing both the kidneys along with their vasculature and ureters.
The donor is heparinized and the sequence of harvesting is modified where kidneys are procured first, one by one, followed by hepatic and cardiac procurement simultaneously. This technique can be performed only in stable donors, and multivisceral procurement of pancreas and small bowel are not feasible.
Results: 12 multivisceral (liver and kidneys in all and heart in four) procurements have been performed. The average perfusion fluid volume for liver was 3.4 litre, WIT during procurement was 3 minutes. There were no procurement injuries. Recipient median age was 52 years, median MELD 15. The mean CIT 145±42 minutes and WIT 31.6±10.6 minutes. All liver recipients recovered and were discharged with a median hospital stay of 15 days.
Conclusion: Our technique has not affected the outcomes in the recipient and has multiple benefits. These include use of less preservation solution and cost reduction, avoiding the drill of ice packing and cooling the abdomen and chest, decreasing bench surgery time and complexity, and avoiding the propensity of procurement injuries during cold phase dissection.

Surgical Video ePosters 5

eP-017

Robotically created jejunogastrostomy to regain endoscopic access to Roux-en-Y hepaticojejunostomy after right lobe live liver transplant

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Introduction: Biliary strictures are common after live donor liver transplantation. When a roux limb is used, Endoscopic Retrograde Cholangiography (ERC) is commonly not possible. Percutanous Cholangiography Tubes (PTC) are the second choice, but they are morbid and often unsuccessful in resolving strictures.
Case report: Patient is a 22 year old female with combined Primary Sclerosing Cholangitis (PSC). She received a right lobe live liver transplant. Biliary reconstruction was done with two independent hepaticojejunostomies to a roux limb. Anastomotic strictures developed at both ducts about a year later. PTC was tried, only one duct was successfully cannulated. Attempted ERC failed due to anatomy. After multiple failed PTC´s and episodes of cholangitis we decided to devise a surgical approach. Options were revision of the biliary anastomoses, which was the highest risk option, Hutson loop, which will commit her to a stoma, or open jejunogastrostomy (JG). We elected to perform a side to side JG using robotic assisted surgery. This allowed access far from the original field of surgery. This was immediately accessible in the OR. Four weeks later we started ERC´s and both ducts were stented. Less than six months later patient is stent free with no episodes of cholangitis.
Conclusions: Robotic assisted surgery can be a valuable tool to perform complex new operations like one mentioned above. The magnification and reticulation offered by the technology allows the minimally invasive technique to applied safely.

eP-018

The first robotic left lateral sectionectomy for pediatric living donor liver transplantation at the King Faisal Specialist Hospital (KFSHRC), Saudi Arabia: description of the technique

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Objectives: The adoption of laparoscopic living donor hepatectomy technique in our institution in April 2013 We describe in this video our first robotic left lateral sectionectomy for pediatric LDLT.
Methods: The donor was positioned in a supine split leg position and in 30° reverse Trendelenburg position. A 12mm trocar was placed in the umbilicus as “assistant port”; four 8mm trocars were placed on a“semilunaris line” from the right to the left flank with 8 cm distance between each. An Xi da Vinci robotic surgical system was docked. Opening the falciform ligament, the liver hilum was dissected to identify S 2-3 and 4 arteries, the left portal vein and the branches to the caudate lobe. The parenchyma transection was done using the harmonic scalpel. Few hem-o-lock clips were applied. After cutting the hilar plate, the transection was done till the left hepatic vein (LHV). The S2-3 artery stump was secured by two Hem-O-lock clips, the left portal vein and the LHV transected and secured by the 45 mm vascular robotic stapler after preparing a small Pfannestiel incision allowing the positioning of an endobag beside the graft. The donor’s procedure lasted 5 h with a, estimated blood loss of 50 ml.
Results: The recipient was an 11 months’ boy with a diagnosis of irresectable giant hepatoblastoma. The transplant was uneventful. The donor was successfully discharged at the POD 4. Remarkably low pain score during the first two POD with the VAS evaluation of 5+/- 3.
Conclusions: Robotic left lateral sectionectomy is the ultimate evolution of minimally invasive donor hepatectomy. with the increased number of procedures its intrinsic value for the surgeon (better ergonomic, stable view, detailed anatomy), the donor (safety and pain) and the quality of the graft (few manipulations) can be better defined in a near future.

eP-019

Full laparoscopic left lateral sectionectomy with graft reduction in paediatric living donor liver transplant

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This video is a demonstration of laparoscopic left lateral sectionectomy (LLS) with graft reduction performed for adult donor to paediatric recipient living donor liver transplant. Pre-operative imaging such as Computed Tomography (CT) scan, CT Volumetry and Magnetic Resonant Cholangiopancreaticography (MRCP) were performed to delineate donor liver's hepatic artery, portal vein, hepatic vein, and biliary anatomy to determine suitability for organ donation and operative planning. The operation began by performing gallbladder dissection and intra-operative cholangiogram for biliary anatomy confirmation. Ligaclips® were placed at the left hepatic duct hilar area to mark the landing zone of left bile duct transection plane. Dissection of the liver hilum was performed to isolate the left hepatic artery and left portal vein. Branches from the caudate lobe were also ligated to fully mobilise the left lobe and achieve a longer left portal vein length. Ultrasonography was used to determine the course of left and middle hepatic veins. The falciform ligament was taken down and a Surgitie® was applied. Retraction of the falciform ligament and right lobe created an "open door" effect. Parenchymal transection was performed using Cavitron Ultrasonic Aspirator and Harmonic® scalpel. An in-site graft reduction was performed to ensure optimal graft to recipient weight ratio. The left hepatic duct was cut after operative cholangiogram ascertained the optimal location, and the remnant donor left duct was suture ligated. A small Pfannestiel incision was made in preparation of graft retrieval. Once the recipient was ready, the left hepatic artery was clipped and divided, left portal vein stapled and divided, followed by stapling of the left hepatic vein and delivery of the graft. A check cholangiogram was performed to ensure integrity of the remnant donor bile duct, and laparoscopic intraoperative ultrasound was performed to confirm the patency of the inflow and outflow of the remaining liver.

Surgical Video ePosters 6

eP-021

Right trisegmentectomy with caudate lobectomy combined with portal vein reconstrucion for hilar cholangiocarcinoma

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Background: R0 resection is the only curative treatment for advanced hilar cholangiocarcinoma (HCCA), especially when involving the caudate lobe and the portal vein (PV). Here, we described right trisegmentectomy with caudate lobectomy combined with portal vein reconstruction for advanced hilar cholangiocarcinoma.
Methods: A 51-year-old female was admitted to hospital with obstructive jaundice. Preoperative CT scan showed the widely extension and involved the caudate lobe and portal veins (PV). According to extension of HCCA, right trisegmentectomy with caudate lobectomy combined with PV resection and reconstruction was performed. The main portal vein involved by the tumor was removed and end-to-end anastomosis was performed. Then, biliary enteric anastomosis was completed between the left hepatic duct and the jejunum in an end-to-side way, the R0 operation had been achieved and the patient was discharged without any severe complication.
Results: Operative time was 4 hours. bleed loss was 500ml. Postoperative course was uneventful. Hospital stay was 20 days. The pathology showed cholangiocarcinoma with no lymph nodes metastasis. No evidence of recurrence was detected at 3 months after surgery.
Conclusions: Right trisegmentectomy with caudate lobectomy combined with portal vein resection can be safely performed and Aggressive surgical resection may improve the prognosis of the patient with HCCA.

eP-022

Extended right hemihepatectomy with anterior approach for infant hepatoblastoma

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Background: Hepatoblastoma is the most common liver malignancy in children with the incidence about one per million children. Radical resection plays a key role in the successful treatment of children with hepatoblastoma. However, the feasibility of radical resection is relatively difficult when the tumor is huge and invades hilar structure. This video showed early extended right hepatectomy for infant huge right lobe hepatoblastoma.
Methods: Preoperative CT suggested the huge mass was found in right lobe of a 28-month-old female infant. The laboratory examination showed AFP was >1210ng/ml. Three-dimensional (3D) reconstruction showed the middle hepatic vein (MHV) was obviously compressed and pushed to the left lobe. The remaining liver volume after 3D simulated surgical excision was 39.7%. According to the accurate preoperative evaluation, this patient was successfully performed with extended right hepatectomy using anterior approach.
Results: Operative time was 4 hours. Blood loss was 100ml. The tumor size was 12cm*10cm*7.5cm. The pathology suggested mixed epithelial mesenchymal hepatoblastoma. The patient obtained rapid recovery and was discharged 15 days after surgery.
Conclusion: According to the accurate preoperative evaluation, radical resection instead of chemotherapy was technically safe and offers potential cure for hepatoblastoma.

eP-023

Pure laparoscopic hepatectomy in extreme anatomical variations with reference to hanging maneuver and portal vein suture technique and danger management

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Anatomical variations in living donor liver transplantation requires special attention from the operator. In particular, structural anomalies that can harm donors require more careful attention. In this video, we will introduce a living donor case with variation of portal vein, hepatic vein, and bile duct.
The donor is 36-years-old female whose Rt. ant. portal vein branches from Lt. portal vein, and also has a variation of Rt. hepatic vein joining IVC through 2 branches. You should be very careful not to damage the Rt. hepatic vein during hanging maneuver. If damaged, you can carefully proceed midplane dissection first, and then repair the injury. For dual portal vein, in order to prevent stenosis in donor side or shortening of portal vein in recipient side you can use suture technique. When it comes to bile duct variation, ICG fluorescence image can help you.

ILTS 2019

Late Breaking Abstracts

Concurrent Oral Abstract Session Latebreaking Abstracts I

LB 0-001

AntagomiR-199a intravenous injection enhances liver protective effect of hypoxiapreconditioned BM-MSCs in a rat model of reduced-size liver transplantation

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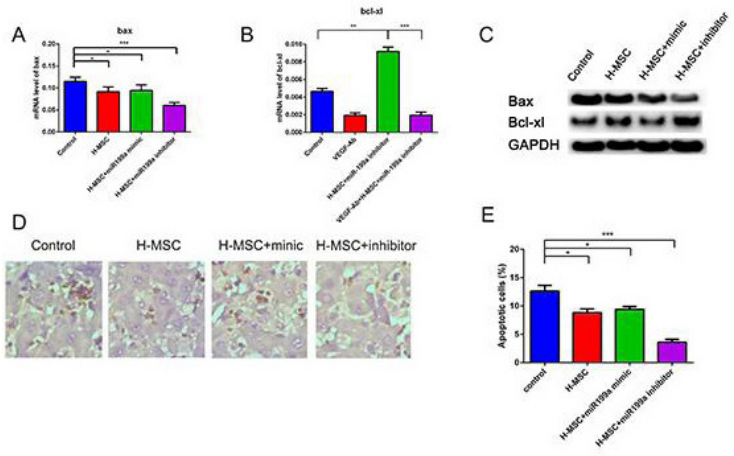

[AntagomiR-199a increased the anti-apoptotic effect of H-MSCs. Liver samples were collected as previo]

Background: Reduced-size liver transplantation was invented to overcome the shortage of donor livers; however, it was proved to be more susceptible to ischemia-reperfusion injury.
BM-MSCs infusion was shown to be protective after liver transplantation. Optimization
of MSCs infusion have been made, among them hypoxia precondition and miRNA
modulation were proved promising. This study was intended to explore whether mir-
199a inhibition enhances the protective effect of BM-MSCs in a rat model of reduced-size liver transplantation model and the underlying mechanism.
Methods: A reduced-sized liver transplantation model was constructed for experiments. Hypoxiapreconditioned MSCs were injected intra-portally. AgomiR-199a, antagomir-199a wereinjected through tail vein after liver transplantation. Apoptosis level as well as pro-inflammatory cytokines were measured 7 days after LT. VEGF antibody was further injected to explore the underlying mechanism.
Results: Mir-199a inhibition not only significantly decreased ALT and AST 24h, 48h, 72h after LT, but also ameliorated apoptosis level. Agomir-199a diminished the protective effect of BM-MSCs infusion. In term of mechanism, the liver protective effect of miR-199a inhibition was abolished by VEGF neutralize antibody treatment. VEGF antibody also increased the level of apoptosis when treated with hypoxia-preconditioned MSCs.
Conclusion: AntagomiR-199a injection enhanced protective effect of BM-MSCs via activation of Hif-1α/VEGF axis.

LB 0-002

A novel genetic EIP classification system for tailoring tacrolimus administration in the early postoperative period in Chinese liver transplantation patients

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Backgrounds & aims: Tacrolimus clearance had significant difference between individuals, which may easily lead to side effect caused by overdosage or underdosage. In this study, we explored a prospective genetic EIP classification method based on these genetic loci to guide clinical medication in the early period after liver transplantation.
Methods: Patients from 3 transplant centers were enrolled in this study. The recipients and their corresponding donor livers from center 1 (n=114) were genotyped using Affymetrix DMET Plus microarray, the association analysis between genotypes and concentration/dose ratios (CDR) were performed. The candidate associated loci were then sequenced using Sequenom MassARRAY platform in center 2 (n=93) and center 3 (n=77) patients for verification.
Results: A clinical classification method based on CDR can effectively divide patients into fast elimination group (FE group), intermediate elimination group (IE group), and slow elimination group (SE group), which we called it clinical FIS classification. In SE group, blood trough concentrations in early postoperative period

were higher than those of FE and IE groups, which could lead to delayed recovery of liver (P=0.0373) and kidney function (P=0.0135) and higher infection rate (P=0.0086). The prediction accuracy of current CPIC EIP classification based on recipient CYP3A5 rs776746 genotype for clinical FIS classification was only 35.56%. Prediction coincidence of adjust EIP classification combined of donor and recipient CYP3A5 rs776746 genotype for clinical FIS classification was 58.45%. Our newly established genetic EIP classification system based on major effect genetic factors (donor and recipient CYP3A5 rs776746) and minor effect genetic factors (recipient SULT1E1 rs3775770, and donor SLC7A8 rs7141505) allows 73.2% overall consistency with clinical FIS classification.
Conclusions: Our study presented a novel tacrolimus clearance classification system, clinical FIS, and then proposed a prospective genetic EIP classification model for precisely predicting the FIS which is possible to become a new clinical guide for tacrolimus medication.

LB 0-003

Acidic microenvironment regulates regulatory T cells in hepatic ischemia reperfusion injury model through PI3K-mTOR signal

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Hepatic ischemia/reperfusion (I/R) injury is a major complication of liver surgery, including liver resection, liver transplantation, and trauma surgery. Much has been learned about the inflammatory injury response induced by I/R, and regulatory T cells(Tregs) play an important role in regulating I/R injury. It is crucial to understand and consider the microenvironment which regulate Tregs during the pathogenesis of I/R injury as Tregs decreased at the early phage of I/R injury and increased later which reduced the inflammatory cytokines production and liver injury. In this study, we found that hypoxia leads to the formation of acidic microenvironments in liver I/R injury, pondus Hydrogenii(PH) decreased to 6.5±0.2 in mice I/R model compared with sham group(7.0±0.1) and Tregs in liver decreased according to low level of PH, while increased when PH was improved at later phase of reperfusion. Feeding with NaHCO3 improved liver function accompanied while less PH was decreased and more Treg was observed. We also checked the Treg generation with acidic microenvironment in vitro, lower PH lead to lower Treg differenation and lower Treg function in T cell expansion test.
The decrease of Treg differenation could be altered with NaHCO3 addiction or higher PH culture media was added in the culture system. Mechanism study showed that proton pump inhibitor could suppress the decreasing of Tregs and PI3K-mTOR signal as well was involved in Tregs differenation caused by the change of PH. This study will help us to understand the pathogenesis of I/R injury the immune injury induced by I/R injury. It will also provide new targets and theoretical basis for clinical alleviation and intervention of liver IR injury.

LB 0-004

Magnetic-driven microrobot-assisted cell therapy and embolization is a precise approach for hepatocellular carcinoma treatment

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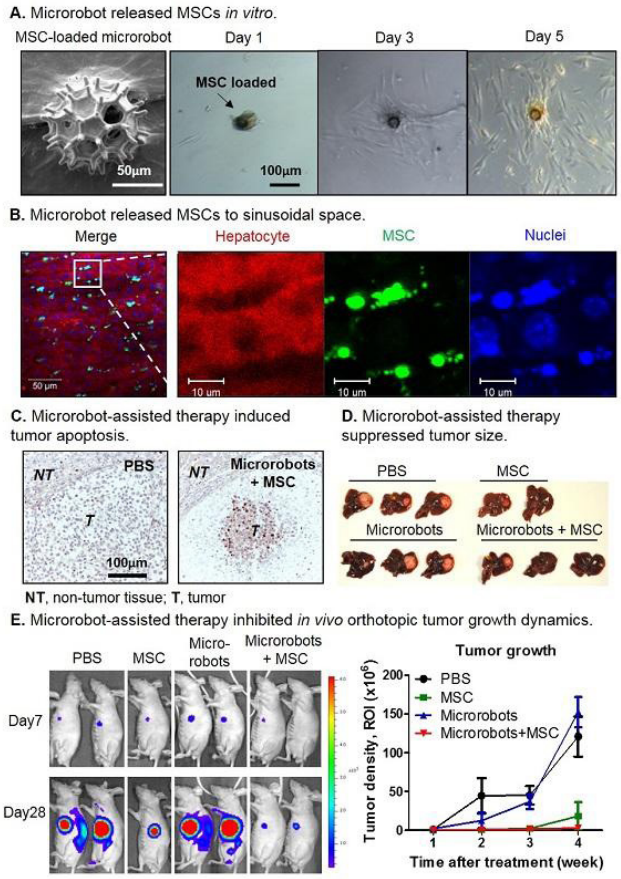
Background: Transarterial chemoembolization is an effective down-staging approach for liver cancer patients waiting for liver transplantation. However, lacking of precision dampened the efficacy and safety to functional liver remnant.
Method: We employed a magnetic-driven degradable microrobot to assist therapeutic cells delivering to tumor site. The microrobot was loaded with therapeutic iPSC-MSC-GPx3^{hi} cells (Qi et al., 2016) by in vitro co-cultivation. Cell-loaded microrobots were injected via portal vein and navigated by magnetic force to the tumor site in an orthotopic liver cancer mouse model. Efficacy of cell release was examined by intravital confocal imaging. Therapeutic effect for tumor growth inhibition was monitored by IVIS Spectrum in vivo imaging longitudinally in an orthotopic HCC mouse model.
Results: The microrobot was designed and fabricated by 3D printing using degradable polyethylene glycol diacrylate (PEGDA) added with 2% Fe_3O_4 nanoparticles. About 50 iPSC-MSC-GPx3^{hi} cells were successfully loaded to each single microrobot (diameter = 95μm), and were fully released in vitro after 5 days (**Figure A**). By magnetic force driven, about 200 cell-loaded microrobots were delivered to left hepatic lobe with tumor nodule, and cells were released to surrounding tissue (**Figure B**). More tumor apoptosis was found after microrobot-assisted cell therapy (**Figure C**). As the result of treatment, the progression of orthotopic liver tumor growth as well as final tumor size was significantly inhibited by iPSC-MSC-GPx3^{hi}-loaded microrobots treatment compared with negative control and sole MSC or microrobot treatment groups (**Figure D-E**).
Conclusion: The new approach using magnetic-driven microrobot-assisted cell therapy and embolization may provide an effective precise adjuvant therapy for bridging the HCC patients to liver transplantation.

Reference: Qi, X., et al., The Clinical Significance and Potential Therapeutic Role of GPx3 in Tumor Recurrence after Liver Transplantation. Theranostics, 2016. 6(11): p. 1934-46



[Figure. Magnetic-driven microrobot-assisted cell therapy for HCC]

LB 0-005

Progress and single-center summary of liver transplantation for intrahepatic and hilar cholangiocarcinoma

Ma E., Zhang Q., Tao Y., Li R., Ma Z., Li J., Li L., Chen T., Jin Y., Wang Z.

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Objective: To investigate the clinical characteristics and prognostic risk factors of intrahepatic and hilar cholangiocarcinoma patients receiving liver transplantation based on single-center clinical data.
Methods: Retrospective analysis of clinical data of 20 patients with intrahepatic and hilar cholangiocarcinoma admitted to General Surgery Department of Huashan hospital affiliated to Fudan University from June 25, 2014, to October 31, 2018. The treatment and follow-up results were analyzed. The survival rate was calculated by the Kaplan-Meier method and the survival curve was drawn. Cox regression model was used to analyze the prognostic factors.
Results: The overall perioperative survival rate was 100%, the 1-year survival rate was 60%, and the 3-year survival rate was 40%. The cumulative recurrence rate of stage I and II patients in AJCC stage was significantly lower than that of stage III and IV patients in AJCC stage; the cumulative recurrence rate of stage I and II patients was 0%, while the cumulative recurrence rate of stage III and IV patients was 76% (p=0.042). Cox regression analysis showed that CA19-9 was the only factor affecting prognosis, and high-level CA19-9 was associated with a high recurrence rate after transplantation (HR=1.001; CI: 1.000-1.001; P = 0.035).
Conclusion: The incidence of cholangiocarcinoma is low and the diagnosis is difficult. The recurrence rate of advanced cholangiocarcinoma receiving liver transplantation is higher and the prognosis is worse. Higher CA19-9 is an independent risk factor for poor prognosis after liver transplantation for intrahepatic and hilar cholangiocarcinoma.

LB 0-006

New and different expanded criteria for liver transplantation in hepatocellular carcinoma: Malatya criteria

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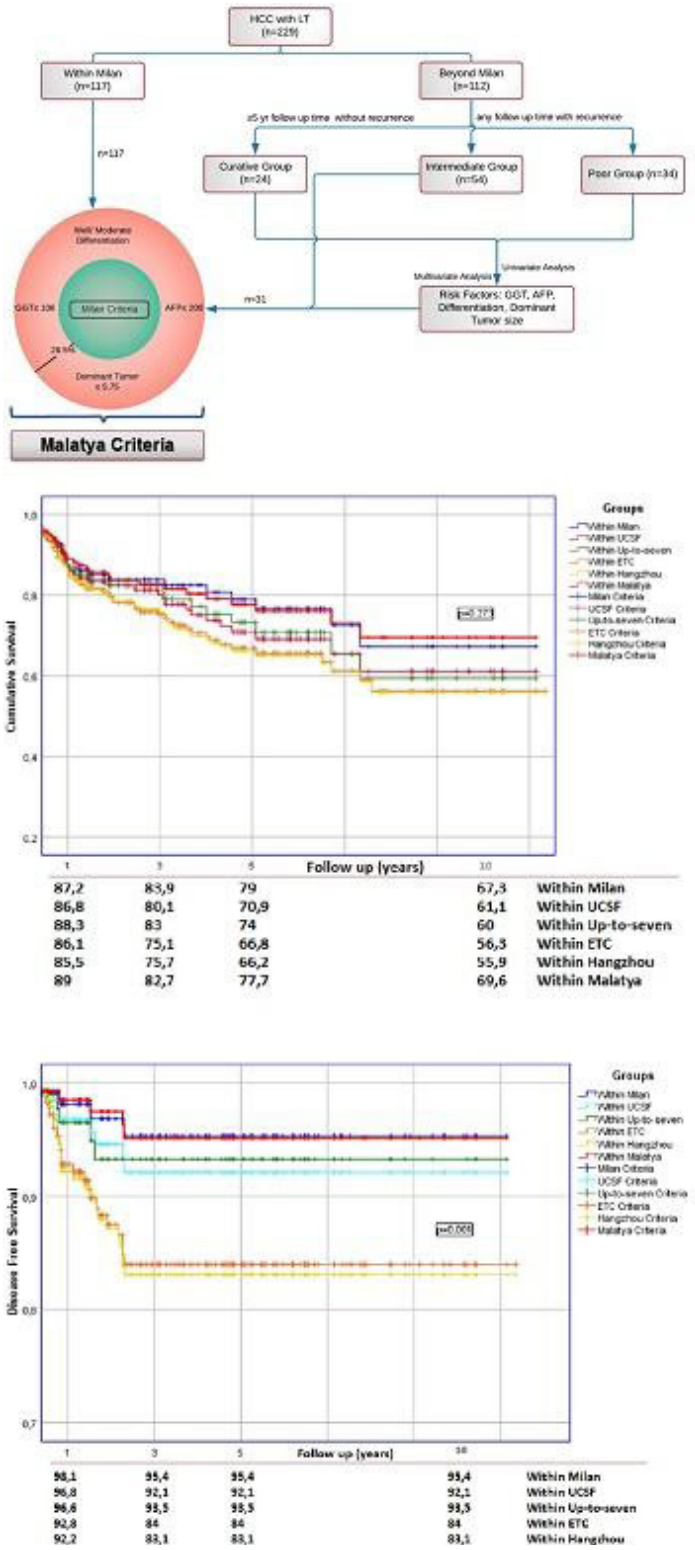
Aim: This study aims to present Malatya criteria which provides better long time survival for HCC patients and contains a brand-new parameter and approach which is not present in the previous extended criteria.
Methods: 229 patients with HCC undergone LT between April 2006-August 2018 included the study.Prospectively recorded data were analysed retrospectively.Beyond Milan criteria(MC) patients were divided into three subgroups according to presence of tumor recurrence:
(i) Curative group:Patients with a tumor-free survival more than 5 years (n=24),
(ii) patients with a tumor-free survival, but did not yet complete the 5 years follow-up period(n=54),
(iii) Poor group:Patients with a tumor recurrence at any time following LT(n=34).
Curative-group and Poor-group were compared with univariate and multivariate analysis according to the long time tumor free survival

and independent risk factors identified. Malatya criteria was defined using these factors and survival analysis was calculated. Survival rates with Malatya criteria,MC and the remaining present extended criteria (UCSF,Up-to-seven,ETC,Hangzhou) are compared,any result was considered significant when the corresponding p value was less than 5%.

Results: Comparison of Curative versus Poor-group based on tumor recurrence with multivariate analysis revealed GGT (OR:14.77,p=0.003),differantiation (OR:14.07,p=0.02),AFP (OR: 10.2, p=0.03), and dominant tumor size (OR:13.9,p=0.008) as independent risk factors. An analysis consisting four of the independent risk factors defined above detected 31 patients in the beyond MC group.Malatya criteria (n=148) are defined by these 31 patients and the 117 patients of the within MC group.According to within Malatya criteria,overall survival rates at 1, 5, and 10-year were 89%, 77.7% and 69.6% consecutively.

Conclusion: Among all extended criteria,highest 5 and 10-year survival rates are achieved with Malatya criteria. Furthermore, 10-year survival rate was higher even from within MC group.As a result,we would like to emphasize that extension of the criteria for HCC should not exclude the patients within MC and additional, diverse parameters such as GGT would be used.



[Flow chart and survival graphics]

LB 0-007

Genetic landscape of hepatocellular carcinoma and cholangiocarcinoma in Chinese population

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Background: Hepatic malignancy is one of the most frequent Malignancies in China and the accurate landscape of Hepatic malignancy in Chinese population need to be explained.
Method: To identify the genetic mutations landscape of hepatocellular carcinoma (HCC) and cholangiocarcinoma (ICC), we performed the Whole Exome Sequencing (WES) in a total of thirty-six pairs of HCC samples and four pairs of ICC samples.
Results: Overall, a total of 4231 somatic SNVs, 192 somatic Indels and 12 somatic CNVs were detected in thirty-six HCCs. Among ICC patients, a total of 240 somatic SNVs, 14 somatic Indels and 4 somatic CNVs were detected in four ICCs. The mean numbers of SNVs, Indels and CNVs of each patients were 60, 3.5 and 1, respectively. TP53 was the most high frequency of genes in both HCCs and ICCs (61.1% and 100%, respectively). Except of TP53, the frequency of candidate genes was greatly different between HCCs and ICCs. NBPF10 and CSMD1 in HCCs and AGBL1 in ICCs are novel candidate genes observed in our study. Furthermore, our results may reveal that KMT2C and ARID1A were significantly associated with the prognosis of HCCs. Meanwhile, five genes (MAP4K3, COX5B, ACTN3, CFTR and LRRC7) and two genes (PRKCG and SENP3) were predicted as new driver genes associated with early-recurrence and late-recurrence of HCCs, respectively. We also found the limited treatment effect of Sorafenib in HCCs.
Conclusion: The somatic mutations spectrum in HCC and ICC in Chinese population is characteristic and novel genes are associated with HCC and ICC in Chinese population.

LB 0-008

Utility of liquid biopsy (CTCs), Matrix metalloproteinase-1 (MMP-1) and Asialoglycoprotein receptor 1 (ASGR1) after liver transplantation (LT) in cirrhotic patients with hepatocarcinoma (HCC)

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Background: New markers associated with angiogenesis and tumor metastasis, such as circulating tumor cells (CTCs), are opening up new avenues in cancer management from the laboratory.
The Aim of this work is to determine the number of CTCs and MMP-1 and ASGR1 expression in patients included in waiting list for LT with HCC and to study its possible association with the AFP marker and with clinical variables.
Method: Peripheral blood of 36 patients suffering hHCC once included in waiting list for LT was obtained. 29 of them were transplanted, 27 of whom had blood extracted one month after the transplant, 19 of them after 6 months and one year after the transplant and 11 of them two years after the transplant.
Results: A statistically significant positive correlation was found between the pre-transplant levels of CTCs and the days on waiting list. The CTCs were not correlated in a significant way with the AFP concentration, number of tumors and time since diagnosis. Out of the 29 transplanted patients, 2 showed vascular invasion in liver. Differences in the levels of CTCs were found between the patients with and without vascular invasion.
Conclusion: The levels of CTCs and MMP-1 expression could be an unfavourable prognostic factor associated to longer waiting times and to the presence of vascular invasion with an increased risk of relapse and post-transplant metastasis. The expression of ASGR1 after LT decreases coinciding with the absence of post-LT tumor disease. In addition, we can see how their levels decrease significantly after transplantation. It would be necessary to increase the number of patients in the study, as well as the follow-up time, in order to achieve greater clinical evidence for its utility.

LB 0-009

Diagnostic performance of MRI texture features in prediction of microvascular invasion in HCCs of pre-transplant patients

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Background: Diagnosis of microvascular invasion (MI) is crucial in HCC, especially in patients on liver transplant (LTx) waiting list. MI has shown to be related with higher rate of recurrence after LTx. Available imaging and laboratoray techniques are insufficient in prediction of MI.
Texture analysis (TA), a computer aided diagnosis system has been recently introduced which provides quantitative analysis of images reflecting pixel based content of the image. It offers important advantages for the assessment of tumor biology. It has been successfully employed in the field of oncology and there is increasing interest within the field in defining association maps between tumor heterogeneity and imaging features. In the present retrospective research, we tried to evaluate the diagnostic performance of MRI TA parameters in prediction of MI in patients undergoing LTx.
Method: Fifty pre-transplant MRI of patients transplanted for HCC (26 negative and 24 positive MI according to histopathologic evaluation of explant) were evaluated. TA was performed on arterial phase contrast enhanced MRI obtained by 1.5 MR Scanner (Siemens, Erlangen, Germany). Upto 300 texture features were extracted by MaZda software version 4.6 (Technical University of Lodz, Institute of Electronics).
Results: Features under 3 sigma normalisation scheme through Fisher test denoted high performance in classifiying HCCs with and without MI, specifically for GrKurtosis, GrSkewness and WavEnHH_s-1 features (Fig. 1, Fig. 2). ROC analysis yileded sensitivity of 95.8% and specifity of 92.3% with area under the ROC curve (AUC) of 0.970 for GrKurtosis.
Conclusion: TA provides efficient classification of HCC lesion in regards of MI and could be uitilized for pre-transplant patients to determine cases requiring further pre-transplant locoregional treatments in order to decrease the risk of subsequent recurrance following LTx.

Concurrent Oral Abstract Session Latebreaking Abstracts II

LB 0-010

The incidence and risk factors for persistent unconsciousness following liver transplantation for acute liver failure

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Aim and background: Persistent unconsciousness in the post-transplant period is a major indicator of mortality in patients with acute liver failure (ALF). Preoperative prediction of such conditions will prevent many unnecessary transplantations. The aim of the present study is to evaluate the factors resulting in postoperative persistent unconsciousness following liver transplantation (LT) for ALF.
Patients and methods: The patients with ALF who received LT for ALF according to King's College Criteria in the last 6 years were retrospectively evaluated and patients who did not gain consciousness in the postoperative period were included in the study. Demographic data, severity of encephalopathy, laboratory data, graft type, etiology were retrospectively analyzed.
Results: Hundred and forty-eight patients were received emergency LT for ALF. Twenty-seven patients (18%) did not regain consciousness. All 27 patients(100%) had dismal prognosis and expired. Presence of preoperative Grade 4 encephalopathy was a major risk factor for postoperative persistent unconsciousness. Persistent unconsciousness was 16% in patients with Grade 2-3 encephalopathy while it was 52% in patients with Grade 4 encephalopathy ($p< 0.01$). In patients with Grade 2 and 3 encephalopathy female gender, re-transplantation, split donor transplantation had significantly higher unconsciousness rate. Cadaveric grafts had higher unconsciousness rate when compared to living donor grafts but this was not significant (21% vs 11%,$p=0.3$).
Conclusions: The number of patients for extraction of definitive data is not enough however preoperative Grade 4 encephalopathy is a major risk factor for persistent postoperative consciousness.

LB 0-011

Mitofusin2, a rising star in acute-on-chronic liver failure, controls the balance of apoptosis and autophagy via mTOR signaling pathway

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Background/aims: Acute-on-chronic liver failure (ACLF) is a life-threatening syndrome with poor prognosis. Several studies have begun to prove that mitochondria play a crucial role in liver failure. Mitofusin2 (Mfn2) plays an indispensable role in mitochondrial fusion and adjustment function. However, the role and underlying mechanisms of Mfn2 on apoptosis and autophagy of ACLF remain unclear. Our aim was to explore the effect of Mfn2 on several biological functions in ACLF.
Methods: In this study, we constructed an ACLF animal model and a hepatocyte autophagy model, using adenovirus and lentivirus to deliver Mfn2 to liver cells, in order to assess the effect of Mfn2 on autophagy and apoptosis in ACLF. Furthermore, we explored the biological mechanism of Mfn2-induced autophagy of ACLF using western blotting, RT-PCR, electron microscopy, and transient transfection of a GFP-LC3-expressing construct.
Results: Mfn2 significantly attenuated ACLF, characterized by ameliorated gross appearance and microscopic histopathology of liver, reduced serum AST, ALT and TBIL levels. Mfn2 improved the expression of LC3-II, Atg5 and Bcl-2 and downregulated the expression of Bax in ACLF. Like rapamycin, Mfn2 also significantly inhibited the expression of p-PI3K, p-Akt and p-mTOR in ACLF.
Conclusion: Our findings suggest that Mfn2 influences multiple biological functions of ACLF via the PI3K/Akt/mTOR signaling pathway. This study will provide a reliable theoretical basis for the application of Mfn2 as an effective target for ACLF treatment, reversing or delaying the process of ACLF.

LB 0-012

Donation after cardiac death grafts have a similar incidence of major intraoperative complications as donation after brain death grafts in orthotopic liver transplantation

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Background: Donation after cardiac death (DCD) liver grafts are an alternative source of organs in this era of increasing waitlist mortality and organ shortages. While there has been significant improvement in reducing rates of ischemic cholangiopathy and graft loss, there are still concerns of an increased incidence of intraoperative events in this patient population (e.g arrhythmia requiring cardiopulmonary resuscitation, post-reperfusion syndrome, hyperkalemia). Mayo Clinic Florida has been performing DCD liver transplantation since 1999, with good outcomes, so we aimed to show that DCD grafts have a similar incidence of intraoperative events when compared to donation after brain death (DBD) grafts.
Methods: Retrospectively, we collected recipient, donor, intraoperative, and postoperative data for 235 DCD patients from 2006-2017. We then performed a 1:1 propensity match to a DBD cohort by patient age, etiology of liver disease, and MELD score at time of transplant, and compared both groups.
Results: The DCD and DBD group had no significant differences in incidence of arrhythmia requiring cardiopulmonary resuscitation ($p = 0.65$), postreperfusion syndrome ($p = 0.75$), and treatments for hyperkalemia ($p = 0.83$) There was a statistically significant difference in amount of total intraoperative and postreperfusion blood products ($p < 0.05$ for all products), as well as inotropes and vasopressors used ($p < 0.05$ for all infusions). In terms of postoperative outcomes, there was no significant difference between both groups in patient ($p = 0.49$) and graft survival ($p = 0.10$) at 1, 3, and 5 years. (Patient Survival DCD: 93.5%, 88.9% and 81.2%; DBD: 92.6%, 87.9% and 85.6%/Graft Survival DCD: 90.5%, 86.1% and 77.1%; DBD 92.2%, 87.6% and 85.1%)
Conclusion: DCD grafts when compared to a matched cohort of DBD grafts have a similar low incidence of major intraoperative events. Centers should continue to look at DCD grafts as a viable source of liver grafts.

LB 0-013

Peak Workload during Cardiopulmonary Exercise Testing is predictor of one year survival following liver transplantation

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Background: Cardiopulmonary exercise testing (CPET) is the gold standard for the objective assessment of functional status prior to liver transplantation (LT) surgery in UK. Suboptimal CPET results are known to be associated with poorer outcomes and decreased 90-day survival. Little is known regarding predicting longer survival and hospital readmission rates.
Methods: We retrospectively analysed CPET data collated from 165 adult patients undergoing LT at a single centre. Demographic (Age, gender, height, weight and Body Mass Index (BMI)) and CPET data (Anaerobic threshold (AT), Peak Oxygen Consumption (VO2) and Peak Workload (PW)) and MELD scores at pre-assessment and LT were collected. Primary outcomes were length of hospital stay (LOS), cumulative readmission duration, 30-day, 1 and 5 year survival. IBM SPSS version 21 was used for uni and multivariate analysis.
Results: Median patients' age was 50.6±12 years, male/female ratio 68/32, and median BMI was 26.3±5.1.
Outcomes: Median LOH was 15 days (Min 3, max 162). Thirty day, 6 months, 1 and 5 year survival were 98.3, 97.7, 96.1 and 81.7% respectively. Median cumulative readmission day was 0, range 0 to 216 and 36.6% of patients were readmitted within 2 years of LT. CPET data: Of all CPET parameters, MVO2, Anaerobic Threshold and Peak Workload were predictors of 30 day, 1 and 5-year survival in univariate analysis. In multivariate analysis, Peak Workload was predictor of 1 year ($p=0.030$), but not 5-year survival ($p=0.757$).
Conclusion: This is the first study that has identified one of parameters observed during CPET test (Peak Workload) as predictor of 1 year survival. Neither of CPET parameters was predictor of LOS, cumulative readmission duration and 5-year survival. Further studies are required to predict long term survival and readmission to hospital following liver transplantation.

LB 0-014

Increasing trans-hepatic caval pressure gradient is associated with acute kidney injury after liver transplantation, irrespective of surgical technique

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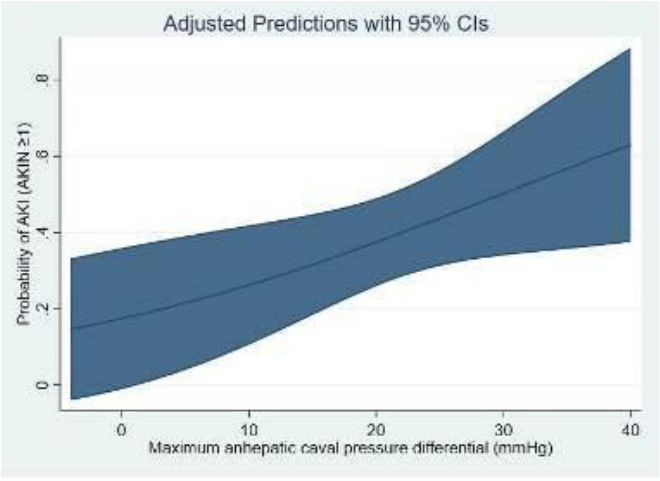
Background: During the anhepatic phase of liver transplantation (LT), inferior vena cava (IVC) clamping leads to decreased venous return and distal venous engorgement. This can impair renal perfusion pressure and result in acute kidney injury (AKI). Piggyback technique (PB) is proposed to offer some protection over caval replacement (CR) due to partial clamping and preserved venous flow. However, the extent of IVC occlusion during PB varies, so we propose that it is the pressure differential across the IVC that determines the risk of AKI, not necessarily the surgical technique.

Aims:

1. To describe the anhepatic IVC pressure differentials in PB and CR techniques
2. To quantify the association of maximum caval pressure differential (dPmax) with AKI

Methods: This was a retrospective, single-centre study of consecutive adult patients undergoing LT between January 2013 and June 2014. Exclusions were super-urgent transplants, preoperative creatinine >100μmol/L, or absent IVC pressure data. The primary endpoint was the development of AKI at 72hrs (AKIN ≥1) and its association with dPmax.
Results: After exclusions, 75 patients were included. PB was used in 48% of cases (22% of which used portocaval shunt) and CR in 52%. No patient underwent veno-venous bypass. In both CR and PB techniques, at least 25% of patients had a dPmax of >26mmHg (IQR 20-27mmHg and 9-26mmHg respectively).
Incidence of AKI was 39%. Controlling for donor and recipient factors, every 1mmHg increase in dPmax was associated with an 18% increased odds of AKI (OR 1.18 (1.04-1.34), p= 0.01). The probability association is demonstrated in Figure 1.
Conclusion: Increasing pressure differential across the IVC during the anhepatic phase of LT is associated with increased risk of AKI at 72hours postoperatively. Substantial caval pressure gradients are frequently encountered even when the piggyback surgical technique is employed.



[Figure 1. Maximum anhepatic caval pressure differential (dPmax) and the probability of AKI]

LB 0-015

Donation after cardiac death liver transplantation without Ischemic cholangiopathy: Facing the challenge

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Background: Liver transplantation (LT) with controlled donation after circulatory death (cDCD) has been associated with a high incidence of ischemic cholangiopathy (IC) and other perioperative complications such as primary non-function and hepatic artery thrombosis. Development of IC leads to multiple hospitalizations and finally, up to 70%, required re-transplantation or die. The use of post-mortem normothermic regional perfusion (NRP) has been reported to decreased the incidence of IC in cDCD LT. In 2015, we implemented a program of cDCD LT with premortem cannulation and NRP. Herein, we present the experience an outcomes of this program.
Methods: This is a retrospective study of prospectively collected data from a date base of cDCD LT preserved with NRP, in our hospital.
Results: From January 2015 to December 2018, 101 potential cDCD donors were connected to the NRP system. Eighteen livers were rejected mainly due to a suboptimal macroscopic aspect during NRP and 83 were finally transplanted (83% liver recovery rate). The median warm ischemia time was 10 min (6-22) and the median donor age was 62 (16-79). Nineteen donors (23%) were aged over 70. The median posttransplant peak in alanine transaminase was 919 U/L (220-6683 U/L). Ten patients (10%) presented postreperfusion syndrome and eighteen (18%) showed early allograft dysfunction. During the follow up two patients died with normal graft function. With a medium follow-up of 22 months, no cases of ischemic cholangiopathy were diagnosed and no graft loss was observed.
Conclusions: The use of post-mortem NRP in cDCD appears to help us in selecting good quality grafts avoiding the development of ischemic cholangiopathy, even when using elderly donors.

LB 0-016

Liver transplantation without donation - exchange of partial livers between two patients with different inherited metabolic liver disease

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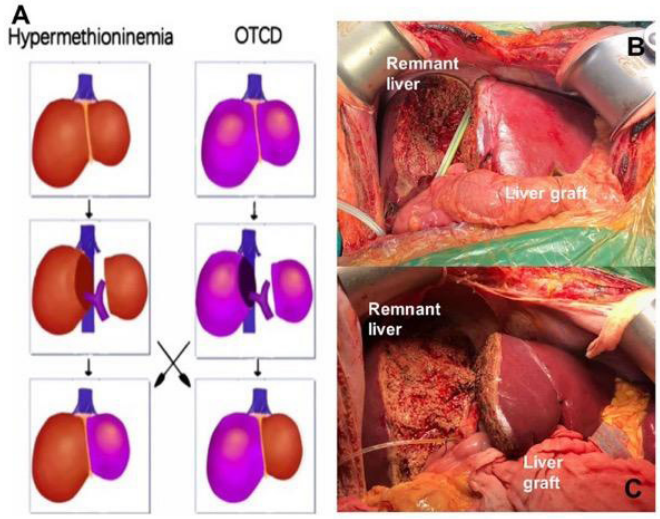
Introduction: Non-cirrhotic inherited metabolic liver diseases are characterized by an enzyme deficiency with normal liver parenchyma and liver function. We report two cases of domino cross-auxiliary liver transplantations, during which partial livers from two patients were exchanged for the first time.
Methods: Patient 1 was diagnosed with hypermethioninemia at the age of 7 months. Despite internal treatment, he suffered from hypomnesia at the age of 7 years. After that, increased T2 signal in bilateral cerebral hemispheres MRI scan was found. Patient 2 experienced several times of consciousness disorders and coma every year from the age of 9 years. Then OTCD was diagnosed in 2013. Levocarnitine and a protein-restricted diet did not prevent development of disease. He was in a coma at the age of 19 years and presented to us.
The left lobe of each patient was removed and transplanted to the other patient as a domino graft, thereby completing the domino cross-auxiliary liver transplantation.
Results: The recovery of both two patients were uneventful. For patient 1, at 1-month follow-up, blood methionine reduced dramatically from the preoperative highest level of 1253 umol/L to 50.97 umol/L, and his serum ammonia remained normal on an unrestricted protein diet. For patient 2, on the 28th postoperative day, his serum ammonia was 45 umol/L and serum methionine was 52.63 umol/L on a normal diet. Their liver functions, Doppler ultrasounds, and abdominal CT scans were normal. These results indicated residual native and transplanted liver mutually compensated for methionine adenosyltransferase defect and ornithine carbamyl enzyme defect.
Conclusion: Domino cross-auxiliary liver transplantation completed by exchange of partial liver between patients with different complementary non-cirrhotic inherited metabolic liver disease could be practical.Liver transplantation without donation can be achieved in this way.



[A. The schematic diagram; B-C. The intraoperative photo of the patient 1 and 2]

LB 0-017

Preventive administration of ursodeoxycholic acid after liver transplantation for primary biliary cholangitis prevents disease recurrence and prolongs graft survival

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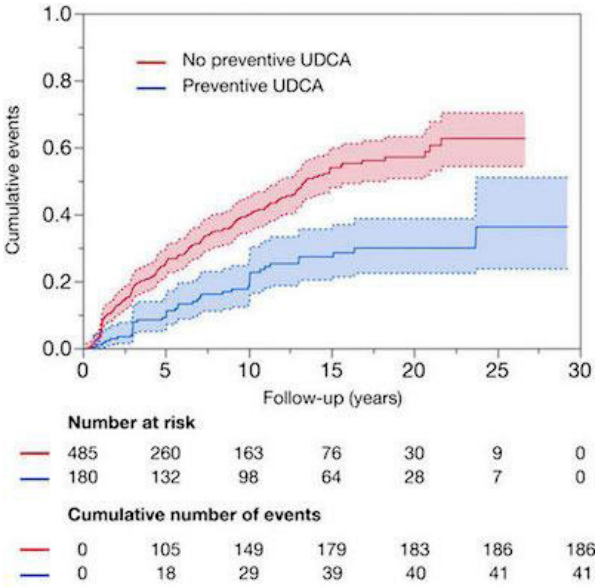
Background and aims: Primary biliary cholangitis (PBC) frequently recurs after liver transplantation (LT). Recent data have shown that PBC recurrence impairs graft and patient survival. Ursodeoxycholic acid (UDCA) has been suggested to prevent PBC recurrence but data supporting this effect are limited. Our aim was to assess in a multicenter international cohort the impact of UDCA administered preventively after LT on the incidence of PBC recurrence and long-term outcomes.

Method: Data from 941 patients (88% female; mean age: 54 years) who underwent LT for PBC over the past three decades were retrospectively analyzed. Among these patients, 211 (22%) have been treated with UDCA (10-15 mg/kg/d) continuously from the first 2 weeks post-LT (preventive UDCA). Recurrence of PBC was diagnosed histologically. Cox models and restricted mean survival time analysis were used to study the factors associated with PBC recurrence and long-term outcomes.

Results: Over an average of 10 years, 264 PBC recurrences, 111 graft losses, and 298 deaths occurred. In patients who had had at least 1 biopsy during follow-up (n=667), the factors associated with PBC recurrence in a multivariate analysis included absence of preventive UDCA (p< .0001; Figure), younger age at LT (p< .0001), use of tacrolimus vs. cyclosporine (p< .001), and use of protocol vs. clinically driven biopsies (p< .05). Preventive UDCA and cyclosporine use were independently associated with survival without graft loss or PBC recurrence. Hazard ratios (95%CI) associated with preventive UDCA with respect to PBC recurrence, graft loss, and death were 0.42(0.30-0.59), 0.44(0.26-0.76), and 0.67(0.51-0.89) respectively. Preventive UDCA was associated with a survival gain without graft loss or PBC recurrence of 21.1 months(12.6-29.5) at 12 years and 42.8 months(27.9-57.7) at 20 years.

Conclusion: Preventive administration of UDCA after LT for PBC prevents disease recurrence and prolongs graft survival.



[Cumulative probability of PBC recurrence (95% confidence interval)]

LB 0-018

Noninvasive early diagnosis of acute rejection after liver transplantation using phosphatidylcholine: single institute, prospective study

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Background: Acute rejection is a serious and frequent complication of liver transplantation (LT), and its diagnosis is contingent on the invasive procedure of the allograft biopsy. A noninvasive diagnostic test for rejection could improve the outcome of LT.
Methods: We obtained 55 serum samples from liver-allograft recipients with a biopsy-confirmed episode of acute rejection, and 87 samples without evidence of acute rejection. Phosphatidylcholine (PC) was isolated from the serum. PC was measured using a using Liquid Chromatography-tandem Mass Spectrometry. We measured serum PC levels for all patients at the 1st, 2nd, 3rd, and 4th weeks. Our results indicated that the level of PC correlated with the allograft status.
Results: There was no difference at sex, age, alcoholic, presence of HBV or HCV, HCC, liver cirrhosis, and MELD score, between rejection and control groups. Serum levels obtained were 34:0 PC, 34:1 PC, 34:2 PC, 36:4 PC, and 18:1 Lyso PC; there was no difference between the two groups up to 4 weeks. However, the concentration of 36:0 PC, 36:1 PC, 36:2 PC, 36:3 PC, 16:0 Lyso PC, 18:0 Lyso PC, 18:2 Lyso PC, and 18:3 Lyso PC were statistically different between the two groups.
Conclusions: Measurement of PC in serum offers a noninvasive means of diagnosing acute rejection of liver allografts. If such correlation between liver biopsy and level of serum PC is confirmed in larger studies, PC should help obviate the need for liver biopsies.

Poster Round II, Session 1, 2, 3: Latebreaking Abstracts

LB P-001

Intraoperative transesophageal echocardiography use in the diagnosis of cardiac tamponade during liver transplantation

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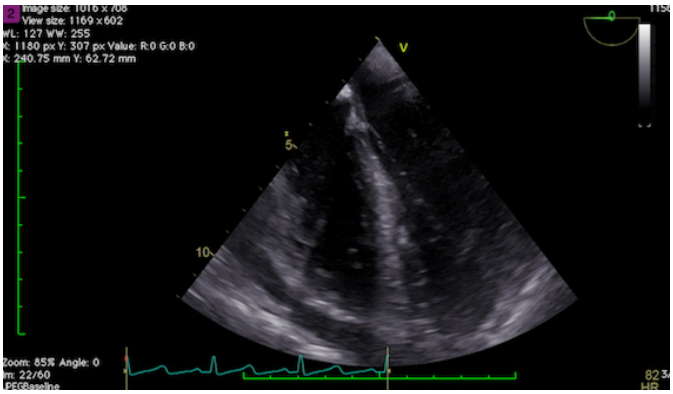

[Pericardial effusion]

Iatrogenic cardiac tamponade is a rare complication during liver transplantation. Transesophageal echocardiography (TEE) is lifesaving during this situation. We present the case of a 58 years old gentleman with cryptogenic liver cirrhosis MELD14 who underwent living related liver transplant on March 2018 at King Fahad specialist Hospital. After placing ASA monitoring and arterial line, general anesthesia induced using modified rapid sequence. Ultrasound guided double right internal jugular cannulation done using 7 Fr triple lumen central line and Swan catheter through 8.5 sheath. Correct placement was confirmed with chest x-ray. The hepatectomy phase was difficult and long due to SBP and adhesions. At the end of hepatectomy, patient developed severe and persistent hypotension and stroke volume didn't normalize after multiple volume challenges. TEE showed significant pericardial effusion around the right ventricle free wall with total right heart collapse during systole. Pericardial window was made by the surgeon to decompress the heart. one liter of blood was released and the patient's hemodynamics improved. Surgery continued with challenging hemodynamics and the use of triple pressors. pericardial drain continued to bleed one to two letters per hour. Our differential diagnosis included iatrogenic cardiac tamponade related to central catheter or Swan catheter ,so, both catheter tips identified by TEE. After vascular anastomosis, cardiothoracic surgeon opened a median sternotomy but no source of bleeding identified.
TEE permitted immediate diagnosis and surgical intervention. Iatrogenic needle penetration of cardiac structure may occur during hepatic surgery due to the left lobe relation to Rt ventricle. In our case, no structural injury related to catheter or suture needle identified. We believe that the pericardial effusion and tamponade was related to blunt trauma during difficult hepatectomy. The patient was extubated on third day and discharged home in three weeks.

LB P-002

Rhabdomyolysis as an unusual contributor to lactic acidosis after pediatric liver transplantation for hepatopulmonary syndrome: a case report

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Hepatopulmonary syndrome (HPS) is a known complication of liver disease. Liver transplantation (LTX) is an effective treatment, however the perioperative course can be turbulent(1). We describe a case of a 12-year-old male with HPS with a significant lactic acidosis after LTX.
A previously healthy 12-year-old male collapsed at school. Evaluation led to the diagnosis of severe HPS (room air PaO2 41 mmHg) and liver disease of unknown etiology. A living donor related LTX was performed, and the patient was taken to the ICU on nitric oxide and minimal vasopressor support.
Four hours after arrival, the patient developed a significant lactic acidosis. While an abdominal ultrasound was reassuring, the patient underwent an urgent re-exploration. Neither significant bleeding nor thrombosis was found. Concurrently, his urine was noted to be abnormally dark. Creatine kinase (CK) returned at 12913 U/l, concerning for rhabdomyolysis.
Generous hydration and diuresis were initiated. Lactate peaked at 7 hours post-transplant and returned to normal levels at 15 hours. CK levels peaked 24 hours postoperatively. An MRI on POD# 4 showed patchy myositis of the left bicep, both thighs, and right pectoral muscle. His CK normalized over the following week.
A rising lactate level after LTX deserves a thorough evaluation. The many possible contributing factors for this patient included factors

leading to excess lactate production (hypoxemia, rhabdomyolysis) and reduced lactate clearance (graft thrombosis). These concerns were addressed with re-exploration, hydration, diuresis, bicarbonate, oxygen supplementation, and nitric oxide. Rhabdomyolysis has been documented during prolonged surgeries, however is more often associated with positioning, morbid obesity, and is generally found in dependent areas(2). This patient had none of these risk factors, and the patchy distribution of myositis in both anterolateral thighs, left bicep, and right pectoral muscle is unusual.

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LB P-003

Cognitive aid and clinical guide for safety and efficient intraoperative use of transesophageal echocardiography during liver transplant

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Patients undergoing orthotopic liver transplantation (OLT) can be challenging to manage due to significant preoperative comorbidities, sudden and severe intraoperative hemodynamic shifts, and occasional unexpected findings such as pulmonary embolism. Transesophageal echocardiography (TEE) is a minimally invasive alternative method to monitor cardiac function which has expanded its role outside the cardiac surgery setting and currently represents an invaluable tool during the perioperative period to assess key aspects such as chamber sizes and function, ventricular hypertrophy, diastolic dysfunction, pericardial or pleural effusions, and valvular abnormalities in patients undergoing OLT. Other applications reported include assistance in the difficult placement of pulmonary arterial catheters and safe catheterization of great vessels for external veno-venous bypass placement. Unfortunately, the TEE during OLT is highly underused partially explained for the lack of familiarity and training, safety concerns and logistic reasons. We develop an easy to implement clinical guide accompanied by a cognitive tool for the operating room to safely and efficiently use the TEE during the liver transplantation in Western University and London Health Sciences Centre. We highlight the contraindications checklist and safety precautions. We display a user-friendly tool to improve the performance using the most relevant views for continuous intraoperative investigation and real-time therapy assessment of hemodynamic instability, acute hypoxemia or malignant arrhythmias in OLT.
The guide will efficiently help the anesthesiologist and intensivist to enhance the use and gain confidence in the safety use of the TEE while successfully discriminate common situations associated with intraoperative hemodynamic instability in LT patients such as intraoperative hypovolemia, right ventricular strain, left ventricular failure, low afterload syndrome and left ventricular dynamic obstruction among others causes of intraoperative unexplained life-threatening circulatory instability.

LB P-004

Use of continuous octreotide infusion in pre anhepatic phase of orthotopic liver transplant

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Background: Orthotopic liver transplantation (OLT) can be associated with significant intraoperative blood loss and transfusion of blood products. Studies have suggested that massive transfusion is associated with increased morbidity and mortality. Octreotide, a somatostatin analogue causes a reduction in splanchnic blood flow, it has been hypothesised that the use of octreotide infusion could reduce intraoperative blood loss and transfusion requirements.
Methods: We retrospectively analysed OLT cases using a pre anhepatic octreotide infusion compared to those without between 2015-16. We matched patients for age, MELD, sex, aetiology and starting haemoglobin concentration and platelet count. We compared total volume of transfused blood products, total volume of fluid given, post- operative haemoglobin, duration of surgery and length of hospital stay.
Results: Table 1

Control		PRBC	FFP	LOS	AGE	INR	Hb(pre op)	Platelet	TXA
Non Octreotide	Median	667	803	13	57	1.36	117	111	1000
	IQR 25	0	0	11.5	48	1.21	93	64.5	0
	IQR 75	1891.75	1671	22.5	61	1.505	127	161.5	1000
Octreotide	Median	341	0	15	53	1.8	103	95	1000
	IQR 25	0	0	12	50	1.4	79	61	1000
	IQR75	1149	1365	22	67	2.5	121	140	1000

[MEDIAN/IQR Two Groups]

We ran Man Whitney U test on each independant variables which suggested there was no significant difference between the two groups.

Conclusion: Our results do not currently support the routine use of octreotide infusions in the preanhepatic phase but they may be of value in those with significant portal hypertension to reduce splanchnic circulatory flow and blood loss. We are prospectively collecting more data on patients with portal hypertension and use of octreotide in preanhepatic phase. Further investigation with a larger prospective study may be warranted in future.

LB P-006

Anesthesia for liver transplant in a patient with sickle cell disease

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Sickle cell disease is frequently associated with liver affection ranging from hepatitis, liver cirrhosis, end stage liver disease, up to acute liver failure.(1) Liver transplant might be the only treatment available. Surgery and anesthesia for patients with sickle disease are considered to carry greater risk for perioperative complications. (2)
We report a case of 57 years old male who had, sickle cell disease, NIDDM, hypertension, and cryptogenic liver cirrhosis. His MELD score was 21, he had moderate ascites, no encephalopathy, and mild coagulopathy. The patient had undergone liver transplant from a deceased donor. Hemoglobin was raised before surgery to 10g/dl as advised by hematology and was maintained intraoperative between 8 and 10 g/dl. Anesthesia was conducted as our routine protocol for liver transplant, normothermia, and adequate hydration were maintained for the whole procedure. Blood loss was estimated to be 2.5 liters, and the patient received 2.5 liters of albumin 5%, 5 liters of crystalloids (plasmalyte) , and 4 units of packed RBCs. Transplanted liver was functioning well after perfusion evidenced by correction of laboratory work up and copious amount of produced bile on table. The patient was transferred to ICU and extubated few hours later.
Conclusion: Liver transplant is well tolerated in a properly selected and managed sickle cell disease patients. Care should be taken to maintain normothermia, adequate hydration, and hemoglobin level at 8-10g/dl.
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LB P-007

Successful OR to ICU handoff for complex surgical patients: a liver transplant model experience

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Handoff process has been identified as a source of medical error linked to adverse patient outcomes. It requires mastery of several skills including prioritization, communication, teamwork, and organization.
Successful handoff implies, safe transportation and efficient knowledge transference of essential clinical information between multiple clinicians typically in a hectic atmosphere with competing demands. This session summarizes the evidence around the role of the handoff process in perioperative care, highlighting strategies for education, quality
improvement, knowledge translation and implementation exploring a local project of handoff on Liver transplant recipients.
This session summarizes the evidence around the role of the handoff process in perioperative care, highlighting strategies for education, quality improvement, knowledge translation and implementation exploring a local project of handoff on Liver transplant recipients. The lecture will end up presenting the most valuable strategies to develop a safe and efficient handoff process at different levels of healthcare.We will share the experience performing a Quality Improvement (QI)project regarding the OR to ICU handoff process of the deceased donor liver transplants recipients at a tertiary academic hospital. We used a circling approach of implementation and feedback through in-person observations, multidisciplinary focused groups, and education sessions to develop a the novo handoff tool for our institution. The Liver transplant population model was chosen due to the associated complexity of the intraoperative events, dedicated surgical, anesthesia, and OR teams, and universal postoperative transfer to the ICU. The process performed by engaging all relevant clinicians with QI knowledge and experience in the process of interest. A systematic review of the literature and the identification of the ethnographic observations susceptible to be improve were also done. As a result, We describe a stepwise process to assist in better understanding the potential relationships between the handoff and the clinical outcomes presenting a cognitive aid and a Research Project.

LB P-008

Isoglycyrrhinate magnesium rescues biliary IRI through HMGB1 inhibition in a rat model of liver transplantation

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Background: DCD liver transplantation was invented to overcome shortage of donor liver, however, extended warm ischemia period leads to the development of biliary complications. Previously we found Iso facilitated Fk506 in reducing liver IRI after LTx through inhibition of extracellular HMGB1. Besides, it was shown in a retrospective cohort study that iso treatment significantly decreased incidence of biliary complications. Hereby, we hypothesized Iso has biliary protective effect against IRI during liver transplantation.
Method: An in vitro IRI model was constructed on HIBEC cells to mimic biliary IRI in vivo. Iso (1mg/ml) was pre-cultured with HIBEC 24h before IRI model. Recombinant HMGB1 was introduced to mimic HMGB1 accumulation during IRI. CCK-8 assay was conducted to observe cell viability when treated with or without Iso. Cell samples were collected, the level of TNF-α, IL-6 were measured via q-PCR. We further measured expression of HMGB1 in cell medium using ELISA.
Results: IRI significantly decreased cell viability of HIBEC; however, Iso pretreatment preserved cell viability during IRI in a dose dependent pattern. On the other hand, rh-HMGB1 showed a similar effect in elevating inflammatory cytokines with IRI model. Iso significantly decreased expression of TNF-α and IL-6.
Conclusion: Iso decreased biliary IRI and maintained cell physiology through HMGB1 inhibition.

LB P-009

SOCS1 regulates hepatocellular carcinoma P21 P27 ubiquitination

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Hepatocellular carcinoma (HCC) is one of the most common primary malignancy in adults and the sixth most frequent cause of cancer death worldwide, moreover, most of the burden is in developing countries. Suppressor of cytokine signaling 1 (SOCS1) is one of SOCS family proteins which participates in a classical negative feedback system regulating JAK/STAT pathway. Like all SOCS family proteins, SOCS-1 has a central SH2 domain and a conserved carboxy-terminal domain known as the SOCS box. Biochemical binding studies have shown that the SOCS box interacts with the elongin BC complex, a part of the ubiquitin proteasome pathway that forms an E3 ligase. We overexpressed SOCS1 in SMMC-7721 and HCC-LM3 cell lines to detect ubiquitination of P21 and P27 proteins by CO-IP. We found that the ubiquitination of P21 and P27 was significantly increased after SOCS1 overexpression. So we inhibited ubiquitination by MG-132 drug and found that ubiquitination of P21 and P27 proteins were suppressed.

LB P-010

Liver transplant consultant - a new title in India

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Background: Experience of dealing with more than 12000 liver disease patients and coordinating about 900 liver transplants including both live donor and cadaver liver transplants across the country.
Body: In an under developed, not very rich and not very literate country like India, where cost of liver transplantation means a lot and people are not aware of pros n cons related to this very complex procedure of liver transplant. Where most of the transplant centres are in Private Corporate hands. There was a strong need of a Patient Education Program and a very specific consultancy service for patients and their families to resolve their dilemma.
Conclusion: After working as a senior liver transplant coordinator in a high volume liver transplant centres in India and been in the field

of liver transplant right from the inception of liver transplantation in India. To create a Patient Centric Atmosphere and solve patient dilemmas, a neutral, experienced Liver Transplant Consultancy started and proved to be a huge success.

LB P-011

Recruitment maneuver in a patient with hepatopulmonary syndrome during liver transplantation surgery

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The recommended cut off values for HPS diagnosis are partial pressure of arterial oxygen (PaO2) < 80 mmHg or PAaO2 (the alveolar-arterial oxygen gradient) >15 mmHg. The European Respiratory Society Task Force has classified HPS severity into the following stages: mild, PaO2≥80 mmHg; moderate, ≥60 to < 80 mmHg; severe≥50 to < 60 mmHg; very severe, < 50 mmHg (1).
General anesthesia causes atelectasis in 100% of patients due to the abolishing the sigh reflex. The intraoperative effects of atelectasis include increases in the PAaO2, and increase in pulmonary shunting, decrease in SpO2. Alveolar recruitment maneuvers (RM) increase gas exchange, and improve PaO2. PEEP should be adjusted on the basis of respiratory system mechanics and oxygenation.
A 15 years-old female patient with cryptogenic liver disease+HPS underwent cadaveric LT. Preoperative PaO2 and SpO2 were 58.2 mmHg, 84%, respectively. After tracheal intubation, mechanic ventilator settings adjusted to 60% O2, 40% medical air, 1 MAC sevoflurane, 5mmHg PEEP. PaO2 increased to 80.4 mmHg in the blood gas sample taken at the dissection stage and SpO2 was 93%. SpO2 (93% to 88%) and cerebral oximeter (Left: 72% to 66%, right: 75% to 62%) progressively dropped towards the end of the dissection stage. Crepitation and B-line (USG) were detected in lung examination (Figure-1). We decided to make staircase RM with PEEP titration to improve oxygenation and hemodynamic status was sufficient for this procedure. After RM, SpO2 increased to 93%, cerebral oximeter values reached 72%(left) and 71%(right). Hemodynamic problems did not appear during the RM (Figure-2). Optimal PEEP determined as 7 mmHg according to RM. The patient was taken to the intensive care unit (ICU) after surgery without complications and mechanic ventilation treatment continued for three days in ICU.
RM should be considered in patients with HPS undergoing LT due to beneficial effects.

LB P-014

Predictors of acute kidney injury in liver transplant recipients at a single centre: a retrospective review

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Background: Renal dysfunction after liver transplantation (LT) is a major cause of morbidity and mortality. Hepatorenal syndrome (HRS) is a common cause of renal dysfunction in this population and can improve after LT. We sought to determine risk factors for acute kidney injury (AKI) after LT and hypothesized that preoperative renal function is inversely associated with postoperative AKI.
Methods: We performed a retrospective chart review of all patients at our center who received a liver transplant from January 1, 2004 until June 30, 2018. Patients with a GFR < 30 ml/min/1.73m^2 were not included in the final analysis. The main outcome was AKI at 72 hours post-transplant and was defined by the KDIGO criteria. Statistical analysis was performed using SAS 9.4. Categorical variables were summarized as frequency (percentage) and continuous variables as means (SD). Independent predictors of AKI were identified by multivariable logistic regression analysis.
Results: There were 1012 patients who received a LT and had a preoperative GFR > 30 ml/min/1.73m^2. The mean age was 54 years and 20% were female. The incidence of AKI at 72 hours was 44% (n=108) in the group with GFR > 60 ml/min/1.73m^2 and 33% (n=256) in the group with GFR between 30 and 60 ml/min/1.73m^2. After multivariable logistic regression the risk factors associated with postoperative AKI at 72 hours were NaMELD, BMI, diabetes requiring insulin, surgical duration, and red blood cell transfusion ($p< 0.05$). Preoperative creatinine and living donor graft were both inversely associated with postoperative AKI ($p< 0.05$). The accuracy of the prediction model for postoperative AKI was high (area under the curve [AUC] = 0.689).
Conclusions: AKI at 72 hours after LT was positively associated with NaMELD, BMI, diabetes requiring insulin, surgical duration, and red blood cell transfusion, and negatively associated with preoperative creatinine and live donor LT.

LB P-015

Use of venous conduct in grade III and IV portal vein thrombosis in liver transplantation: a single center experience from northeastern Brazil

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Background: Portal vein thrombosis (PVT) is a complication associated with the severity of liver disease. Its prevalence varies from 5 to 26% in patients awaiting liver transplantation (LT). There is no consensus on the best management in grade 3 and 4 (according to Yerdel classification) ranging from thrombectomy, thromboendovenectomy and venous conduits. The aim of the present study is to analyze the survival and complication results in patients submitted to LT, in a single-center experience, in which extra-anatomic mesoportal jumping grafts (JG) were performed.
Method: Retrospective study, with data collection from review of medical records. The study included patients who underwent liver transplantation who performed JG, as treatment for grade 3 and 4 PVT, in our service from January 2009 to August 2018. TheJG was performed as decribed by Tzakis.
Results: Of 361 patients undergoing LT in this period, 16 required JG. The main indications were alcoholic cirrhosis and cryptogenic cirrhosis, 5 cases. The mean calculated MELD was 20. Cold ischemic time was 6.3 hours. Warm ischemic time was 46 minutes. AST peak and ALT was 2582 and 1537, respectively. 12 patients were diagnosed with PVT in the preoperative period. Four patients were diagnosed during transoperative period. Three patients showed cancer, one cholangiocarcinoma and two hepatocarcinomas. All four deaths occurred in the first 30 postoperative (PO) days. Two, on 2 and 3 PO days, due to graft primary non-function (PNF), and another two, on 13 and 25 PO days, due to sepsis. The overall survival was 73.3%, with a maximum follow-up of 84 months.
Conclusion: In our case series, we observed a better survival rate than that reported in the literature, as well as a lower incidence of grafts PNF. JG in our series was effective in treating grade 3 and 4 portal thrombosis.

LB P-016

Diagnosis of donor derived infection by metagenomic next-generation sequencing in orthotopic liver transplantation

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Background: Orthotopic liver transplantation (OLT) is considered the therapy of choice for liver cancer or end-stage liver failure. The degree of risk for donor derived infection (DDI) in OLT is largely unknown and the ideal assays to use in screening to prevent such transmissions is unknown. Metagenomic next-generation sequencing (mNGS) is a comprehensive approach for sequence-based identification of pathogenic microbes. However, diagnosis of DDI using mNGS in OLT has not been reported.
Methods: From February 2018 to October 2018, we applied mNGS to detect the presence of pathogenic microbes applied to preservation fluid, blood, liver tissue, perihepatic tissue from donor and preoperative postoperative blood, drainage fluid from recipient in 42 pairs of OLT. We determined the thresholds for the unique reads required to identify the infectious pathogens. The diagnostic performance of DDI was compared between mNGS and traditional methods.
Results: When compared to traditional methods (4.76%, 2/42), DDIs in 19.0% (8/42) patients were identified by mNGS ($P < 0.05$). Positive rate of mNGS for detecting pathogen is 45.2% (19/42), 39.0% (16/42), 32.0% (13/42) and 28.6% (12/42) respectively in preservation fluid, blood, liver tissue and perihepatic tissue in donor. Interestingly, the positive rate of mNGS was superior to that of culture (45.2% vs 19.1%; $P < 0.05$) in preservation fluid, but not in perihepatic tissue.
Four recipients with occult virus infection were identified by mNGS preoperatively, and the transmission of recipients derived virus were confirmed postoperatively by mNGS, which were excluded DDI.
Conclusions: mNGS is a powerful tool to early diagnosis the presence or absence of DDI in OLT patients, so that early intervention after operation can be given for reducing the incidence of related infection after transplantation.

LB P-017

Hepatic artery and celiac trunk dissection during endovascular treatment of SASS after liver transplantation

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Introduction: Celiac trunk and hepatic artery dissection is a possible complication following endovascular embolization procedures. The risk of this complication increases with subsequent angiographies. Patients qualified for liver transplantation (LTx) due to hepatocellular carcinoma (HCC) sometimes require several transarterial chemoembolization (TACE) procedures.
Case study: This case explores a 42 - year - old man who underwent liver transplantation due to HCV/AIH induced liver cirrhosis and HCC. The patient had two TACE procedures prior to LTx because of HCC. Doppler ultrasounds (USs) of the liver were performed according to our protocol on the 1st and the 3rd day following the LTx . Control USs revealed changes in the portal vein (PV), hepatic artery (HA) and splenic artery (SA) flows (mean PV velocity increased from 30 cm/s to 110 cm/s, HA RI increased from 0.6 to 0.9 and SA PSV increased to 140 cm/s). A splenic artery steal syndrome (SASS) was suspected and partial emoblization of the spleen was performed. During the procedure, angiography revealed celiac trunk and hepatic artery dissection. Therefore, two stents (Biotronik bare metal stent 7x15mm, Innova Boston Scientific nitinol stent 6x40mm) were implanted into the dissected arteries. Control angiography performed after two weeks confirmed proper arterial flow in the stents and embolization of 60% of the splenic volume. Doppler US after four months confirmed correct HA, PV and SA flows. Liver function tests remained normal.
Discussion: This case suggests increased risk of arterial complications following LTx in patients that underwent TACE prior to LTx. SASS is a rare complication of LTx and should be considered in the case of Doppler US abnormalities even without clinical symptoms and with normal liver function tests. An approach through the celiac trunk was necessary for the SASS endovascular treatment. Frequent endovascular access via the celiac trunk increases its risk of dissection.

LB P-018

Controlled donation after circulatory death up to 80 years for liver transplantation

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Background: Nowadays the results obtained with controlled donation after circulatory death (cDCD) are similar to those achieved with donation after brain death (DBD) in liver transplantation (LT), although in the case of cDCD there's a higher percentage of rejections of the donor during the evaluation and organ retrieval. The best results in cDCD-LT have been obtained with < 50years donors, total warm-ischemia-times (TWIT) < 30 minutes and cold-ischemia-times (CIT) < 5 hours. Our aim was to compare the results obtained between cDCD and DBD groups in our hospital and the influence of age on the results of cDCD over 70 years and up to 80 years.
Method: A prospective study of all cDCD-LT performed between Nov-2014 and Sept-2018. The results in terms of clinical and analytical parameters were compared with a control group, formed by DBD-LT carried out immediately after each cDCD-LT. The results obtained within the cDCD were also analyzed according to the age of the donors (cut-off 70years). A super-rapid recovery (SRR) retrieval technique was used.
Results: Both groups were similar in terms of pre-transplant and donor characteristics. We only found statistically significant differences in the rate of biliary complications (higher in the DCD group).

	DCD >70 (n=30)	DCD <70 (n=40)	p
Hepatic Artery Thrombosis (HAT)	3 (10%)	2 (5%)	0.421
Retransplantation	3 (10%)	6 (15%)	0.536
Overall Survival (1 year)	78%	79.8%	0.464
Graft Survival (1 year)	74.6%	69.2%	0.382

[Data obtained comparing DCD >70 years vs DCD <70 years]

Conclusion: Graft survival of the cDCD group wasn't inferior to the DBD group. However, we found a higher rate of biliary complications in the cDCD group. Age wasn´t a negative factor to cDCD success and probably, as happened with DBD, it would no longer be an exclusion criteria allowing to increase the donor pool.

LB P-019

Failed ability to donate under donation after circulatory death protocol

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A shortage of donor organs exists in many countries around the world, including the United States. In the past 2 decades, there has been resurgence in the use of donation after circulatory death (DCD) donor organs in an attempt to try to help meet this need. The four bioethical principles of autonomy, beneficence, non-maleficence, and social justice are each fundamentally important when discussing the rationale for the use of DCD organ donors. We sought to explore the percentage of potential DCD organ donors at Mayo Clinic and our regional organ procurement organization (OPO) who were unable to donate because the patients did not expire within the allowed time frame. Following Mayo Clinic Institutional Review Board approval, we obtained the total number of DCD attempts at our institution since enactment of our DCD program from our OPO administrator from August 1, 2013 through August 31, 2018. At Mayo Clinic, 7/23 (30%) of our potential DCD donor pool failed to donate compared to 34/250 (14%) of patients at other hospitals within our OPO due to this time restriction. Of the 7 potential DCD donors that did not expire within the allowable timeframe at Mayo Clinic, 3 expired 4-6 hours after withdrawal of support, 1 expired after 10-23 hours, 2 expired greater than 24 hours after withdrawal of support, and this information was not recorded for 1 patient. Without a more certain means of predicting the death of patients over a relatively short time period, any concrete exploration of premortem procurement from patients failing to meet DCD criteria to increase the number of transplantable organs would further risk public trust in transplantation practices and may lead to more harm than good.

LB P-020

A case of severe abdominal infection after liver transplant caused by donor-derived carbapenem-resistant klebsiella pneumoniae

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The donor-derived carbapenem-resistant klebsiella pneumoniae (CRKP) has become one of risk factor for graft dysfunction and receptor death after liver transplant. Here, we report the case of a 39-year-old male with allogeneic liver transplantation in our hospital due to acute exacerbation of alcoholic cirrhosis and chronic liver failure. The donor brain died from a traffic accident. He had experienced pulmonary infection but cured afterwards by antibiotic treatment in ICU. the routine culture of donor liver perfusion fluid showed positive for CRKP and Escherichia coli on 4th post transplantation day. We found that the same kind of CRKP and Escherichia coli were detected in the peritoneal drainage and sputum culture. On 7th day, we used antibiotics treatments such as tigecycline and amikacin according to the drug sensitive tests. However, the patient developed severe abdominal infection and septic shock. We performed an emergency abdominal exploratory and removed a large amount of necrotic tissue surrounded liver. On the 27th day post surgery, the transplanter had a high fever again, and MRCP showed a bile leakage. We did a third operation to repair it and removed recent generated necrotic tissue. The patient's symptom disappeared and was cured on day 49 post-operation dramatically. We found the combination of beta-lactamase inhibitors and other sensitive drug such as ceftazidime-avibactam maybe a promising agent for CRKP infections in patients undergoing organ transplantation, and surgical debridement should be considered as a necessary treatment for severe local infection.

LB P-021

Liver transplantation for intrahepatic cholangiocarcinoma: Chinese experience

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Indications for intrahepatic cholangiocarcinoma (ICC) for liver transplantation (LT) are controversial. LT for ICC has a high recurrence rate and low long-term survival rate. Most transplant centers list ICC as a contraindication to LT. Recent studies have shown that small-volume ICC tumor patients with single lesions achieve good long-term survival after LT. We conducted the retrospective study composed of 87 patients during 2015 to 2018 from China Liver Transplant Registry who were transplanted for ICC. After a median follow-up of 9.3 months, the 1-year, 2-year, and 3-year cumulative and tumor-free survival rate were 77.01%, 72.41%, 72.41% and 70.59%, 65.52%, 65.52%, respectively. The tumor recurrence and survival were significantly associated with larger tumor size, multiple lesions, implementation of neoadjuvant chemoradiation, etc. Patients with "very early" ICC (single tumor ≤ 2cm) may become candidates for LT. In summary, accurate evaluation of tumor morphological, biological and other prognostic factors, and establishment of standardized selection criterion are the main research direction of LT for ICC.

LB P-022

Portal vein thrombosis is not a contraindication in liver transplantation

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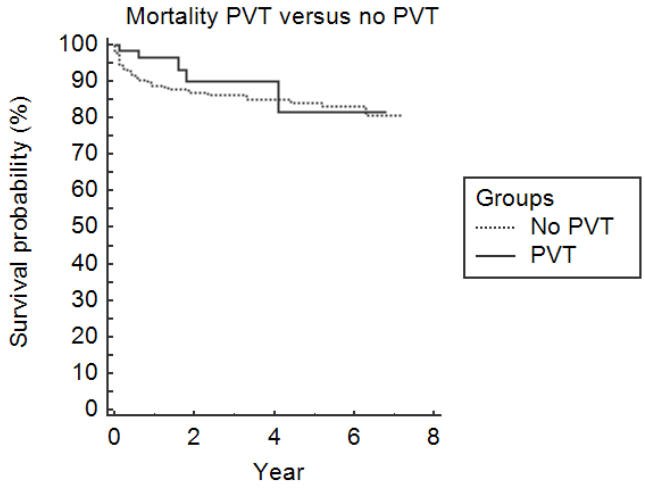
Introduction: Portal vein thrombosis (PVT) is common in the cirrhotic population and no longer considered an absolute contraindication to liver transplantation in many centers.
Methods: Retrospective analysis of 500 consecutive cases of liver transplantation from 2011-2018 at a single center. Characteristics and long-term outcomes of patients with portal vein thrombosis (PVT; n=64) confirmed at the time of liver transplantation were compared with patients transplanted without portal vein thrombosis (noPVT; n=436).
Results: Recipients with PVT were older (59 vs 56 years; p< 0.05). There was no statistically significant difference in the 2 groups in the proportion of male patients, BMI, incidence of diabetes mellitus, malignancy, and pre-transplant functional status. The PVT group waited longer for their liver transplantation (336 vs 228 days; p< 0.02). The mean MELD score was 24 vs 26 (PVT vs noPVT; p=0.13). Similar proportion of recipients in both groups received living donor vs deceased donor grafts. 42% of thrombi were unsuspected on pre-operative imaging and detected intraoperatively, 35.9% were occlusive thrombus and 15.6% had clot extension into the SMV or splenic vein. 63 patients underwent an eversion thrombectomy; in 2 of these patients, flow could not be reestablished and their graft portal veins were anastomosed to varices in the area of the liver hilum. There was no significant difference in the cold ischemic time, length of hospital stay, or incidence of early graft failure. Patients in the PVT group had a significantly higher rate of post-operative portal vein thrombosis formation (4.7% vs 0.46%; p=0.002). 5-year patient survival were similar between the 2 groups.
Conclusion: Large series of PVT in transplanted patients revealed an incidence of 12.8%. Adequate flows can be reestablished in most patients with eversion thrombectomy and long-term survival is comparable with patients transplanted without PVT.



[5-year Recipient Survival PVT vs noPVT]

LB P-024

Organs donation and potential donor: knowledge of USCS' medicine scholars

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Background: The 2014 national curricular guidelines, of Brazil, does not advocate that specific competences related to the context of organs transplant and flow of notification must be developed in medical courses. The professional who has recently graduated may suffer a lag regarding this subject, resulting in the difficult and mistaken diagnosis of Brain Death, reducing the number of potential organ donors. This study intends to understand the aspects related to transplant knowledge in medical students.
Methodology: Descriptive-exploratory study, developed in the Municipal University of São Caetano do Sul (USCS), with a sample of 374 students (95% CI and error margin of 3%), through an instrument

of 15 items. The sample is composed by 66.84% of female students, with minimum age of 22.
Results: 44% of the students received some information about the process of organ donation during their undergraduate studies; 91% affirm that the subject should be mandatory in the undergraduate program; 81% believe they were not prepared to pass on information about the subject and 53% don't know how to explain the concept of brain death. It was calculated the correlations (Spearman) between: the knowledge about the subject (bad, regular, good and great) and being prepared to pass on information about the subject (0.5 p-value < 1% for the 7th semester of the course); to know how to explain the concept and characterize brain death (0.4 p-value < 1% for the 6th semester of the course); to have the subject discussed during the course (0.4 p-value < 1% for the 5th semester of the course).
Conclusion: It was concluded that the instruction and training of the medical students and of the medical team to conduct the talk with the donor's relatives is an alternative to increase the rate of organ donation and of the understanding about the donation-transplant relation.

LB P-025

Liver transplantation using a graft from a deceased brain donor with Rendu-Osler-Weber syndrome: first time ever performed

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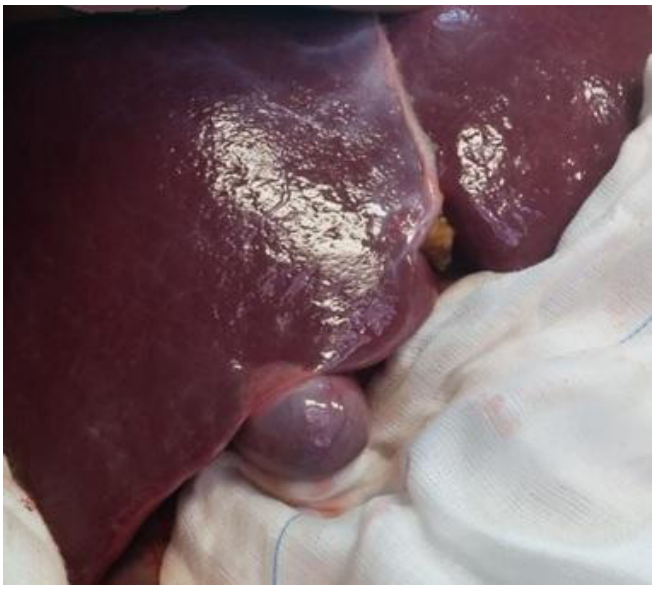
Background: Rendu-Osler-Weber syndrome, or hereditary hemorrhagic telangiectasia (HHT), is a rare autosomal dominant genetic vascular disease characterized by pathological angiogenesis causing a fibro-vascular systemic dysplasia, arteriovenous malformations, fragility of the vascular wall, dilatation and consequent rupture of the vessels. Whereas the number of organs is largely insufficient to transplant all the patients who need it, ISMETT tried to resolve this issue from its inception, and has developed the process of liver transplantation with organs from extended criteria donors.
Case report: We report the notable first liver transplantation recipient who received a whole liver graft from a young deceased brain donor affected by HHT, to introduce a broader concept in this field of medicine where HHT is usually a primary etiology for liver transplantation. Donor´s imaging evaluation and histological examination of liver biopsy had confirmed before surgery the absence of the HHT hepatic involvement without any signs of tiny teleangiectases or substantial vascular malformations.



[Macroscopic examination of the liver during the donor surgery.]

To date, the recipient recovered well after the surgery and has undergone imaging screening test, which has been negative. A Doppler ultrasound will be performed every three months for the first year after LT and thereafter every 6 months., according to International Guidelines for the Diagnosis and Management of HHT.
Discussion: The novel and unique clinical observation made on this case could have important implications for the interpretation of donors' comorbitidities and might convey generalizable insights about the practice of liver transplantation.

LB P-026

Evaluations for liver transplantation in patients with class II and III obesity

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Introduction: A higher proportion of patients with end-stage liver disease who require evaluation for liver transplantation are obese due to overall increased incidence of obesity.
Methods: This is a retrospective analysis of 633 consecutive patients who underwent evaluations for liver transplantation at a single center from 2011-2018. Data collected included demographics, indications for transplantation, length from start of evaluation to presentation at liver waitlist candidacy committee, and outcomes of

evaluations. We compared patients with BMI< 35 (non-obese or Class I obesity; group 1, n=499) to patients with BMI≥35 (Class II and III obesity; group 2, n=134).
Results: 21.2% of patients who presented for evaluation had Class II and III obesity; 7.3% had severe obesity. Average age was 56 vs 58 (group 1 vs group 2; p=0.25). The average BMI was 27.6 vs 29.2 (group 1 vs group 2; p< 0.05). The average weight was 81.8kg (42.6-133.8kg) in group 1 and 112.4kg (84.4-165.1kg) in group 2. The most common primary indication for liver transplantation was end-stage liver disease secondary to alcoholic cirrhosis in group 1 and hepatitis C cirrhosis in group 2. The average MELD was similar between the 2 groups. Group 2 patients took 29 days to complete the evaluation vs 20 days for Group 1 patients (p< 0.05). Almost all Group 2 patients met indications for workup of obstructive sleep apnea which required extra treatment by the pulmonology team. Similar percentages of patients in each group were listed for liver transplantation (73.5 vs 75.3%, group1 vs group 2) and eventually transplanted (42.7 vs 41.0%, group 1 vs group 2).
Conclusion: Evaluation of patients with Class II and III obesity for liver transplantation waiting list candidacy took an average 9 days longer than less obese patients. This did not affect the proportion of patients who were eventually listed and transplanted.

LB P-027

miR-142-3p regulates survival and function by regulating H3K27me3 demethylation through targeting KDM6A in induced regulatory T cells

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In vitro induced human regulatory T cells (iTregs) have in vivo therapeutic utility. MicroRNAs (miRNAs) are a family of approximately 22-nucleotide non-coding RNAs that are processed from longer precursors by the RNases Drosha and Dicer. miRNAs regulate post-transcriptional protein expression through mRNA destabilization or translational silencing; miR-142-3p regulates natural Treg (nTreg) function through autophagy. We hypothesized that this miRNA may also have an iTreg regulation function. Antagomir-mediated knockdown of miR-142-3p improved Foxp3 expression, regulatory function, cytokine expression, and apoptosis of iTregs in vitro, with or without inflammatory cytokine stimulation. miR-142-3p knockdown increased ATG 16L1-mediated autophagy. Target prediction and luciferase assay results indicated that miR-142-3p binds directly to KDM6A, which resulted in demethylation of H3K27me3 and in turn, upregulated expression of the anti-apoptotic protein Bcl-2. Based on these results, we propose a novel strategy that uses knockdown of miR-142-3p to enhance apoptotic ability and function of iTregs by increasing KDM6A and Bcl-2 expression. This approach might be used as a treatment to control established chronic immune-mediated autoimmune and inflammatory diseases.

LB P-028

The risk facotrs of mortality following liver transplantation in acute liver failure: Single center experience

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Background: Acute liver failure (ALF) is due to massive hepatocyte injury, coagulopathy and encephalopathy in an individual without prior history of liver disease. In irreversible damage, the liver transplantation (LT) is the only viable treatment. The aim of the present study is to evaluate and determine the factors related with mortality in patients that received LT in accordance with King's College criteria (KCC) for ALF in our institute.
Methods: Hundred and forty-eight patients with ALF that received LT according to KCC were included in the study. Ninety-day mortality and factors related with mortality such as age, gender, transplantation data and the etiology of ALF, severity of encephalopathy, laboratory data were retrospectively analyzed.
Results: In total 148 patients were analyzed (53% male, 53% pediatric). Ninety-day mortality was 34%. Preoperative bilirubin levels in survivors and non-survivors were 18±10 mg/dl and 23±12 mg/dl; respectively (p=0.03). The mortality rate of the patients with bilirubin levels above and below 20mg/dl were 38% and 30%; respectively. The mortality rate in patients with preoperative encephalopathy grade 4 (intubated) and grade2-3 were 56% and 28%; respectively (p=0.04). Postoperative persistent cerebral edema and reduced consciousness was an independent strong risk factor for mortality (%100 vs %19, p< 0.01). We found a significant difference in terms of mortality among female and male gender (%47 versus %21, p=0.001). In pediatric patients, mortality rates were similar among living donor and cadaveric donor transplantations (31% versus 27.8%, p=0.7). However, in adult patients with ALF cadaveric donor transplantations had significantly higher mortality rate than the living donor transplantations (52% versus 27.5%, p=0.046).
Conclusion: Grade 4 encephalopathy (need for intubation) was the preoperative parameter with strongest correlation with the postoperative mortality. Furthermore, female gender was also associated with significant mortality risk which may be related with higher body mass index in these patients.

LB P-029

Caudal repositioning of right hepatic vein anastomosis corrects severe outflow kinking in adult right lobe liver transplantation

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Background: Outflow obstruction after Right Lobe LDLT presents postoperatively with cholestasis and ascites. Wide anastomosis with triangulation of cavotomy prevents anastomotic narrowing. Torsion of large right lobes may occur in recipients with atrophic native liver and no ascites. We report severe outflow obstuction due to graft torsion recognised on intra op doppler and managed by graft reimplantation.
Methods: 56 year male with HBV related Childs B cirrhosis, 4.2 cm HCC (Left liver) portal hypertension, jaundice and GI bleed underwent living donor ABO Compatible right lobe transplant (graft weight 880 gm; GRWR 1.15). Vascular anastomosis were RHV to RHV, MHV +V8 connected to Y limb of cadaveric iliac artery to separate cavotomy, RPV to MPV and RHA to RHA. Post reperfusion Arterial patency was confirmed by opening the graft cystic artery.
Intraop doppler showed monophasic low volume flow in RHV and gradual dampening of RHA and PV flow with graft swelling. Repeat doppler (10 mins) after attempting graft repositioning showed no outflow,reduced inflow and thrombosis of RHA. The doppler suggested that the graft was rotating post reperfusion, the resultant torsion obstructing the outflow with sinusoidal congestion and artrerial thrombosis. Anastomoses were dismantled, graft removed and reflushed on back bench. RHV anastomosis was shifted caudally on IVC; the graft now lying without rotation. Long limb of Y graft (MHV +V8) to IVC, portal vein and arterial anastomosis were redone. Repeat doppler and postop (d1- d5) doppler showed normal inflow and outflow.
Conclusion: Although intra-op doppler is predominantly used for monitoring arterial anastomosis and portal flow, it may also detect outflow kinking. Prompt correction can prevent subsequent graft congestion, vascular thrombosis and graft loss.Caudal positioning of large right lobe graft can avoid RHV kinking that can occur despite a wide anastomosis.

LB P-030

Mixed venous and arterial patch: an option for the reconstruction of the hepatic veins in the domino liver transplant

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Domino liver transplantation is an accepted strategy to increase the pool of donors, implanting the liver of a patient affected by Amyloid Polyneuropathy to an elderly patient with a terminal liver disease. The most important technical peculiarity is obtaining a good outflow to avoid a budd-chiari syndrome. When carrying out the hepatectomy in the donor, the section of the hepatic veins to be short in length and since we must preserve the stump for the subsequent suture, is performed practically at the level of the entrance of the veins in the hepatic parenchyma. This flush section causes the hepatic veins to be independent and may cause a venous drainage obstruction.
To avoid this situation, different technical resources have been described, from a classical technique with vena-venous bypass resection and cava, to reconstruction with a vena cava vein patch, with an inverted Y-shaped iliac bifurcation, venous patches and reconstruction. with arterial patch.
We expose an alternative for the reconstruction of the outflow when we do not have the necessary graft for this type of reconstructions described. We present a case with a segment of short iliac vein and segment of common iliac artery with moderate atheromatosis as the only available grafts with which we made a new wide cuff that encompasses the area of the 3 ostiums of the hepatic veins and that we anastomose in bank surgery performing an end-to-end anastomosis on the anterior and posterior faces of the hepatic veins of the graft, thus ensuring the drainage.

LB P-031

Implementing a North American protocol of adult-to-adult Live Donor Liver Transplant (LDLT) program in Latin America. Our experience in Chile

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Introduction: Donation rates in Latin-America have been historically low. In Chile, it was only 6.6 donors per million during 2018. In order to decrease waitlist mortality, an adult-to-adult LDLT program was created in our center.
Methods: Initial experience was established in a high volume hepatobiliary and deceased donor liver transplant center, with the help of an experienced proctor from Brazil who guided the team through the first cases of adult-to-adult LDLT. Two years after beginning the process, we achieved the consolidation of a full-time surgical and medical team, including a surgeon and a hepatologist with formal LDLT training in North America. The new protocol was adapted from the University of Toronto and included: standardization of the surgical technique with hidrojet dissection, right lobe donation with middle hepatic vein preservation, pre-clamp infusion of iv heparin, use of volumetric software, having a dedicated live donor coordinator and weekly LDLT meetings.
Results: Between April 2016 and January 2019, a total of eleven adult-to-adult LDLT were performed. The last 5 cases were done after the implementation of the protocol. 90-day mortality was seen in 2/11 (18.2%), none of them after adaptation of the protocol. Postoperative complications of the recipient included 1 HAT, 1 PVT, 5 bilomas (one required reoperation) and 1 hospital-acquired pneumonia. All donors were discharged within 8 days. Two donors (18%) presented postoperative complications, both of them bilomas. Since the implementation of this protocol, there has been a significant increase in referrals, evaluations and LDLT cases per month.
Conclusion: Learning from high volume LDLT centers is extremely important to accelerate the personal and institutional learning-curve. Good LDLT results can be achieved by adapting a North American LDLT protocol in Latin America, by combining the hepatobiliary/transplant experience with specific LDLT training of some of the members of the team.

LB P-032

Cold ischemic hepatic preservation in rabbits after static conservation in a hypothermic solution based on powdered coconut water (ACP-405)

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Background: Preservation of the graft is crucial in the management of the transplant. There are many worrying points, but those of greater relevance are the reduction of cold ischemia time and the reduction of the reperfusion injury. Because of this, preservation solutions are extremely important. Surching for a solution that adds quality and a good cost-benefit relation is constant. The use of bio-based coconut water has become interesting because of a potential in the preservation of cells and its low cost. We analyzed hepatic morphological preservation in rabbits after static conservation in a hypothermic solution based on powdered coconut water (ACP-405).
Methods: We performed in situ hepatic perfusion of 10 rabbits, hepatectomy and tissue maintenance in hypothermic solutions SPS-1 (standard solution) and ACP-405 for up to 18 hours. Morphological evaluation of the degree of ischemic lesion was comparative at the predetermined times (T0-0h, T6-6h, T12-12h and T18-18h), performed blindly, evaluated as absent, mild, moderate and severe for each time.
Results: At the analysis of each time, the two solutions presented similar degree of injury. There was an increase in the overall score with the time progression of analysis in a similar way between the solutions. In all cases, there was not a statistically significant difference between the lesion grades when comparing the solutions evaluated by Mann-Whitney test and Friedman test (T0 - p 0.735; T6 - p 0.23; T12 - p 0.517; T18-0, 11).
Conclusion: After the histopathological evaluation at the determined times, it was concluded that the ACP-405 solution was similar to the SPS-1 solution in the hepatic morphological preservation during the period of cold ischemia. The suggestion of a natural, low-cost product is very promising and should be studied more deeply.

LB P-033

Characteristics of energy metabolism in patients with hepatocellular carcinoma on the basis of hepatitis B cirrhosis

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Methods: The subjects were patients with hepatitis B virus-associated cirrhosis (LC group) and patients with Hepatocellular carcinoma (HCC group) treated at the Beijing YouAn Hospital from January 2016 to June 2017.
Results:
1. Characteristics of energy metabolism in patients with HCC: normal metabolism (REE%, 95.58±19.65%) in patients with HCC. The oxidative energy supply of carbohydrates decreased, mainly by fat oxidation. As Child-Pugh grade gradually worsened, RQ showed a decrease in

HCC group (0.85±0.06 vs 0.82±0.07 vs 0.80±0.08), and CHO% showed a decrease (39(33-58)% vs 34(26.5-48)% vs28(21-49)%), while FAT% showed elevated performance (40(24-52%vs 41(29-59)% vs 55.5(34-70)%) .With the progress of tumor staging, the RQ and CHO% showed a decrease, while the FAT% showed an increase.
2. Comparison of energy metabolism between patients in HCC group and LC group: CHO% decreased (35.5(27-51)% vs 49 (31-62)%, P=0.013), FAT% increase (41(29-58)% vs 33(18-52)%, P=0.030).
3. Correlation analysis between liver function and energy metabolism: AST, GLOB, CHE, gamma-GT, AKP, TBA, TC were positively correlated with energy metabolism index, and CHE was positively correlated with RQ, CHO and CHO% (P< 0.05), negatively correlated with FAT, FAT% (P< 0.05), AKP was negatively correlated with RQ, CHO and CHO% (P< 0.05), and positively correlated with FAT, FAT% (P< 0.05). TBA was negatively correlated with RQ and CHO, and positively correlated with FAT (P< 0.05).Multivariate analysis showed that PA was an independent risk factor for RQ, CHO% and FAT%(P< 0.05).
Conclusion: The proportion of three major nutrients in patients with hepatocellular carcinoma was significantly imbalanced, the carbohydrate oxidative energy supply decreased, and the fat oxidative energy supply was the main source. The proportion imbalance of three major nutrients in patients with severe liver injury and advanced hepatocellular carcinoma was more obvious. CHE, AKP and TBA are related to energy metabolism. PA is an independent risk factor of RQ, CHO and FAT%.

LB P-034

Liver transplantation offers a therapeutic possibility to unresectable Klatskin tumors

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Katskin tumor (TK) or hilar cholangiocarcinoma is a tumor with a nefarious prognosis that as the only cure and most accepted treatment is radical hepatic resection (RH).
The majority present a stage advanced to the diagnosis where the possibility of carrying out a curative resection is scarce. Liver transplantation (TH) as a therapeutic indication for unresectable Klatskin is not clear due to the discrepancy of results in the published series.
Present results of TH in patients with unresectable Klatskin tumor non-disseminated and compare the results in patients with surgical resection (RQ) and in those where we chose palliative treatment (unresectable scattered and inoperable).
This is a retrospective study, with 124 patients diagnosed with KT from 1993 to April 2018.
20 were inoperable. Operable patients underwent exploratory laparotomy; in 62 HR was performed, 20 were classified as unresectable non-disseminated, opting for TH and 22 was unresectable disseminated susceptible to palliative treatment.
Survival was analyzed by the Kaplan-Meier method and the long-rank test.
In the TH group we obtained an overall survival (SPVG) at 1, 3 and 5 no differences compared to RT 79, 61 and 48% and 73%, 55% and 45% respectively. Disease free survival (DFS) 1, 3 and 5 was significantly higher than the group RT; 81, 74 and 47% vs. 73, 49 and 42% respectively.
Patients with unresectable tumor palliative treatments had a survival rate significantly lower than that of patients with unresectable tumors receiving TH (p < 0.001).
Some prognostic factors analyzed statistically significant were: Vascular invasion (p < 0.005). Advanced stages (p < 0.001). Perineural invasion (p < 0.001)
In conclusión patients with TK with unresectable not spread, the TH achieves similar to patients with RT, increased SLE SPVG and clearly improves the life expectancy of these patients with palliative treatments.

LB P-035

Liver transplant for ASIA syndrome. Recurrence after trasplant and inmunosuppression therapy

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Background: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) is frequently characterized by myalgias, myositis, arthralgia, neurological manifestations, fever, and cognitive alterations. In the range of clinical conditions related to ASIA syndrome, siliconosis after breast implants has been reported.
Method: We report a case of hepatic infiltration by silicone in a patient with ASIA syndrome. A 45-years-old woman with a 10-year-old mammary prosthesis and rupture of one side of the prosthesis four years ago. After 1 month of moderate abdominal pain in the right hypochondrium, hyperthermia, chronic fatigue, and myalgia, she was admitted to the hospital. Regarding laboratory findings, hepatic enzymes were elevated inluding bilirrubine (27 mg/dl). The viral infection panel and anti-smooth muscle antibody were negative. Liver transplant was needed because of a severe and

progressive liver failure. Patient was discharged afterr 12 days, inmunosupressed with tacrolimus and micophenolate. Histologic findings showed portal spaces expanded by the presence of silicone. There were also rare granulomas containing the foreign material.
Results: One year after transplant, micophenolate was discontinued, and, in two weeks, patient was adimited with a new ASIA syndrome with bilirrubine in 18 mg/dl. MNR and PET-CT scan showed a strong inflamatory disease in breast where prothesis was removed. Liver biopsy diagnosed macrofagic infiltration. Re-introduction of micophenolate in treatment resolved jaundice and symptoms was dissapeared.
Conclusion: ASIA syndrome should be part of the differential diagnosis of a patient with liver failure, nonspecific symptoms, a history of exposure to an adjuvant, and development of an autoimmune disease. Micophenolate could be important to avoid recurrence in liver graft. We present laboratory findings and imaging and histologic pictures of this patient.

LB P-036

Hemostatic balance in pediatric patients during and after liver transplantation

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Background: In adult patients with liver failure concurrent changes in both pro- and antihemostatic pathways occur, resulting in a rebalanced hemostatic system which can easily be tipped towards thrombosis or bleeding. Pediatric patients though, have a still maturing hemostatic system, different liver disease etiologies and higher incidences of thrombosis post-transplantation. The aim of this study was to assess the hemostatic balance in pediatric patients undergoing liver transplantation.
Methods: We collected serial blood samples from 20 pediatric patients (≤16 years) undergoing a primary liver transplantation in our center between September 2017 and October 2018. Samples were taken from the start of transplantation until post-operative day 30. Routine hemostasis tests, thrombomodulin-modified thrombin generation assays and clot lysis assays were performed and plasma levels of selected hemostatic proteins were measured. To determine reference values an age-matched control group of 20 healthy children was included.
Results: Thrombocytopenia was present in study patients. However, highly elevated levels of the platelet adhesive protein von Willebrand factor (VWF) and decreased levels of the VWF-regulating protein ADAMTS13 were present during and after transplantation, up until day 30. The prothrombin time and activated partial thromboplastin time were significantly prolonged during transplantation. In contrast, thrombin generation was intact in study patients at baseline, but decreased significantly during reperfusion. Post-transplantation thrombin generation capacity was reduced under continuous heparin administration. Although coagulation proteins and thrombin generation had largely normalized at day 30, fibrinogen levels were still substantially elevated. Clot lysis time was elevated at the start of surgery and at all post-operative time points.
Conclusion: Pediatric patients with end-stage liver disease are in a hemostatic balance. During transplantation a temporary hypocoagulable state is present, which rapidly converts to a hemostatic balance with clear hypercoagulable features that persist until day 30. These hypercoagulable features may contribute to the risk of post-transplant thrombosis.

LB P-037

Encouraging outcome of pediatric liver transplantation: a single-center experience

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Background: Liver transplantation (LT) has become the definitely curative therapyfor pediatric patients with end-stage liver diseases, acute liver failure and some metabolic diseases. Here, in this study, we aimed to explore the prognosis of children after LT.
Methods: The clinical data of 105 children who underwent LT in Huashan Hospital affiliated to Fudan University, School of Medicine from September 2014 to October 2018 were collected retrospectively. The baseline characteristics including age, height, weight, primary diseases, PELD score, graft source, graft weight and graft-to-recipient weight ratio(GRWR) were evaluated. Postoperative cumulative survival rate was estimated by the Kaplan- Meier method and all the complications were also analyzed.
Results: The cohort comprised 47 boys and 58 girls with a median age of 11.6 months, a median height of 70.6cm and a median weight of 8.5kg. Biliary atresia was the leading indication for LT, accounting for 50.5% (53 children). 77 patients received living donor grafts and the left 28 received deceased donor livers. No hepatic artery complications were developed during follow-up but 3 portal vein complications and 1 outflow tract complications were observed. Compared to the vascular complication, the rate of

biliary complication was relatively higher (7.6%, 4 bile leakage and 4 anastomotic stricture). 1 patient suffered from PTLD. By the end of the follow-up, 9 children died and the 1-year and 3-year cumulative survival rates were both 90.6%.
Conclusion: In our center, the overall outcomes of pediatric LT are promising. Most patients can regain an healthy life after LT.

LB P-038

Texture analysis features in prediction of HCC grade at explant

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Background: Histologic grade of Hepatocellular Carcinoma is one of the most important predictors of recurrence following liver transplantation. Radiologic estimation of tumor grade has been evaluated through differenet conventional imaging modalitites in several studies. Recently, texture analysis (TA) has been introduced which is a pixel based computer aided analaysis of radiologic images. Is has been seccueefully implemented specialy in oncology field for evaluation of tumor biology.
In this retrospective study we aimed to evaluate the efficacy of TA features in prediction of HCC at explant.
Materials and methods: Sixty three histopathologically proven HCC lesions were registerde. All patients were examined by a 16-slice multidetector computed tomography scanner (Siemens Somatom Sensation 16, Erlangen, Germany). TA was performed on arterial phase contrast enhanced CT images by MaZda software version 4.6 (Technical University of Lodz, Institute of Electronics).
Results: HCC lesions with Edmonson histopathologic grade of I or II were classified as low, and grade III or IV were classified as high grade lesions. Features under 3 sigma normalisation scheme through Fisher test yielded high performance in classifiying low and high grade HCCs specially for Gray Level Co-ocurrence Matrix (GLCM) features.
Conclusion: Texture analysis features specially Gray Level Co-occurrence Matrix (GLCM) are able to predict HCC grade prior to liver transplantation which facilitates selection of cases at higher risk of tumor recurrence after liver transplantation.

LB P-039

Single center experience with biodegradable stents in treatment of refractory biliary strictures after living donor liver transplantation

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Introduction: Biliary anastomotic stricture is the most common biliary complication following living donor liver transplantation (LDLT). Endoscopic treatment may be challenging in LDLT recipients due to the complex nature of the duct-to-duct reconstruction. In such situations, percutaneous transhepatic treatment may be an important alternative. Multiple sessions of balloon dilation, and serial exchanges of biliary drainage catheters may be required to achieve satisfactory clinical results.
Biodegradable biliary stents (BBSs) may provide the beneficial effects of stenting while avoiding the issues related to subsequent removal.
We aimed to present our experience with BBSs in treatment of post-LT benign biliary strictures refractory to standard bilioplasty.
Material and methods: Two patients with symptomatic benign biliary strictures after LT treated with biodegradable Ella (ELLACS, Hradec Králové, Czech Republic) biliary stents were included. In both patients, stricture after repeated balloon dilation was observed. For each patient, 2 stents were placed.
Results: No peri-procedural complications related to the stent were observed. Mean follow up period was 12 months. The follow up ultrasound findings and blood tests were unremarkable. No stent migration or major complications such as biliary leakage, cholangitis, pancreatitis and gastrointestinal bleeding occurred during the procedures and follow up.
Conclussion: Percutaneous implantation of a BBS provides a safe and effective treatment alternative not just in refractory cases, but also can be implemented as first line choice to avoid long term routine treatment discomfort.

LB P-040

Contrast-enhanced ultrasound for the evaluation of hepatic artery occlusion after liver transplantation

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Introduction: Vascular complications after liver transplantation is a major threat to the survival of recipients.HAT is a major cause of graft loss and patient mortality, with an incidence between 3% to 8% in transplant recipients. Early detection of HAT is critical because urgent revascularization is required to avoid severe graft loss. Ultrasound is the preferred first-line imaging modality in patients with suspected HAT, the accuracy and positive predictive value of Doppler US is low and requires a high level of operator skill.Contrast-enhanced ultrasound (CEUS) provides real-time angiographic-like images of vessels at bed side and allowing the accurate diagnosis of hepatic artery thrombosis. The aim of this study was to evaluate the efficacy of CEUS in detecting HAT after liver transplantation.
Materials and methods: This is a retrospective data of Liver transplantation patients in the Osmania General Hospital, Hyderabad between 2016 to 2018. Status of hepatic vascular assessment following liver transplantation done by conventional Doppler Ultra sonography and Contrast Enhanced Ultrasonography.
Results: 23 cases of post Liver transplantation aged between 4years and 58 years, with a median age of 30 years. There were 20 males and 3 females. 14 underwent DDLT, 7 were LDLT, 1 was split Liver transplantation and 1 was Auto liver transplantation. Doppler US was inconclusive regarding patency of the hepatic artery (HA) circulation in 5 (21.7 %) of 23 patients. CEUS was done in these 5 patients and detected HA thrombosis (HAT) in 2 cases and patent HA in 3 transplants.These 5 were confirmed by CT Angiography / conventional Angiography. The sensitivity, specificity of CEUS were 100%.
Conclusion: CEUS is a fast, non-ionizing imaging modality for the initial exclusion of vascular complications after liver transplantation. It can be performed at the bedside in the ICU and operation theater. It is safe will not cause any nephro toxicity and Radiation.

LB P-041

Liver transplant for heart failure in patient with Rendu-Osler-Weber syndrome. Technical problems

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Background: Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome) is a rare disease characterized by the presence of arteriovenous malformations. Hepatic involvement can lead to life-threatening conditions, and liver transplant is a good therapeutic option for these patients.
Method: A 62-year-old woman diagnosed with hereditary hemorrhagic telangiectasia presented with a severe heart failure. The initial study revealed high-flow heart failure, secondary to the presence of multiple intrahepatic arteriovenous fistulas. Echocardiogram showed moderate dilatation in the atria and right ventricle, dilatation and eccentric hypertrophy of the left ventricle, and a cardiac output of 7.1 l / min. Pulmonary hypertension was not evident. Management of heart failure was performed with sildenafil and bevacizumab, without clinical response, so it was decided liver transplantation.
Results: During liver transplantation, a liver with abundant arteriovenous fistulas and a large diameter (12 mm) of hepatic artery were found, performing arterial revascularization through the patient hepatic artery left branch. The postoperative course was without complications and heart failure resolved in a few days.
Conclusion: In Rendu-Osler-Weber syndrome, successful liver transplantation has been reported in cases of liver failure, extended biliary necrosis, and cardiac failure, all related to intrahepatic AV shunts. Enlarged hepatic artery diameters are present in all the patients, and can complicate arterial anastomoses. Right branch of hepatic artery coul be a solution for this technical problem.We present radiological, histologic and surgical images.

LB P-042

Is the body mass index a risk factor in the liver transplant recipients?

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Introduction: Obesity is a growing global epidemic and one of the leading causes of death. The prevalence of obesity in the candidates for liver transplantation (OLT) is increasing, and therefore it is necessary to analyze if it is a risk factor for morbidity and mortality after OLT.
Methods: Retrospective cohort study of all recipients transplanted at the Virgen del Rocío University Hospital in the years 2006-2016. The variables of the donor have been analyzed: age, sex, weight, BMI, cause of death; receiver variables: age, sex, weight, height, BMI, MELD score, CHILD score, indication; and as outcome variables: postoperative complications, early mortality, graft loss and overall survival.
Results: We analyzed the results of 669 of the 707 OLT performed between 2006-2016. These were grouped by BMI categories: 219 (31%) normal, 266 (37.6%) overweight, 184 (26%) obesity. Overall survival at 5 years was: 81.6% in the normal group, 73.6% in the overweight group and 66% in the obese group, these differences being statistically significant (p = 0.011). Early mortality was 4.1% in the normal group, 6% overweight and 6% obese. No differences were found between groups regarding postoperative complications: hemorrhagic, vascular, biliary, respiratory, hemodynamic, digestive, renal, neurological, rebel ascites and infections. No differences were found regarding the need for reinterventions.
Conclusions: In our group, the overall survival in the OLT decreases as the receiver´s BMI increases; but overweight and obesity do not constitute a risk factor for early morbidity and mortality in OLT.

LB P-043

Portal vein thrombosis and liver transplantation: How far should we go?

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Background: Portal vein thrombosis (PVT) complicates the procedure of liver transplantation (LT) and is considered as relative contraindication with poor survival outcomes. The aim of this study is to evaluate the impact of PVT on short and long-term outcomes in patients undergoing LT.
Methods: Data of 582 consecutive adult patients including 66 with PVT who underwent LT between 2010 and 2017 were analysed from a prospectively maintained database. Patients were divided into complete PVT (CPVT: Yerdel grades II, III and IV n=27), partial PVT (PPVT: Yerdel grade I, n=39) and no PVT (NPVT, n=516). The three groups (CPVT, PPVT, and NPVT) were compared, univariate and multivariate analyses were performed.
Results: There were no differences regarding preoperative data. Operative data showed increased blood loss (ml) in the CPVT group compared to the other two groups (2735, 1475 and 1000, p< 0,001). In the post-transplant course, patients from the CVPT group had higher 90-day mortality (44%, 8% and 5%, p< 0.001) and higher rates of major complications (74%, 41% and 42%, respectively, p=0.004) than those of other groups. Actuarial 3-yr patient survival (PS) and graft survival (GS) rates in the CPVT group compared to PPVT and NPVT was significantly lower (PS: 33%, 79% and 85%, p< 0.001) and (GS: 33%, 76% and 80%, p< 0.001), respectively. After adjusting covariates by multivariate analyses, only CPVT was identified as an independent prognostic factor for poor PS and GS (both, p< 0.001).
Conclusion: In this study, CPVT negatively impacted PS and GS, while PPVT showed similar outcomes compared with NPVT. Further studies are necessary to determine better selection criteria for CPVT patients in order to avoid futile LT.

LB P-044

Primary Graft Non-function in liver transplantation (PNF): Can we predict? A single centre experience

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Background: Primary non-function (PNF) after liver transplantation is a lethal condition requiring immediate re-transplantation. The precise cause is not well known yet. The aim of this study is to determine the incidence of PNF in our liver transplant recipients, potential risk factors and outcome.
Patients and Methods: 248 adult liver transplant recipients from 2014 till 2017 at our Transplant Unit were included. Five patients (2%) had PNF. Donor and graft variables studied including age, height, BMI, Serum Sodium, cold and warm ischemia times, operative time, graft type (Donation after Brainstem Death DBD / Donation after Circulatory Death DCD) and liver biopsy of the graft. Recipients variables including primary liver disease, UKELD score, post transplant biochemistry, potential risk factors including dialysis, inotropes, mechanical ventilation and pre-transplant portal vein thrombosis (PVT), hospital and Intensive Care Unit (ICU) stay and patient survival.
Results: No significant differences were noted in recipient variables between both groups to account for PNF. Donor and graft variables were not significantly different either except for CIT which was significantly longer in PNF group (p=0.003) and notably, all donors in PNF groups were DCD donors. Post transplant laboratory values were strikingly worse clearly indicating an early more pronounced impairment of both liver and kidney functions in the PNF group. Creatinine (umol/l) Day 1, Day 3, Day 5 and Bilirubin Day 5 were significantly different (P values 0.021, 0.020, 0.017 and 0.012 respectively). Hospital and ICU stays were longer in PNF group, with ICU stay significantly longer with median of 7 days versus 2 days for the No-PNF (P value 0.005). We had only one death (20%) in the PNF group.
Conclusion: Main risk factors for PNF were CIT and DCD grafts. Early and worsening hepatic and renal impairments are ominous signs of PNF with still good outcome after early re-transplant.

LB P-045

Simultaneous liver kidney transplantation from brain death and living donor :early experience in 2 cases

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Introduction: Simultaneous liver kidney transplantation (SLK) remains to be the ideal treatment option for patients with decompensated cirrhosis and end-stage renal disease (ESRD) as the reported survival is similar to liver transplant alone recipients without renal dysfunction. After Liver transplantation alone, hepatorenal syndrome can be recovered, whereas chronic kidney disease may be worsened because of perioperative events and calcineurin inhibitor toxicity. Difficult to predict kidney recovery after liver transplantation, indications for SLK are not precisely defined. The parameters for optimal stratification of these transplant candidates remain unclear.
We introduce out early experience of SLK which is performed in small center.
Methods: We did first SLK first liver and kidney from brain death donor at 2014.07.29. Second one was kidney first and liver from living donor at 2018.05.26.
Results: We have two SLK experiences, one SLK from brain death donor, the other son donated liver and spouse donated kidney. All candidates have diabetes mellitus end stage renal disease with peritoneal dialysis for years. One have alcoholic induced liver cirrhosis with hepatic encephalopathy, the other have chronic hepatitis B with liver cirrhosis. Patient donated from brain death organs received liver transplant first and kidney transplant. Who had living donor organs received kidney transplant first and liver transplantation.
All patients recovered well with normal liver function and kidney function after transplant and discharged well.
Conclusion: We had performed 2 cases of SLK who had DM CKD and liver cirrhosis. SLK could be the good treatment option for patients with ESLD and ESRD.

LB P-046

Use of steatotic donor livers for transplantation: Do they affect outcome?

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Background: The exact effect of donor steatosis on post-transplant outcome is not well established. The aims of this study are to evaluate the effect of different grades of cadaveric donor liver steatosis on recipient outcome and to validate the performance of Model of Early Allograft function (MEAF) score in conjunction with donor graft steatosis.
Patients and methods: Adult recipients of 228 livers transplanted between 2014 and 2017 were studied. Livers were divided into three groups according to the grade of histologically determined steatosis; S0: no steatosis (n=162), S1: minimal-mild steatosis < 33% (n=62), S2: moderate and severe steatosis 33%-66% and >66% (n=14). Donor data were analysed. The outcomes of transplant were evaluated including liver and renal function, acute rejection, length of ICU and total hospital stay, and 30 days and 6 months mortality.
Results: Moderate or severe steatosis grade (S2) was associated with older donors (medians of 48, 53 and 60 respectively, p=0.01) and a higher donor BMI (medians of 24.8, 28 and 29.1 , p< 0.001). Postoperative laboratory values displayed higher ALT level in S2, PT and Creatinine were significantly higher in S2 group 14, 15.1 and 19.5 sec (P 0.040) and 85, 96.6 and 112.1 (P 0.018). The incidence of EAD did not differ significantly among groups (P 0.494) despite being higher in S2 group 4/14 (28.57%) but with no concomitant PNFs. No acute rejection episodes in S2 group. The median length of hospital stay was similar, but S0 group had a significant shorter median ICU stay of 2 days after transplantation (0.017). Neither 30 days nor 6 months mortality differed significantly between the three groups.
Conclusion: Steatosis was associated with older, more obese donors, but did not adversely affect the postoperative outcomes after liver transplantation. Steatotic graft recipients had more renal impairment and longer ICU stay.

LB P-047

Post liver transplant bony aspergillosis

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Background: Bony aspergillosis post liver transplant is a rare infective complication.
Method: A 47 year old patient underwent living donor liver transplantation for decompensated alcoholic liver cirrhosis in our hospital . His post operative recovery was uncomplicated and he was discharged on 19th day post transplant. Histology of the explanted liver showed evidence of cirrhosis and there was no evidence of malignancy in the liver. Patient was discharged on Tacrolimus, Mycophenolate and tapering dose of prednisolone. The patient went back to his country (Iraq) and had regular follow ups with the gastroenterologist in his country. The prednisolone was stopped 2 months post transplant. Mycophenolate was stopped 6 months post transplant.
Result: During follow up his liver function (LFT) tests remained normal and he was asymptomatic. Seven months post transplant , the patient had severe low back pain. An MRI done in Iraq showed evidence of a destructive lesion in his lumbar vertebra. He came to our hospital for further investigations. A PET-CT scan revealed a hypermetabolic destructive lesion in L2 vertebral body as well as lytic lesions in the lateral aspects of the right clavicle and right 8th rib. A biopsy was carried out from the soft tissue mass around the lytic lesion in the right rib. The biopsy revealed a non caeseating granulomatous inflammatory lesion. The culture of the tissue grew Aspergillus fumigatus. The patient was treated with liposomal Amphotericin B for two weeks and with oral voriconazole for 6 months. The patient became asymptomatic after one month of treatment. The patient remains asymptomatic 20 months after initiating treatment. An MRI scan done 18 months since the diagnosis of Aspergillous osteomyelitis has not shown any recurrence of disease
Conclusion: Although rare bony aspergillosis following liver transplant can be treated with a long course of appropriate antifungal a

LB P-048

Denovo hepatocellular cancer in a liver graft following living donor liver transplant

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Background: Denovo hepatellular cancer (HCC) in a patient following liver transplant is very rare. Usually denovo HCC is associated with recurrence of HBV and HCV in the graft leading to cirrhosis.
We describe a case of development of denovo HCC following right lobe liver transplant.
Method: Case report of a 47 year old male patient underwent an uncomplicated living donor liver transplant for decompensated cirrhosis due to alcoholic liver disease using right lobe graft without middle hepatic vein. The patient had an uncomplicated recovery. Patient was discharged in 3 weeks. Immunosuppression - Tacrolimus, Steroid and Mycophenolate(MMF). Steroid stopped after 3 months and MMF after 6 months. Patient continued on Tacrolimus monothearpy.
Result: Two and half years following liver transplant the patient developed severe back pain and hemoptysis. Graft function was normal.
Result: MRI scan showed multiple bony lesions. He underwent biopsy of thoracic vertebral lesion. Histopathology showed a poorly differentiated adenocarcinoma. Immunohistochemistry showed tumour expressing Cytokeratin, EMA, CK-20 & CK- 7 and were immunonegative for CDX2, TTF-1, Napsin A, CA19.9, CD30, LCA, HMB 45 and Melan A, glypican and PLAP.
PET CT scan showed heterogenous moderate to high grade activity in multiple nodular lesions in both lungs and in bony lesions.
Tumour marker - Alfa fetoprotein was raised to 1544, CEA, Ca19-9 were normal..On the basis of histology and raised AFP levels diagnosis of metastatic HCC arising from the graft was made.
Patient was treated with localized radiation to the spine for pain control and Sorafanib was started.
Patient is alive after 5 months since diagnosis of the malignancy.
This reported case is unique as there was no predisposing factor for de novo HCC.
Conclusion: Denovo HCC in liver graft is rare. It may develop in the graft without HCV or HBV infection and without changes of cirrhosis.

LB P-049

Risk factor for initial poor graft function in deceased donor liver transplantation

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Background: Aim of this study is to identify factors predictive of early postoperative poor graft function.
Methods: We retrospectively collected the medical records of 82 adult patients who underwent orthotopic liver transplantation (OLT) form Dec 2009 to Dec 2018. IPF was defined using Nanashima´s classification: (1) ALT and/or AST levels above 1500 IU/L within 72 hours after OLT. Those with values below 1500 IU/L were assigned to the non-IPF group.
Results: IPF occurred in 22 recipients (26.8%) and non-IPF in the other 60 (73.2%). Univariate analysis revealed that recipients' gender, CTP score, MELD score, preoperative ventilator use, preoperative renal replacement use, preoperative vasopressor use, and primary liver disease were not associated with IPF. Only donor age (>60 years) and graft fatty change (>30%) was risk factor for IPF group in univariate analysis.
In operation related factor, there was no significant difference in total operation time, warm ischemic time, and RBC transfusion between the IPF group and the non-IPF group. But, there was significant difference in warm ischemic time between the IPF and non-IPF group (41.1min vs 64.5min, p=0.04)
Logistic regression were performed for parameter with univariate analysis result p< 0.05 (donor age >60 years, graft fatty change >30%, and warm ischemic time > 42min). But, multivariate analysis revealed there was no significant difference between the IPF and non-IPF group.
Conclusions: The results of this study suggested old age donor, moderate or severe steatosis, and longer hepatic warm ischemia times are potential risk factors for initial poor graft function.

LB P-050

Direct-antiviral agents (DAA) treatment in HCV liver transplant candidates with end-stage liver disease: correlation between clinical-virological changes and histopathological features

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Background: Viral eradication by direct antiviral agents (DAAs) before liver transplant (LT) in HCV-LT candidates prevents graft reinfection and might lead to delisting in those with improved clinical scores.
Aim: To evaluate the impact of DAA on clinical and histopathological features at the time of transplant.
Materials and methods: From January 2014 to December 2018 all consecutive HCV transplanted patients were studied. MELD and Child´s scores were evaluated before DAA and at transplant time; native livers were analyzed for necroinflammation/fibrosis by Ishak/Metavir scores, Laennec classification of cirrhosis, degree of sinusoidal fibrosis and collagen proportionate area (CPA).
Results: 94 LT candidates were transplanted (82% males, 57 years, 70% HCCs); 69 (71%) DAA-treated (median=20 weeks) with a SVR rates=98% and 25 untreated (HCV-RNA at LT= 56822 UI/mL). MELD and Child's scores at transplant were significantly higher in untreated patients compared with treated ones (15 vs 11: p=0.0008; 10 vs 7: p=0.001, respectively). At explant pathology, 96% of the LT recipients showed features of cirrhosis (F4-A=13%, F4-B=66%, F4-C=17%) with a median CPA value of 20% (range 6-40%). A significant correlation was found between CPA value, Laennec stage (p< 0.0001), Child-Pugh (p< 0.0001) and MELD (p=0.0003) scores but at the explant pathology the proportion of Laennec stages and CPA values were similar in DAA-treated and untreated LT-recipients. However, untreated LT-recipients showed both higher necroinflammation scores (p< 0.0001) and degree of sinusoidal fibrosis (p=0.001) compared to treated ones. Interestingly, by splitting the DAA-treated patients according to the time lag between treatment and transplant, the group of 27 patients treated ≥24 weeks before LT showed a significantly lower CPA values (p=0.012), necro-inflammation (p< 0.0001) and sinusoidal fibrosis (p=0.002) at the explant compared to those untreated.
Conclusions: The correlation between clinical scores and explant pathology findings of our cohort of HCV-LT candidates confirms a DAA-induced, time-dependent benefit of viral suppression in this setting.

LB P-051

Diamond-shaped patch technique for right hepatic vein reconstruction in living-donor liver transplant: A simple method to prevent stenosis.

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Patency of the right hepatic vein (RHV) of the liver graft is essential for successful living-donor liver transplant (LDLT). We developed a simple technique for RHV reconstruction that does not require the use of cadaveric veins or additional time to prevent stenosis. Of 159 patients who underwent LDLT at our institution between May 2010 and April 2016, we included 152 in this study. Conventional RHV reconstruction was performed in 100 patients, while the diamond-shaped patch (D-patch) technique was performed in 53. For the D-patch technique, the posterior aspect of the RHV needs to be dissected from the liver parenchyma during donor hepatectomy, which prevents stenosis due to liver rotation after graft regeneration. A D-patch obtained from the hepatic vein of the recipient liver was used on the anterior aspect of the RHV for reconstruction. The Student´s t test and χ test were used for statistical analysis.Rates of intervention for RHV stenosis during the first month were significantly different between the conventional reconstruction and D-patch groups (19.2% vs 3.8%; P=.01). The time taken to perform the D-patch technique was similar to that for conventional reconstruction (anhepatic period, 104.9±47.3minutes vs 106.7±42.0minutes; P=.82).The D-patch technique for RHV reconstruction in LDLT is a simple, fast, and feasible surgical technique that can be performed without using cadaveric or saphenous veins.

LB P-052

Monitoring phosphorylation of p70S6K to assess the efficacy of mammalian target of rapamycin inhibitors in liver transplant patients

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Background: The activity of p70S6 kinase located downstream of the mammalian target of rapamycin (mTOR) pathway is sensitive to mTOR inhibitors. However, the methods of assessing p70S6 kinase activity are still unclear. This study aimed to investigate p70S6 kinase activity in CD4-positive cells of liver transplant patients.
Methods : Liver transplant patients treated with mTOR inhibitors were recruited from Beijing Chaoyang Hospital between October 2016 and October 2018. The influence of mycophenolic acid (MPA) derivatives and prednisone on p70S6 kinase phosphorylation in CD4-positive cells was examined in liver transplant patients and healthy controls (HCs). The phosphorylation of p70S6K in CD4 + CD25hi regulatory T cells (Treg cells) and CD4 + CD25- T effector cells was analyzed by phospho-flow cytometry.
Results: The phospho-flow technique detected a significant loss of p70S6 kinase phosphorylation in CD4-positive cells of patients treated with mTOR inhibitors compared with HCs. MPA derivatives and prednisone did not affect p70S6 kinase phosphorylation significantly. No significant difference in p70S6 kinase phosphorylation was observed when the whole blood was stored within 3 h at room temperature. The phosphorylation of p70S6K was significantly lower in CD4 + CD25hi Treg cells than in CD4 + CD25-T effector cells in HCs. After liver transplant patients were treated with mTOR inhibitors, p70S6K phosphorylation was more reduced in CD4 + CD25-T effector cells than in CD4 + CD25hi Treg cells.
Conclusions: This study confirmed the stability and feasibility of phospho-flow cytometry. The phosphorylation of p70S6 kinase in CD4-positive cells reduced in liver transplant patients treated with mTOR inhibitors.

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LB eP-001

Vascular jump graft from superior mesenteric vein for inflow in living donor liver transplantation

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Complete portal vein occlusion poses a challenge for inflow in liver transplantation. More so in living donor liver transplantation. Extensive collaterals pose difficulty during recipient Hepatectomy. Superior mesenteric vein(SMV) jump graft is an option which tends to be a long course. Options are limited. Presenting a video of a liver transplantation recipient to whom the vascular access as a substitute was gained through a jump graft from the SMV. The left lobe graft was transplanted. Good inflow was noted. Patient initially behaved as a small for size graft recipient although over a course of 32 days recovered. Challenging yet technically feasible. Careful selection is required in dealing with portal vein thrombosis patients for living donor liver transplantation.

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LB eP-002

Hot hydrodissection in a case of redo liver transplantation surgical video presentation

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Surgeons may hesitate about approaching to transplantated liver graft due to increased risk of bleeding and difficulty to achieve proper exposure, because of prominent fibrotic tissue around the previous graft. In these cases, each adhesive layer must be clearly identified to achieve optimal exposure. In the literature, normal saline hydrodissection procedures have been utilized to separete various anatomic planes to reduce tissue injury.
In this video we will present an Indian male patient with history of living donor liver transplantation (LDLT). Six years after, he was referred to our institution for liver retransplantation. After abdominal wall incision, prominent-dense fibrotic adhesions and venous collaterals around the prior liver graft were found. The adhesiolysis around the graft with hot water and scissor was performed to expose the graft, than recipient hepatectomy was performed. Operation was successful without any complication such as intestinal or vascular injury.
In conclusion, we believe that, using gentle manual hot hydrodissection to seperate graft from extended surrounding adhesions from the previous surgery, provides reduced tissue damage, risk of hemorrhage and results in good exposure.

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LB eP-003

Do we need patent native IVC for LDLT? Transdiaphragmatic dacron graft replacement leaving native thrombosed IVC in LDLT, surgical video presentation

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We present our method of replacement of transdiaphragmatic venous graft in right lobe adult living donor liver transplantation (LDLT) with total inferior vena cava (IVC) thrombosis due to prior inappropriate placement of TIPS stent.
Our case is a 49-year-old female patient with TIPS. Pre-transplant imaging examination with IV contrast-enhanced CT revealed total thrombosis of both suprarenal IVC and TIPS stent which was propagated to right atrium. There was also dilated azygos and retroperitoneal-paravertebral varices draining lower extremities. During the surgery, thrombosis of IVC was confirmed till its junction with the right atrium. According to team concensus, a Dacron venous graft was positioned between right hepatic vein and right atrium via transdiaphragmatic approach without sternotomy, leaving the native IVC intact. The portal vein, hepatic artery, and bile duct were anastomosed in standard fashion. Intra-operative Doppler-US showed patent graft lumen and cavo-atrial anastomosis. Operation was successful without any complication.
The placement of the IVC in LDLT is technically challenging. In case of removal of the native IVC, the diaphragm and pericaricardium should be opened after sternotomy to expose the IVC opening into the right atrium. In this video we will present our safe, simple, and time saving technique in details. We also discuss preoperative and postoperative radiologic images of this case.

LB eP-004

Importance of small hepatic vein drainage (≤3 mm) to prevent small for size syndrome surgical video presentation

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In this video, we will present our approach of anterior complex venous drainage in a living donor liver transplantation (LDLT) case with limited donor graft volume for recipient weight (≤0.6). Pre-transplant imaging examination of donor liver with IV contrast enhanced CT revealed two and three venules draining into middle hepatic vein (MHV) smaller than 3 mm in segment 8 and 5, respectively. Drainage of these small hepatic venules is importat to increase graft size.
The donor hepatectomy was performed without the MHV to increase donor remnant liver volume. We decided to preserve each small venule of anterior sector to increase recipient graft volume to avoid small for size syndrome. We provided good exposure of anterior sector dranaige with meticulous dissection, so segment 8 and 5 small venules could be seperated from MHV. Then, vascular clamp test was performed for each venule to show parenchymal congestion. After the donor hepatectomy, all small venules of anterior sector were conjoined to form on single outflow tract, which was reconstructed with a Dacron graft at the back table. This Dacron graft was anostomosed with the recipient inferior vena cava to provide effective anterior sector venous drainage. We also present preoperative and postoperative radiologic images of this case.

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