OS007 PRELIMINARY RESULTS ON IMPACT OF DIFFERENT MACHINE PERFUSION STRATEGIES ON EARLY RENAL FUNCTION IN A PORCINE DCD AUTO-TRANSPLANT MODEL

Tom Darius[1], Pierre Gianello[2], Antoine Buemi[1], Luc De Pauw[1], Martine De Meyer[1], Michel Mourad[1]

[1]Cliniques Universitaires Saint Luc, Belgium; [2]Cliniques Universitaires Saint Luc, Université Catholique De Louvain, Institut De Recherche Expérimentale Et Clinique, Belgium

Background: Hypothermic machine perfusion (HMP) and end ischemic *ex vivo* normothermic perfusion (EVNP) have demonstrated improved early graft function compared to static cold storage (SCS). The aim of our study was to evaluate the impact of several machine perfusion variables on early graft function.
Methods: A porcine auto-transplant model was used. The left kidney of female Landrace pig (35–40 kg) was exposed to 30 min of warm ischemia by vascular clamping and preserved by 1 of the 6 study groups: 1) 22 hrs SCS, 2) 22 hrs HMP, 3) 22 hrs oxygenated HMP, 4) 20 hrs HMP + 2 hrs EVNP, 5) 20 hrs SCS + 2 hrs oxygenated HMP, and 6) 20 hrs SCS + 2 hrs EVNP. The LifePort Kidney Transporter® (Organ Recovery Systems) was used for all machine perfusion strategies. The left kidney was auto-transplanted in a right orthotopic position. The primary endpoints were kidney function and graft survival at 2 weeks.
Results: 34 auto-transplants were performed (minimum 5 pigs per study group). Peak serum creatinine at day 3 after transplantation was significantly lower both in the 22 hrs oxygenated ($p = 0.0025$) and non-oxygenated HMP ($p = 0.0134$) group compared to the other study groups. There was no significant difference between 22 hrs oxygenated and non-oxygenated HMP groups ($p = 0.7480$). Use of delayed machine perfusion strategies, oxygenated HMP as well as EVNP, yielded higher serum creatinine peaks compared to continuous HMP strategies. Renal function at 1 week and 13 days was comparable between all groups. EVNP provided the highest renal blood flow compared to other machine perfusion groups. No difference was found in perfusate biomarkers (AST, LDH, glucose) between machine perfusion groups.
Conclusion: HMP strategies only when applied from time of kidney procurement until transplantation until transplantation and irrespective of supplemental oxygenation, led to a positive effect on early graft function. End ischemic EVNP contributed to higher renal blood flow, but did not affect early graft function.

OS008 *EX VIVO* NORMOTHERMIC RENAL HEMO-PERFUSION: A FUNCTIONAL EXPLORATION OF PERFUSION, FILTRATION, TRANSPORT AND RESPIRATORY PERFORMANCES OF PIG KIDNEYS AFTER SHORT-TERM COLD-STORAGE

Jacques Kaminski[1], Ludovic Mercier[1], Arjan Van Der Plaats[2], Rutger Ploeg[3], Thomas Minor[4], Henri Leuvenink[5], Thierry Hauet[1], Patrick Hannaert[1]

[1]Irtomit, Inserm Umr 1082, Chu De La Milétrie, Poitiers, France; [2]Organ Assist Bv, Groningen, The Netherlands; [3]Department of Surgery, Nuffield Department of Surgical Science, University of Oxford, United Kingdom; [4]Department For Surgical Research/General Surgery, University Hospital Essen, Germany; [5] Department of Surgery, University Medical Center, University of Groningen, The Netherlands

Background: To preserve or recondition lower quality organs, *ex vivo* normothermic perfusion (EVNP) gains interest, but mechanisms are unclear and experimentals show strong heterogeneity. We explore the functional status of cold-stored kidneys next submitted to 2 h-EVNP with Krebs-Henseleit (KH) vs. plain whole-blood (WB). To reduce the use of animals, we use Pig kidneys from transplantation studies and WB from end-protocol controls.
Methods/Material: Kidneys flushed and cold-stored (SCOT15®; 3 h); WB were cold-stored in CPDA-1 bags. The kidney was mounted for perfusion flow (PEF mL/(min/g)) and urine production (UP, μL/(min.g)) monitoring, at constant 80 mmHg pressure (PP); renal resistance RR = PP/PEF. Perfusion media were equilibrated with 95%O2/5%CO2 (KH, 60% BSA). Na fractional reabsorption (FRN) was calculated from glomerular filtration rate (GFR; μL/(min.g) = creatinine clearance), Na transport (μmol/(min.g)) and excretion (μmol/(min.g)); av-QO2 consumption (QO2, μmol/(min.g)) was calculated from PEF and arterial and venous O2 levels. Results given as mean ± SD(*n*).
Results: (Hep = Heparin): 1) KH-BSA yields the highest PEF and QO2, but low GFR and UP, and insignificant Na reabsorption and TNa/QO2 (a measure of transport efficiency). 2) When perfusing with WB-250 UI/l Hep, PEF decreases, but GFR, TNa, FRN and UP increase; conversely, QO2 is reduced (TNa/QO2 increased). 3) Increasing Hep to 5000 IU/l, PEF remains similar, but GFR, UP, TNa, FRN, and transport efficiency strongly increase (2–6 fold).
Conclusion: EVNP optimal conditions remain to be established. Using a Pig preclinical model of static cold storage, we show a strong decoupling between (high) perfusion (high) and function (very low) with KH-BSA, which thus appears unsuitable for renal function. Conversely, properly heparinized whole-blood yields better function, approaching "physiological" values, especially in terms of transport respiratory efficiency. On behalf of the COPE consortium.

	n	PEF	RR	GFR	UP	TNa	FRN	QO2	TNa/QO2
KH-BSA	6	2.9 ± 1.0	0.24 ± 0.10	3.5 ± 3.0	2.1 ± 2.0	0.0 ± 0.1	11 ± 8	1.5 ± 0.5	0.0 ± 0.1
WB-250	5	0.8 ± 0.6	1.70 ± 1.1	7.4 ± 6.8	5.3 ± 2.7	2.4 ± 1.0	64 ± 6	0.4 ± 0.4	4.3 ± 2.0
WB-5000	4	1.0 ± 0.3	0.67 ± 0.24	48.1 ± 26	11.1 ± 7.0	9.3 ± 4.6	80 ± 20	0.9 ± 0.2	10.1 ± 4.8

(units above).

Translational Kidney Immunology

OS009 GENERATION OF NATURAL ANTIBODIES POST TRANSPLANT AND ASSOCIATION WITH KIDNEY ALLOGRAFT LOSS

Sarah See[1], Alexandre Loupy[2], Olivier Aubert[2], Yokarla Veras[1], Xaxier Lebreton[2], Baoshan Gao[3], Christophe Legendre[2], Dany Anglicheau[2], Emmanuel Zorn[1]

[1]Columbia University Medical Center, United States; [2]Hopital Necker, Université Paris Descartes, France; [3]The First Hospital of Jilin University, Changchun, China

The development of donor specific antibodies (DSA) reacting to mismatched donor class I and class II HLA is a prominent risk factor for kidney graft loss. Over the past few years our lab investigated the implications of a different type of antibodies referred to as natural antibodies (Nabs) in the outcome of kidney transplant alongside DSA. These antibodies are polyreactive IgG binding to multiple immunogenic determinants, including oxidized epitopes. Here, we assessed Nabs in 1462 serum specimens collected from 635 patients immediately pre-transplant and either at time of biopsy proven rejection within the first year post-transplant or at one year post-transplant in patients without immunological event. This large prospective observational cohort from Necker Hospital in Paris, France, includes patients transplanted between 2005 and 2010. All specimens were tested blindly from the patient clinical information. Nabs were assessed by ELISA through their reactivity to malondialdehyde (MDA). A univariate Cox regression model identified the development of Nabs

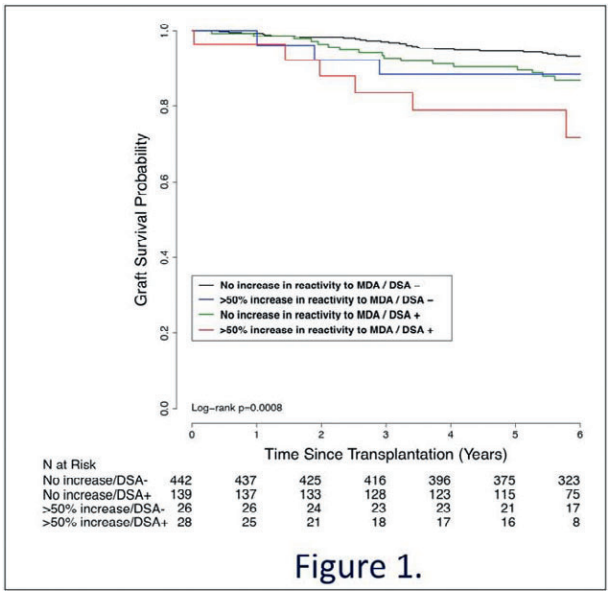

Figure 1.