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EDITORIAL

# Liver resections for liver transplantations

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## Abstract

Split-Liver and living-related donor liver transplantation are the newest and both technically and ethically most challenging developments in liver transplantation and have contributed to a reduction in donor shortage. We report the technical aspects of surgical procedures performed to achieve a partial graft from a cadaveric and a live donor.



**Key words:** Living-related liver transplantation; Split liver transplantation; Liver resections; Liver transplantation; Liver surgery

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## INTRODUCTION

Segmental liver transplantation based on cadaveric splitting or living related donation has been developed as a valuable treatment for patients with end-stage liver disease. It is also a means of overcoming the shortage of organs, and mortality on the waiting list. In a country such as Italy, with a population of 55 million and with 500 000 infants born each year, it can be estimated that the need for liver transplantation is between 1650 cases and 4400 cases per year in adults[1]. The imbalance between the need and the availability of liver grafts has been a powerful stimulus for the development of innovative surgical techniques to increase the pool of organs for transplantation. Clearly, living-related donor liver transplantation (LRLT) is the natural evolution of other surgical procedures, namely, reduced-size liver and split-liver transplantations. It is based on the segmental anatomy of the liver and its peculiar capacity to regenerate[2]. Living-related donor transplantation is the newest and both technically and ethically challenging development in liver transplantation and has contributed to a reduction in donor shortage. We report the technical aspects of the surgical procedures performed at our center to obtain a partial graft from live and cadaveric donors.

## ISMETT SERIES

Since July 1999 we have performed 601 liver transplantations in our center. Many different types of grafts were used including Domino Liver Transplantation, grafts coming from Extended Criteria Donor and partial graft

resulting from complex liver resection in both live and cadaveric donors.

During the period from June 2003 to November 2009, 125 grafts resulting from conventional *in situ* split liver procurement were transplanted in 85 pediatric recipients (left lateral segments) and 40 adult recipients (extended right graft-Coineaud segments 4-8). We performed 1 split liver donor procedure with 2 adult recipients; the first receiving the right lobe (Coineaud segments 5-8) and the second the full left lobe (Coineaud segments 2-4).

From January 2002 to November 2009, LRLT was performed in 90 adult and 3 pediatric recipients. We recorded 91 living-related liver donors: one of them underwent to aborted operation; two adult patients received a full left lobe (segments 2-4) and 85 received a right lobe (segments 5-8); all 3 pediatric recipients received left lateral segments (segments 2 and 3).

## SPLIT LIVER TRANSPLANTATION: THE SHARING OF A CADAVER LIVER

The technique of liver splitting as it is used today by most centers is performed during organ procurement from heart beating, brain dead donors[3,4]. Leaving the hepatic vasculature intact, the liver parenchyma and left bile duct are transected close to the right side of the falciform ligament.

The abdominal organs are then perfused through the aorta with cold preservation solution, the left portal and hepatic veins are dived. The right hepatic artery (HA) is transected close to its origin from the common HA and the left lateral segment is removed. The right part of the liver is then excised with the usual technique used for whole liver procurement[5].

Only cadaver donors without risk factors (age > 60 years, hemodynamic instability and no macroscopic steatosis) are considered for liver splitting. The left lateral segment is almost exclusively transplanted in children. Ideally, the ratio between the body weight of the donor and that of the pediatric recipient should be below 12. Otherwise the graft might be too large, making abdomen closure problematic[6]. Should that occur, abdominal closure can be temporarily performed using a synthetic mesh and definitive closure postponed[7]. The cadaveric liver graft can be split either during the procurement procedure (*in situ*) or on the back-table after a conventional donor procedure (*ex situ*). For ex-situ splitting of the liver, the whole organ is retrieved and grafts are then prepared in the recipient transplant center. Although this technique is the most widely used method to transplant 2 patients with 1 liver, extended cold ischemic time and some rewarming due to the longer back-table procedure as compared to conventional liver transplantation increase the risk of graft dysfunction in the recipient. The *in-situ* splitting technique is closely related to the techniques established for living related donor procurement. Its application is limited due to a more time-consuming and technically more demanding explantation technique[4].

### *Cadaveric left lobe split livers*

Reduced-size liver transplantation shows outcomes in line with, if not superior to, whole-liver transplantation and has become an essential part of the technical expertise of pediatric transplant centers. The development of this technique has led to almost total elimination of child mortality on the waiting list, through the utilization of an adult liver cadaver donor. Its main limitation is that it withdraws organs from the larger adult recipient pool. For this reason, after the development of living-related and split-liver transplantation (SLT), reduced-size live transplantation is used increasingly rarely, and should not any longer be considered an option for pediatric liver transplantation. The European Liver Transplantation Registry (ELTR) reports liver transplantation activity in Europe, and recorded 5895 children transplanted between 1988 and 2005. Overall 1-year patient and graft survival was 84% and 73%, respectively, in patients older than 2 years at the time of transplantation, and 81% and 71%, respectively, in children < 2 years of age. Ten-year patient and graft survival rates for the same age groups were 75% and 61%, and 74% and 60%, respectively. Similarly, united network for organ sharing (UNOS) reported survival rates of the 9064 pediatric patients transplanted between 1997 and 2004. Overall 1-year patient and allograft survival reported to the Studies of Pediatric Liver Transplantation (SPLIT) registry, recorded 1611 patients, who reached 88% and 82%, respectively, while the rates were 83% and 74%, respectively, 4 years after transplantation. Specific factors influencing early survival include age, diagnosis, severity of illness, and possibly allograft type[8].

### *Cadaveric right lobe split livers*

Extended right grafts (ERG) can be transplanted in adult patients. However, ERG are still considered marginal grafts and are only used for primary transplantation in stable patients[9].

Nonetheless, single center and multicenter reports have clearly shown that the outcome of adult patients transplanted with whole liver grafts and ERG are not significantly different. In centers with substantial experience, ERGs have been successfully used both for high risk patients (i.e. fulminant liver failure) and retransplantation[10-12].

The American Society of Transplant Surgeons has performed a survey of 89 North American transplant centers participating in the UNOS scientific registry for transplant recipients on the utilization of SLT. In these historical series, the overall incidence of right trisegment graft complications was 26%, with biliary complications being most frequent, followed by vascular complications, and post-transplant hemorrhage. The most frequently reported vascular complication was HA thrombosis with 5 reported cases of HA pseudoaneurysm and 1 anastomotic disruption. There was a 4% incidence of primary nonfunction and a 15% incidence of mortality with more than one-half of deaths being attributed to graft-related complications[13].

The surgical technique of ERG transplantation is almost

identical to the one used for whole liver transplantation with the only exception being the arterial anastomosis when the celiac trunk is procured with the left lateral segment. In this case, the right HA of the ERG is anastomosed directly to the recipient right HA. When this is not technically feasible, as it can happen in retransplantation, a jump graft to the infrarenal aorta can be performed using the cadaver donor iliac artery.

Until very recently, split liver transplant operations were performed using adult donors only[14-16]. With increased experience livers from pediatric cadaver donors have also been successfully split and transplanted in two pediatric recipients of different body weights and ages[17].

## LIVING DONOR LIVER TRANSPLANTATION (LDLT): DONOR SELECTION AND OUTCOMES

The first patient who was saved by using part of the liver donated by a living donor was a child in Australia with biliary atresia who received a left lateral segment from the mother[18].

Following that seminal case, LDLT prompted an open debate that led to recognition of the procedure as ethically sound, notwithstanding the risk of death and morbidity for the donor[19].

The basic principles of live donation are that the potential donor must be medically fit, genetically or emotionally related to the donor, free from any pressure and material interests (financial or otherwise). In order to reduce the risks associated to donor hepatectomy as much as possible, extensive, multidisciplinary donor evaluation performed on using specific protocols is mandatory.

Medical donor evaluation is conducted by a physician who acts as the donor's advocate, having as sole objective the physical and psychological safety of the donor[20]. An accurate and comprehensive step-by-step work-up protocol for donor evaluation has been designed in our center in order to ensure donor safety and also to confirm that the donor is capable of providing a suitable graft for the recipient. The evaluation process is completed in 3 d, with blood work, ultrasound and consults on the first day; Volumetric Angio computed tomography Scan and Cholangio nuclear magnetic resonance imaging on the second day in order to study potential anatomical abnormality of portal vein (PV), HA, hepatic venous outflow and bile duct. The liver biopsy on the third day has the objective of discovering pathological conditions which might pose a risk both to the donor and the recipient; fatty liver infiltration is the most frequent pathological finding that contraindicated donation if more than 30% of hepatocytes show steatosis. In some transplant centers, only potential donors with a body mass index (BMI) greater than 25 undergo liver biopsy, on the assumption that only in these individuals is there a significant presence of steatosis. However, even in individuals with BMI below 25, steatosis in up to 33% of the cases has been reported. Furthermore, liver biopsy can show the presence of other pathological conditions which contraindicate liver donation.

At our institution, of 256 individuals who underwent evaluation as potential donors, only 80 qualified and donated part of their liver[1]. Donor mortality is a rare but catastrophic event which has an incidence between 0.13% (for pediatric donation) and 0.2% (for adult donation). Most operative complications are minor and are managed medically. Biliary complications range from minor leaks from the cut surface to major leaks and strictures requiring endoscopic, radiological or surgical interventions. Donors and their family need to be fully informed of the risks of live donor liver donation. Currently, in experienced centers, live liver donation can be considered a safe procedure.

Although long-terms studies on the outcome of liver donation are still lacking, it has been clearly shown that within 4 wk to 8 wk liver volume returns to almost its original level with no significant alterations of liver function. Most of the donors return to a normal life in a few weeks.

## LIVE-DONOR HEPATECTOMY: TECHNICAL ASPECTS

### *Adult to adult*

Initially, we performed 2 left hepatectomies (segments 2-4); however, we abandoned this procedure in favor of right hepatectomy, as described herein. The operation was performed using a bilateral subcostal incision with an upper midline extension (Mercedes incision). Mobilization of the right liver lobe and skeletonization of the retrohepatic inferior vena cava with ligation of all accessory hepatic veins was performed using the usual piggyback technique but with preservation of accessory veins larger than 0.8 cm in diameter. Intraoperative cholangiography was always performed, as was intraoperative ultrasound, to confirm the transection plane, which follows the Cantlie line with no vascular occlusion. Isolation of the right HA was always performed, and isolation of the right PV was performed prior to the parenchymal transection only when feasible. The middle hepatic vein always remained with the donor. We should point out that in a few cases other centers left the middle hepatic vein with the right graft for safety reasons and for technical issues related to the anatomy. The following 4 sequential techniques were performed for the hepatic parenchymal transection: parenchyma tissue fragmentation and skeletonization of biliovascular structures with the ultrasonic dissector or water pressure dissector; vascular hemostasis and biliostasis of the minuscule biliary ducts using microsurgical clips and a radiofrequency dissector; sectioning of fibrous and vasculo-biliary structures with electrocautery; and suction of organic and irrigation fluids mixed with parenchymal detritus using an aspirator and the integrated aspirator in the ultrasonic dissector[21-24]. The ultrasonic dissector was set at 90% amplitude, with high tissue selection, and the

irrigation rate was 5 mL/h, with suction set at maximum strength. This was applied after the liver capsule was opened using diathermy, with coagulation at 70 W. The radiofrequency setting was 75 W, and the irrigation rate was 2.5 mL/h to 5.0 mL/h. The division of the biliary duct was performed just before the end of the parenchymal transection, using sharp instruments rather than cautery to avoid damage to the bile duct. Initially, we did not use donors with more than 1 duct draining the right lobe, more than 1 artery for the right lobe, or trifurcation of the PV[24,25].

We later adapted our technique to overcome these anomalies. In the case of a right dominant hepatic vein, when a tributary of the hepatic venous system larger then 5 mm was noted in the transection plane, a test clamp was used to determine whether the liver parenchyma became dusky, after which a decision was made as to whether to preserve the branch. In the case of a double PV for the right lobe, a Y graft to the main bifurcation of the recipient PV was performed on the back-table in 4 cases. Jump grafts for accessory hepatic veins were performed with interposition iliac vein grafts from cadaveric donors, always on the back-table. Once removed, the right lobe was flushed with 3 L of University of Wisconsin solution, only through the portal system.

### Adult to pediatric

In left lateral segmentectomies for pediatric transplantation, the operation was performed with a Mercedes incision or through an upper midline incision, according to the size of the patient. Mobilization of the liver and skeletonization of the left hepatic vein, left PV, and left HA were accomplished using the surgical technique routinely adopted by our team for in situ split-liver harvesting[26].

The subsequent surgical steps of parenchymal transaction were the same as described for right hepatectomy.

## LIVE-DONOR HEPATECTOMY: OUTCOMES

### Recipient outcomes

In a report of the adult-to-adult liver transplantation (A2ALL) consortium from 9 US centers, the one-year graft survival in 385 recipients was 81%. The main factor influencing the outcome was found to be center's experience. In centers with a less than 20 case experience, an 83% higher risk of graft failure ($P < 0.0045$) was reported. The incidence of biliary complication was 30%. In a study comparing the outcome of 764 patients who underwent LDLT with 1470 matched patients receiving cadaveric grafts, 2 years patient survival was similar (79% and 80%, respectively). However, graft survival of LDLT was significantly worse than with cadaveric grafts (64.4% *vs* 73.3%). The "small-for-size syndrome" is a potential complication specifically related to LDLT unless the volume of the donated liver is adequate to meet the recipient's metabolic needs. A Graft-Recipient Weight Ratio (GRWR) greater than 0.8% is essential to avoid the "small-for-size syndrome" and increase the graft's survival.

Due to the regeneration of the donated liver, higher incidence of hepatitis C virus (HCV) recurrence was considered to be a possible drawback of living transplantation. However, at 1 year, 3 years and 5 years after cadaveric liver transplantation recurrent chronic hepatitis in the graft occurred in 20%, 60%, and 80% of the patients respectively. After LDLT, symptomatic HCV recurrence was reported earlier and in a more severe form by several centers and liver regeneration was identified as a possible contributing factor[27].

### Donor outcomes

Donor safety has to be the first priority during the entire process of living-related transplantation, from the first day of evaluation through the entire follow-up period. A recent systematic review that focused on adult donor outcomes concluded that there are small but real risks when using the right lobe for living donors, although it also claimed that nearly all donors returned to normal liver function within 6 mo[28]. Numerous single-institution series have reported their complications for liver living-related donors and a recent large study from the US reported an analysis of administrative data on a group of 433 right- and left-lobe living donors identified as being at risk for perioperative complications[29,30]. The ethical debate over the potential risk to the donor renders this field of surgery controversial and, as a result, we believe, worthy of reports on all single center experiences. A wide range of living donor complication rates are reported in the literature, with an estimated risk of mortality and morbidity after right hepatectomies for living related liver transplantation (RHLD) of 0.4% and 35%, respectively. Overall, the complication rates range from 0% to 67%, with an overall crude complication rate of 31%[31,32]. The literature has reported 11 deaths, and 2 liver transplants in donors who have undergone RHLD. Additionally, one donor is in a persistent vegetative state after donation[20]. Despite the extensive resorting to living-donor donation in South-East countries, only one donor death was reported in Asia[33].

## CONCLUSION

Lortat-Jacob reported the first anatomic right hepatectomy in 1952[21]. Since then, and particularly in the last 2 decades, hepatic surgery has achieved important technical breakthroughs including intermittent portal triad clamping, total vascular exclusion, preoperative PV embolization with 2-stage hepatectomy, and sophisticated methods of parenchymal transection.

In the early 1980s, on the basis of the lessons learned from surgical anatomy applied to oncologic surgical resection, livers procured from cadavers were resected ex situ to develop a smaller left lateral segment graft (segments Ⅱ and Ⅲ) of a size that could be transplanted into small

children. The right part of the cadaver donor liver was discarded. At the end of the 1980s, the conflict between pediatric and adult waiting lists was addressed by further evolutions in the surgical technique of liver transplantation: SLT and living-donor liver transplantation. These procedures had the common objective of enabling transplantation in children without interfering with transplantation in adults.

Split liver and LDLT are the most significant technical evolutions of liver transplantation which, over the last decade, have contributed to dramatically reduce pediatric wait list mortality and the gap between need and availability of liver grafts for adult patients. To further improve the outcome of these complex operations, refinements in the surgical technique and better comprehension of the interrelations between liver regeneration and portal hypertension will be needed. Although improved surgical techniques and perioperative management are now a reality in referral centers for liver surgery, there remain several issues that make this procedure extremely worrisome when performed in healthy individuals such as living donors[31].

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