Letters from the Frontline

Title:

Two-stage recipient hepatectomy and left-liver transplantation to minimize risks in adult-to-adult living donor liver transplantation: new concepts

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Footnote Page

List of abbreviations:

AALDLT, adult-to-adult living-donor liver transplantation;

APLDLT, adult-to-paediatric living-donor liver transplantation;

BMI, body mass index;

CT, computerized tomography;

ELH, extended left hepatectomy;

GRWR, graft-to-recipient body weight ratio;

ICU, intensive care unit;

LH, left hepatectomy;

LOS, length of hospital stay;

LT, liver transplantation;

MRI, magnetic resonance imaging.

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TO THE EDITOR

The combination of two-stage total hepatectomy and partial liver transplantation (LT) for secondary unresectable liver-only malignancies is producing a great quantity of literature. In the first stage, partial hepatectomy leaves a deportalised right liver while left-graft LT is performed. The second stage is scheduled after enough liver regeneration has occurred and consists of residual liver removal.

These strategies alleviate organ shortage in a moment when novel indications are flourishing, while deceased-donor transplantation is stagnating, despite the adoption of marginal candidates and splitting. Additionally, timely total hepatectomy is crucial in oncological surgery, which hardly meets the constraints of the waiting list. The introduction of living-donor LT (LDLT), decades ago, raised great expectations in this context. Unfortunately, after initial interest, most Western centres have progressively disregarded this tricky procedure. We have already reported our whole experience with standard total hepatectomy and LDLT (64 cases) and shown that one in four recipients experienced small-for-size syndrome, one in six arterial complications and one in seven postoperative death.[1] In contrast, a two-stage approach appears a true game changer for LDLT technical hurdles.[2, 3] Based on these assumptions, we have recently performed our first case of two-stage total hepatectomy coupled with left-liver LDLT, the details being extensively reported in Table 1 and Supplementary Materials. With this communication, we report our technical strategy and give a general insight into this topic.

PATIENT AND METHOD

The Donor Procedure

Our experience and standardised surgical technique in adult-to-paediatric LDLT (APLDLT) emphasises that left donor hepatectomy is a highly reliable procedure.[4] The key of APLDLT

is risk minimisation for donors and recipients, because left hepatectomy is traditionally associated with fewer and less severe postoperative complications,[1,5] and small grafts well suit small patients. Comparably, adult recipients with no portal hypertension may settle for tiny left liver grafts.[6] Through an upper midline incision, we carry out an open left hepatic resection with the procurement of the middle hepatic vein.

The Recipient Procedure: First stage (Figure 1)

The first step is the partial removal of the native metastatic liver. We carefully discuss the surgical strategy for partial hepatectomy in advance, based on preoperative imaging. The primary aim is to avoid the transection line to pass through lesions and expose tumour. We thus adapt from standard left hepatectomy (LH) to extended left hepatectomy (ELH). In the first case, the reference plane is the Cantlie line and parenchymotomy is carried out after standard extra-glissonian hilar dissection. In the second case, the section line is identified, after right anterior hilar dissection, by intra-arterial injection of indocyanine green and intraoperative fluoroscopy. After parenchymotomy, the middle and left hepatic veins are dissected well into the liver to obtain a nice cuff for hepatic vein anastomosis during graft implantation. We then divide the vascular pedicles, we remove the specimen, and we reinforce the remnant biliary stump with a running suture. We deportalise the remnant right liver and we resect the main portal convergence. In essence, surgery should adhere to sound anatomical criteria to curb the risk of biliary leakage. The need for a flawless surgery is driven by the risk of a cumulative effect of technical mistakes and possible postoperative complications.

The second step of the first stage is graft implantation. We start by anatomically anastomosing the left and middle hepatic veins confluence of the donor and the recipient, while the graft is cold rinsed and is wrapped in cold-soaked gauzes. Next, we anastomose the recipient's portal trunk and the donor's left portal vein. Then, we arterialise the graft by anastomosing donor and recipient's left hepatic arteries. We check graft inflow through transit time flow measurement and we calculate the intra-parenchymal resistance with echo-colour-Doppler ultrasound scan, after 30 to 90 minutes from unclamping to allow for the arterio-portal buffer response. We proceed with graft inflow modulation if portal flow exceeds 200 ml/min/100 g of graft weight.[7] Firstly, by means of a supra-pancreatic ultrasound-guided approach, we find and ligate the splenic artery at its origin, by placing a Hem-o-lock® without severing the arterial pedicle. The flow rate is double-checked and, if

portal flow still exceeds the threshold, a partial porto-caval shunt is placed. Finally, we prepare the remnant native liver for the second stage, the completion of the hepatectomy. We place one silicone vessel loop around the right arterio-biliary pedicle and one around the right hepatic vein. Then, we ligate and sever all the accessory hepatic veins, so that the inferior vena cava is fully released from the liver. Next, we slip a large silicone sheath to the right side of the VCI, dorsolateral to the liver and against the liver cut surface to encase the remnant. Lastly, graft biliary drainage is restored by hepatico-jejunostomy. We cut the jejunum 40 cm from Treitz and we bring the distal end, the future biliopancreatic limb, into the supramesocolic area in a transmesocolic approach. We anastomose the proximal end to the Roux limb 70 cm far from the future hepatico-jejunostomy. We then anastomose the biliary duct to the bowel in an end-to-side fashion with single-layer separated stitches. We place an internal biliary stent deciding case-by-case based on the quality and diameter of the biliary anastomosis. The hepatico-jejunostomy is preferred to set the delicate graft biliary tract free from the native one, which has to be manipulated a second time later on. The patient is aware of the significant risk of biliary complications, occurring in one out of three liver recipients and, in the setting of adult-to-adult LDLT (AALDLT), even more frequently because of the anastomosis between a biliary side branch and a jejunal loop. Before abdominal wall closure, we restore the falciform ligament continuity to avoid graft tilting and to keep the cut surfaces of the remnant and of the graft well separated. This expedites the subsequent residual native liver extraction by decreasing interhepatic adhesions.

The Recipient Procedure: Second stage (Figure 2)

For the second stage of the recipient procedure, we plan a volumetric imaging a fortnight after the first operation. Accordingly, we complete the native liver resection with laparoscopic right hepatectomy or right posterior sectionectomy. We access the abdominal cavity using the open laparoscopic technique, starting from the inframesocolic compartment to take advantage of the expected absence of adhesions. We progressively cleave the native liver remnant, by hydrodissection, until we find the previously encircled arterio-biliary and hepatic pedicles. We then divide the two vascular pedicles using an Endo-GIA type stapling system, we insert an extraction bag in the abdomen, and we put the liver inside. Lastly, we perform a Pfannenstiel incision and we retrieve the organ. A laparoscopic

second stage carries a risk of conversion to open surgery, which intuitively appears lower than in standard right hepatectomy. If needed, conversion can be easily done by resuming the incision of the first procedure.

DISCUSSION

Two-stage total hepatectomy coupled with LT is a promising technique in liver oncology but the reported experience is still sparse and we wish to draw attention to six specific issues of this literature.

Firstly, all articles concentrate on colorectal-cancer liver metastases.[2, 3, 8] Nonetheless, the concept can be extended to neuroendocrine tumours and hepatocarcinoma in patients without significant portal hypertension and with a favourable liver anatomy.

Secondly, most literature reports triple and quadruple immunosuppressive regimens. Conversely, a minimised immunosuppression with tacrolimus monotherapy (trough levels: 4-6 ng/mL) and without induction is key for oncological LT recipients.[1]

Thirdly, partial LT is reportedly performed with left lateral sectors (segments II-III), from deceased or living donors.[2, 3] However, the preservation of a vascular pedicle that can be anastomosed requires the division of segment-IV vessels, so that the segment IV is completely devascularised and bound to atrophy. Sensibly, the donor procedure should entail proper LH (segments II-IV) because the segment IV, in the donor, is useless, while, in the recipient, adds precious mass, impacting graft inflow modulation need.[7]

Fourthly, in the recipient first stage, hepatectomy can be customised from standard LH to ELH. The aim is to avoid the section plane to pass through metastases and to respect anatomy, in terms of hepatic drainage (segments V and VIII to middle or right hepatic vein), arterial supply and biliary variants, with ELH being preferable to LH for possible anterior biliary sectoral duct draining into the left bile duct.

Fifthly, the portal bifurcation should be resected during the first stage of hepatectomy, as for Klatskin tumours. This adaptation, in contrast to reports proposing simple right portal branch ligature, is oncologically appropriate to secure margins, and technically beneficial. The balance between traction forces of the portal tripod (the trunk, the right and the left branches) after right liver resection is found by aligning the portal trunk and the left branch. Thus, portal anastomosis is less likely to kink if the donor left portal branch is directly sutured to the recipient straightened portal vein.

Sixthly, the second stage can be performed via laparoscopy. The native liver can be fully prepared during the first stage, by wrapping it to prevent adhesions and by marking pedicles. These modifications allow a comfortable residual hepatectomy, with reduced surgical stress. Indeed, a fast postoperative recovery is highly desirable in view of prompt adjuvant chemotherapy.

To conclude, novel two-stage LT strategies appease ethic debates around LDLT as limited donor hepatectomies reduce the risk of liver failure in donors. Likewise, leaving a residual native liver in recipients for a limited time protects from possible temporary graft shortfall or technical failures during the crucial postoperative phase: arterial thrombosis or graft inadequate volume growth and functional insufficiency (the small-for-size or small-for-flow syndrome) can be smoothly managed. This groundbreaking innovation gives small grafts time to regenerate, while native liver acts as a stake, which supports metabolic functions and prevents emergency listing of patients whose primary indication was controversial.

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Legends

Table 1. Clinical detail of the first case

Footnote: * Volume estimation based on MRI and CT scan imaging, obtained through the software Vitrea® (Vital Images Inc., Minnetonka, US-MN); ** Weight estimation based on Vitrea® calculation -10%.

Figure 1 (a-d). The Recipient Procedure: First stage

Extended left hepatectomy in case of central tumour (a). Early resection of the main portal convergence with deportalisation of the remnant posterior sector (b). Graft (segments II, III, and IV) orthotopic implantation (c). Anastomose of recipient's portal trunk with donor's left portal vein (d).

Footnote: Venous drainage stumps of segment V and VIII into the right hepatic vein (v5, v8). Biliary branches of segment VI and VII (b6, b7).

Figure 2 (a-e). The Recipient Procedure: Second stage

The native liver is fully prepared during the first stage: silicone vessel loop around the right arterio-biliary pedicle and around the right hepatic vein (a, c). Large silicone sheath to the right side of the VCI, dorsolateral to the liver and against the liver cut surface to encase the remnant (a, d). Laparoscopic right remnant resection with division of the two vascular pedicles using an Endo-GIA type stapling system (e).

Footnote: Remnant posterior sector (Remnant). Left-liver living-donor graft (Graft).

Supplementary figures.

Figure I. Imaging of volume evolution over time

Figure II. Graphic showing the liver volume evolution over time

Footnote: a, first stage; b, second stage.

Figure III. Digital reconstruction of the left-liver graft based on the 6-month follow-up CT scan

Preoperative data

Donor

Age (y)	48
Weight (Kg)	67
Height (cm)	155
BMI (Kg/m^2)	28
Portal anatomy	Type 2 (trifurcation)
Arterial anatomy	Modal
Biliary anatomy	Modal
Graft volume (ml)*	290
Graft weight (g)**	261

Recipient

Age (y)	55
Weight (kg)	57
Height (cm)	162
BMI (Kg/m^2)	22

Operative data

The Donor Procedure

Operating time (min)	310
Blood loss (ml)	160
Procedure	Open left hepatectomy (II, III, IV)
Graft weight (g)	236
ICU (hours)	24
LOS (days)	14
Dindo-Clavien	I

The Recipient Procedure: First stage

Operating time (min)		
	Hepatectomy	390
	Transplantation	230
Blood loss (ml)		450
Procedure	Open left trisectionectomy (I, II, III, IV, V, VIII)	
Resected liver weight (g)		895
Ischemia time (min)		
	Cold	159
	Warm	38
Hemodynamic data		
	Native portal	
	flow (ml/min)	1100
	pressure (mmHg)	8
	Graft portal	
	total flow (ml/min)	475
	relative flow (ml/min/100 g)	210
	pressure (mmHg)	28
Portal inflow modulation (splenic artery ligation)		Yes
ICU (hours)		36
LOS (days)		15
Dindo-Clavien		I

The Recipient Procedure: Second Stage

Operating time (min)		177
Blood loss (ml)		100
Procedure	Laparoscopic right posterior sectionectomy (VI, VII)	
Specimen weight (g)		485
ICU (hours)		24
LOS (days)		6
Dindo-Clavien		I

Follow-up

Time after transplant (days)	0	10	18	40	90	180
GRWR (%)	0.41	0.80	0.91		1.52	1.44
Graft Volume (ml)	260	449*	577*		963*	918*
Graft Weight (g)	236	404**	519**		867**	826**
Recurrence		No	No	No	No	No

Preoperative data	
Donor	
Age (years)	48
Weight (kg)	67
Height (cm)	155
BMI (kg/m^2)	28
Portal anatomy	Type 2 (trifurcation)
Arterial anatomy	Modal
Biliary anatomy	Modal
Graft volume (ml)*	290
Graft weight (g)**	261
Recipient	
Age (years)	55
Weight (kg)	57
Height (cm)	162
BMI (kg/m^2)	22

Preoperative data	
The Donor Procedure	
Procedure	Open left hepatectomy (II, III, IV)

The Recipient Procedure: First stage	
Procedure	Open left trisectionectomy (I, II, III, IV, V, VIII) and liver transplantation
Operating time (min)	
Partial hepatectomy	390
Implantation	230
Blood loss (ml)	450
Resected liver weight (g)	895
Ischemia time (min)	
Cold	159
Warm	38
Hemodynamic data	
Native portal flow (ml/min)	1100
Native portal pressure (mmHg)	8
Graft total portal flow (ml/min)	475
Graft indexed portal flow (ml/min/100 g)	210
Graft portal pressure (mmHg)	28
Portal inflow modulation (splenic artery ligation)	Yes
ICU (hours)	36
LOS (days)	15
Dindo-Clavien	I
The Recipient Procedure: Second Stage	
Procedure	Laparoscopic right posterior sectionectomy

						(VI, VII)
Operating time (min)			310	Operating time (min)		177
Blood loss (ml)			160	Blood loss (ml)		100
Graft weight (g)			236	Specimen weight (g)		485
ICU (hours)			24	ICU (hours)		24
LOS (days)			14	LOS (days)		6
Dindo-Clavien			I	Dindo-Clavien		I
Follow-up						
Time after transplant (days)	0	10	18	40	90	180
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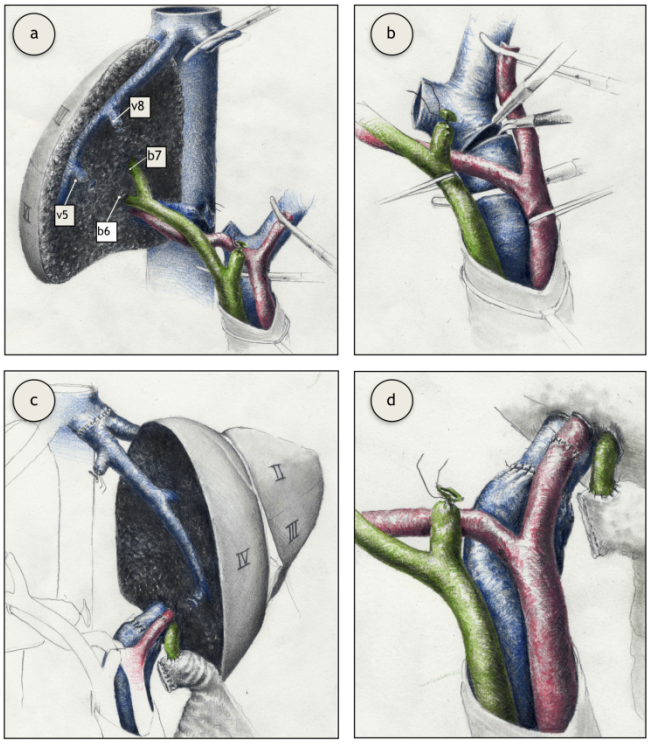

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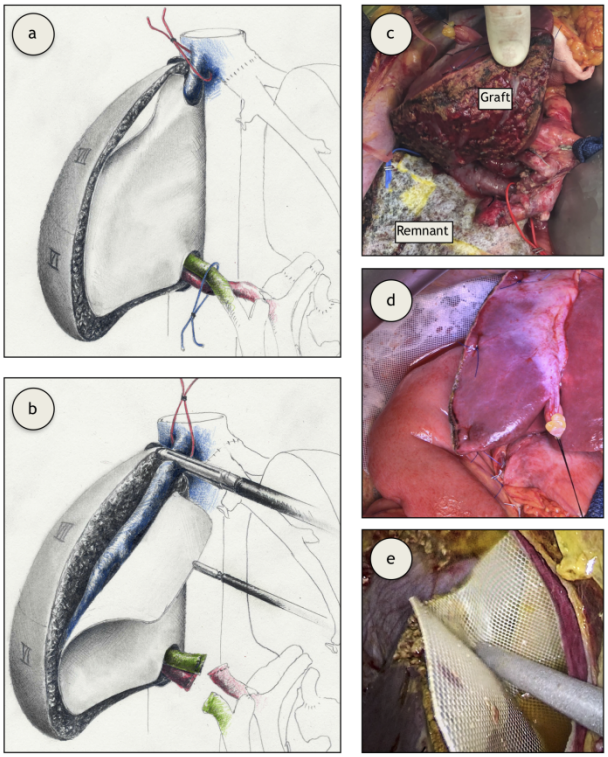

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