

Adult-to-adult living related liver transplantation : initial experience

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Abstract

The number of adult patients on the liver transplantation waiting lists is growing steadily.

Adult living related liver transplantation (LRLT) represents the ultimate means to expand the donor pool.

The success of this model of "small for size" grafting relies on strict donor and recipient selection. The choice of the graft (2 left and 4 right hepatectomies) was made on the minimal ratio between estimated graft and recipient body weights (0.8-1%), necessary to meet the recipient's metabolic demands.

Our experience with six adults is reported. Donor morbidity was minimal (one wound infection); there was no mortality. Four (66%) recipients are doing well, two died of infectious complications. All recipients had a complicated post-transplant course.

Due to its complexity, both in donor and recipient, LRLT should only be developed very carefully in experienced liver transplant centers. (*Acta gastroenterol. belg.*, 2001, 64, 9-14).

Key words : living related transplantation, liver transplantation, adult.

Abbreviations

BW	body weight
(D)-US	(doppler)-ultrasound
GR/WR	graft / recipient weight ratio
GR/LSVR	graft / recipient liver standard volume ratio
HPS	hepatopulmonary syndrome
IVC	inferior vena cava
(O)LT	(orthotopic) liver transplantation
LRLT	living related liver transplantation
SPLT	split liver transplantation

Introduction

More and more adults are becoming candidates for liver transplantation (LT). Due to the shortage of organs however, many patients die on the waiting list. The development of split liver transplantation (SPLT) and more recently of living related liver transplantation (LRLT) represents a valuable source to expand the adult donor pool (1,2,3,4).

Our preliminary experience with adult-to-adult living related liver transplantation is reported here.

Material and methods

During the period January 1998-September 2000, three male and three female adults (> 15 years) underwent orthotopic liver transplantation (OLT) using an allograft originating from an adult living donor. The recipient's median age was 41.5 years (range 15.5 to 58). Indications for LT were primary biliary cirrhosis (2 ×), primary sclerosing cholangitis (1 ×), Wilson's disease (1 ×), cryptogenic cirrhosis (1 ×) and Langerhans' histiocytosis (1 ×).

Two patients were transplanted urgently. One patient had histiocytosis complicated by pronounced hepatopulmonary syndrome (HPS). PaO₂ at room air was 34 mmHg. Transjugular intrahepatic portosystemic shunting, attempted to treat the HPS, led to acute worsening of his condition two months later.

A thirty-year old, deeply jaundiced, lady with primary biliary cirrhosis (Child-Pugh C status) was hospitalized because of septic shock and spontaneous bleeding giving rise to an infected right psoas muscle haematoma and intra-alveolar bleeding.

Transplantation was performed two weeks later when the active infection was "under control".

All donors were first degree family members who had asked for LRLT once faced with the problem of long waiting times for their sick relatives. Donor selection was based on blood group compatibility and on normal, biochemical, medical, radiological and psychological evaluation done by independent staff members of the departments of internal medicine and psychopathology ("donor's advocates"). All six screened donor-candidates fulfilled the proposed criteria.

Hepatic doppler-ultrasound (D-US) was completed with CT-scan or magnetic resonance (MR) imaging with computerized volume measurement. (Fig. 1) (5,6).

The choice of the grafts to be transplanted — right or left liver — was made on the ratio between estimated graft and recipient body weights (GR/RBW), the lower

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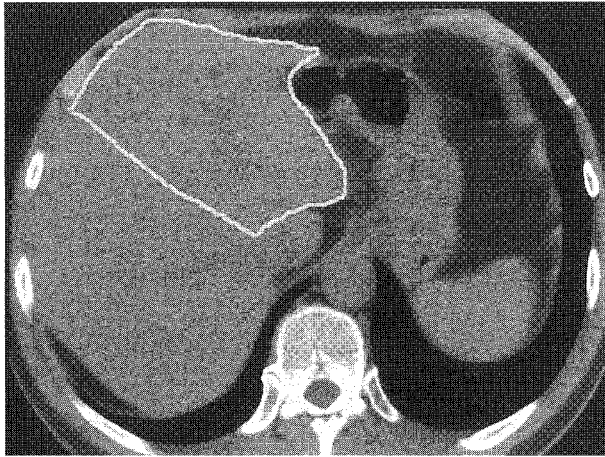


Fig. 1. — Estimated CT-scan volumetry of left hemiliver graft including the middle hepatic vein (OLT 965).

limit being at 0.8-1% (7), and the ratio between estimated graft and liver standard volumes (GR/LSV), the lower limit being at $\geq 40\%$ (8).

Vascular anatomy was defined five times by coeliomesenteric angiography and once by angio-MR. D-US and biochemical controls were done daily during the first postoperative week both in donors and recipients.

Two units of donor blood were generated two and one week before graft procurement. Three months post-donation, all donors had clinical, psychological, biochemical and D-US follow-up as well as CT-scan liver volumetry.

The adult-to-adult LRLT program was approved by the institutional ethics review board. Informed consent was obtained in all cases from donor, recipient and their respective witnesses.

Donor operation

The first two recipients received a left liver graft (corresponding to Couinaud's segments II-III-IV); the latter four received a right liver graft (Couinaud's segments V to VIII) (9).

Bilateral subcostal incision with extension to the xyphoid was performed. After completing cholecystectomy and cystic duct isolation, cholangiography was performed in order to define biliary anatomy. Intraoperative US was used to indicate on the liver surface the course of the middle hepatic vein and to look for intrahepatic parenchymatous and vascular anomalies.

The arterial, venous and biliary elements of the corresponding left or right liver grafts were first isolated. Parenchymal transection was done *without inflow occlusion* using ultrasonic surgical aspiration (Cusa® - USA), monopolar and bipolar irrigation electrocautery (Yamamura Ika-kikai-JPN), Argon beam coagulation (Valleylab - USA) and Ultracision® (Ethicon - USA).

Four donors had normal arterial anatomy; one had a right hepatic artery originating from the superior mesenteric artery and one had two right hepatic arteries originating from the common hepatic artery. Four donors had single biliary duct drainage of the graft; two had two hepatic ducts draining the right liver allograft (Fig. 2). One of the latter patients also had two extrahepatic portal vein branches and one accessory right hepatic vein of 10 mm diameter.

When procuring the right liver lobe several major hepatic veins draining segments V and VIII were severed.

Just before start of perfusion, the donor was heparinized (1000 UI). The liver graft was flushed through a portal vein cannula using successively 4°C-cold Hartmann and UW-solution. The hepatic artery was ligated next and the hepatic vein was transected and sutured progressively using running polypropylene suture (Prolene® - Ethicon - USA).

A cell-saver (Haemonetics - USA) was used in all donor-operations.

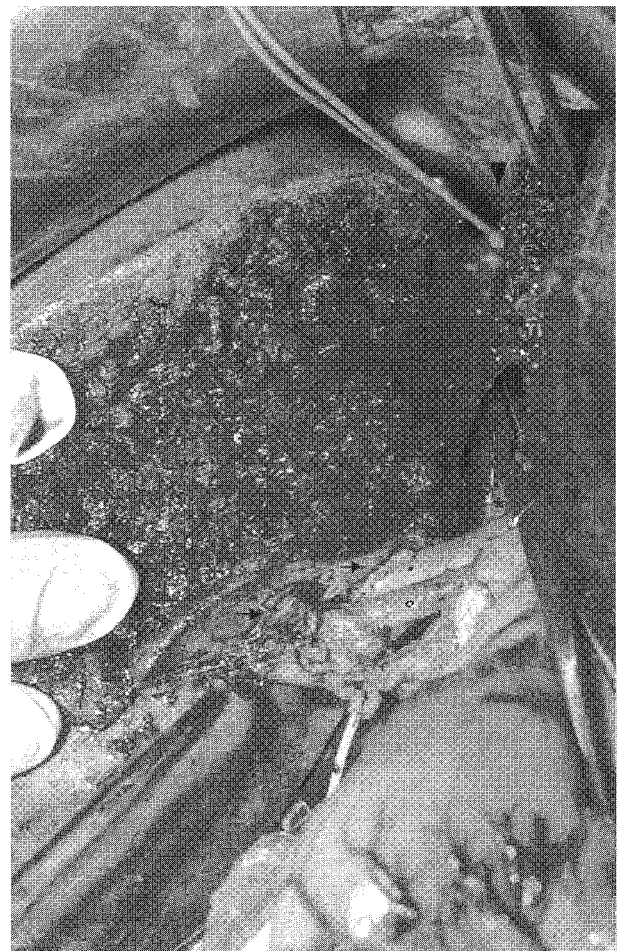


Fig. 2. — Intraoperative view of right liver graft procurement [right hepatic vein (arrow head), right hepatic artery (°) portal vein (☆) and inferior vena cava (*). There were two right hepatic bile ducts (arrow)].

Recipient operation

The recipient operation was started once the feasibility of the donor operation was confirmed.

The native liver was removed whilst preserving the inferior vena cava (IVC) (10). Temporary porto-caval shunting or veno-venous bypass were not used. Grafts were implanted using the piggy-back technique. The hepatic venous cuff of the left liver graft was anastomosed to the recipient's middle and left hepatic veins cuff. The right hepatic vein of the right liver graft was anastomosed to the widened orifice of recipient's right hepatic vein. In one patient a larger (right) accessory vein was reimplanted into the IVC.

Microsurgical reconstruction of the hepatic artery consisted of an end-to-end anastomosis using single stitches of PDS 8/0 (Ethicon - USA). Magnifying loops (5.5 ×) were used in five cases; one 1.5 mm right hepatic artery was anastomosed using operative microscope (B.L.). This patient had two interconnecting small right hepatic arteries; because of the excellent arterial back flow only one vascular anastomosis was performed.

Biliary tract reconstruction was done using Roux-en-Y hepaticojejunal anastomosis (3 ×); direct anastomosis between donor and recipient hepatic ducts (2 ×) and combined duct-to-duct and Roux-en-Y hepaticojejunal anastomoses (1 ×). All biliary anastomoses were made using interrupted PDS 7/0 (Ethicon-USA) stitches. None of the biliary anastomoses was stented.

Immunosuppression consisted of tacrolimus (Prograf® - Fujisawa-JPN) and low dose steroids; the first patient also received anti-LoCD2a antibodies (BTI-322 - Biotransplant - USA). Steroids were withdrawn within a few months once liver tests became stable. All patients had similar peri-operative care.

Results

Donor data (Table I)

Median operative time was 7.55 hours (range : 7.15 to 8.30). All donors were extubated at the end of the operation. Blood transfusion needs were as follows : 290 ml autologous blood in one and reinfusion of recovered blood (435 to 1239 ml) in four patients.

Donor morbidity was very low, consisting only of one E-coli wound infection. Median hospitalisation time was 9 days (range : 7 to 14).

The two left liver grafts weighed 450 and 565 gr; the right livers weighed 725, 760, 850 and 915 gr. All weights fulfilled both the minimal requirements for the GR/BW ratio (range : 0.90 to 1.44%) as well as the GR/LSV ratio (range : 45 to 93%).

The early postoperative evolution of bilirubin, AST and INR is shown in figure 3; two donors had an early bilirubin elevation above 2 mg %.

All donors resumed their normal activities at a median time of 3 weeks (range : 2 to 4).

Recipient data (Table II)

Median operative time was 7.55 hours (range : 5.30 to 14). Three recipients had no blood transfusion; two patients received 217 and 645 ml of recovered blood and one patient received both 500 ml of recovered blood and 930 ml of allotransfusion.

Median hospitalisation time was 22 days (range : 7 to 68).

The first patient (OLT 961) was extubated at day 1 despite severe pre-LT HPS. At day 9 reintubation was necessary and at day 25 a cerebral abscess, caused by streptococcus milleri, was drained surgically. This event

Table I. — Adult-to-adult living related liver transplantation : donor data

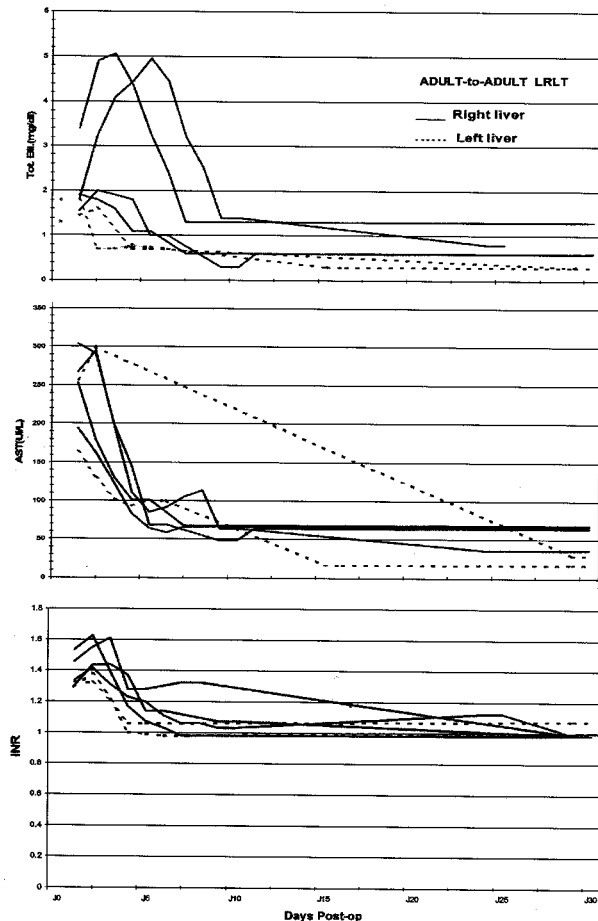
OLT	Donor	Age yrs	Graft		Ratio		Remaining donor liver volume* (Liver W/BW)	Transfusion (ml)		Hospitalisation (days)
			Type	Weight (gr) real (estimated)	Graft / Rec BW	Graft / Rec LSV		Auto	Recup.	
961	Mother	42	left (II-III-IV)	450 (505)	0.90%	45%	931 (2.2%)	Ø	Ø	7
965	Father	58	left (II-III-IV)	565 (410)	0.99%	56%	990 (1.7%)	Ø	850	7
1045	Husband	53	right (V-VIII)	850 (1380)	1.44%	87%	950 (1.8%)	Ø	547	14
1068	Mother	48	right (V-VIII)	725 (790)	1.40%	71%	285 (0.6%)	294	460	9
1069	Son	32	right (V-VIII)	915 (1150)	1.43%	93%	635 (2%)	Ø	435	12
1118	Son	19	right (V-VIII)	980 (760)	1.02%	85%	520 (0.69%)	Ø	1239	10

* (B)W : (body) weight; LSV : liver standard volume
estimated total liver volume - real graft volume.

Table II. — Adult-to-adult living related liver transplantation : recipient data

OLT	Diagnosis	Unos Status	Sex	Age yrs	Implantation technique			Transfusion		Hospitalisation		Outcome
					Hepatic veins	Art.	Biliary	Recup.	Allo.	Intensive care	Total	
961	Histiocytosis X HPS (paO ₂ 34 mmHg)	2	M	15.5	PB	1	1 hep-jej.	Ø	Ø	5	68	d 24 cerebral abscess HPS corrected at 3 mo.
965	Primary biliary cirrhosis	1	F	33	PB	1	1 hep-jej.	Ø	Ø	3	(7)	d 1 bleed cut surface encephalopathy d 7 sepsis †
1045	Primary biliary cirrhosis	3	F	52	PB	1	1 hep-hep.	217	Ø	1.5	30	d 8 rejection encephalopathy renal insufficiency d 9 rupture oesophageal varix; prolonged ascites d 222 anastomotic biliary stenosis
1068	Primary sclerosing cholangitis	3	F	18	PB	1	2 hep-jej.	Ø	Ø	1	9	prolonged ascites
1069	Cholestatic cirrhosis	3	M	58	PB	1	1 hep-hep.	500	930	1	12	d 17 wound dehiscence prolonged, infected ascites d 37 sepsis ‡
1118	Wilson's disease	3	M	52	PB (2 hep. veins)	2	1 hep-hep 1 hep-jej	645	Ø	2 (+ 4)	22	d 3 respiratory arrest d 9 hepatic artery stenosis d 37 CMV-hepatitis prolonged ascites and oedema

HPS : hepatopulmonary syndrome; UNOS : United Network Organ Sharing status 1: intensive care recovery, status 2 : chronic, acutely, decompensated liver disease ; status 3 : chronic liver disease patient at home ; PB : piggy-back allograft implantation.



was attributed to severe pre- and posttransplant hypoxemia. He recovered without any neurological sequelae. HPS was completely corrected three months post-LT. He is doing well 27 months post-LT. The second patient (OLT 905) was reoperated on at day 1 for bleeding originating from the cut surface of the graft. Recovery during the first post-transplant days was complicated with a marked encephalopathy. At day 7 she succumbed due to a fulminant sepsis caused by streptococcus faecium ; this germ had been detected some weeks before LT in a retroperitoneal haematoma.

The third patient (OLT 1045) had a difficult post-LT course due to pronounced cholestasis, prolonged ascites and renal insufficiency. The dose of tacrolimus was lowered because of severe nephrotoxicity. This resulted in rejection needing OKT3 (Cilag-Janssen-USA) treatment. At day 9, an oesophageal varix rupture was treated with endoscopic banding. An anastomotic stricture of the hepatico-hepaticostomy was repaired at day 222 using a Roux-en-Y hepaticojejunostomy. She is doing well 13 months post-LT.

The fourth patient (OLT 1068) had prolonged ascites needing intensive diuretic therapy up to three months post-LT ; she is currently doing well 9 months post-LT.

Fig. 3. — Early postoperative evolution of bilirubin, AST and INR values after living related graft procurement (o o left liver ; x — x right liver).

The fifth patient (OLT 1069) was discharged in good condition at day 12 despite presence of massive ascites. Rehospitalization was necessary five days later because of partial wound dehiscence in the presence of infected ascites. Following parietal surgery, he developed a corticoreistant rejection treated with OKT3. He died of fulminant sepsis at day 37 ; autopsy revealed multiple foci of infected ascites.

The sixth patient (OLT 1118) was discharged at day 22. Respiratory arrest at day 2 due to bronchial obstruction, caused by a mucous plug, was treated with reintubation and bronchoscopy. At day 9, he had percutaneous balloon dilatation because of significant supra-anastomotic arterial stenosis, detected at routine doppler-ultrasound examination. One month post-LT, he developed corticosensitive rejection followed by CMV hepatitis. Ascites and peripheral oedema remained present for 6 weeks.

Discussion

The ever increasing gap between the number of patients on the waiting list and the number of transplanted patients, has obliged surgeons and physicians to look for alternative methods of liver grafting (Table III).

LRLT and SPLT are the only methods allowing enlargement of the adult donor pool. Surgeons having cadaveric organ harvesting at their disposal mainly developed the concept of SPLT (1,11) ; those who didn't, mainly developed the concept of LRLT (3,8). The first successful LRLT was performed in a child by the group of Strong in Sidney (in 1990) (12). The "small for size" liver transplant model needs to follow strict rules in order to fulfil the metabolic demands of the recipient (3,7). In order to do so, the ratio of the liver graft and recipient body weights needs to be > 0,8 - 1% and/or that of the liver graft and recipient standard liver volume (LSV) ≥ 40%. The need to transplant a larger liver mass in cases of markedly impaired condition of the recipient has also become rapidly established. The choice of the graft is thus dependent not only on the recipient's LSV and/or BW but also on the recipient's condition at moment of LT (3). LSV can be calculated either using Urata's or Heinemann's formulae (13,14).

Table III : Expansion of liver donor pool at Cliniques Saint-Luc

- february 1984 - september 2000 : 1120 transplants in 970 patients (retransplantation index 1.16%)			
- innovative techniques of LT			
split	- paediatric	:	42
	- adult	:	27
living related	- paediatric	:	82
	- adult	:	6
domino transplantation		:	1

} 14.1%

The excellent results obtained in paediatric LRLT, especially by Tanaka in Kyoto and Makuuchi in Tokyo, led to the application of the concept of LRLT into the adult population. This shift however made the use of larger grafts mandatory.

The first successful adult-to-adult LRLT was performed by Makuuchi in Shinshu (in 1993) using a left liver (segments II, III, IV) (15) ; the first successful adult-to-adult LRLT using a right liver (segments V to VIII) was done by Yamaoko in Kyoto (in 1994) (16). In order to respect the minimal hepatic mass requirements for transplantation, surgical techniques needed further adaptation ; Fan in Hong-Kong used the right liver lobe (segments IV to VIII) (17) and Makuuchi the left liver including segment I (18). In some cases of insufficient liver mass, the allograft was used as an auxiliary orthotopic graft (19).

The Cliniques St-Luc's experience followed the same evolution. Excellent results of our paediatric LRLT-program, (started in 1993), led to the development of the adult LRLT program in 1998 (20).

Although some deaths have been reported or alluded to (21), the donor operation can nowadays be done safely (3,22). Improved knowledge of liver surgery and technical progress using modern tools such as bipolar irrigation electrocautery and ultrasonic dissection make donor hepatectomy possible without major blood losses. Intraoperative need for transfusion is indeed the most predictive factor of morbidity and mortality in modern liver surgery (8,22).

The recipient operation itself doesn't seem to carry more risks than the usual LT-procedure. Posttransplant evolution is however more difficult in two thirds of the patients reflecting the problem of the "small for size" liver grafting.

Prolonged encephalopathy and ascites formation, variceal rupture and enhanced infectious risk have been described after LRLT ; these problems are related to the reduced hepatic functional capacity. Review of the larger series of adult-to-adult LRLT shows that 70% of early postoperative deaths are related to sepsis (8,22,23, 24,25). The use of an as large as possible liver mass is therefore always mandatory. In order to reduce morbidity and mortality as much as possible, donor and recipient selection must be and should remain very strict.

Further progress in the field of adult liver transplantation will rely on the cross fertilisation of living related liver transplantation and (in-situ or ex-situ) split liver cadaveric transplantation (25,26,27,28). Development of both methods will be the only way to overcome the actual organ shortage, this at the price of a more complicated early (and late) post-transplant course.

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