Liver splitting and living donor techniques

M Malagó, X Rogiers and C E Broelsch
Department of Surgery, Universitäts-Krankenhaus Eppendorf, Hamburg, Germany

Split liver transplantation (SLT) and living related transplantation (LRT) have been developed following advancements in liver surgery. In experienced hands they can yield results comparable to full organ liver transplantation. They are today a reality which has to be implemented and used more widely. LRT is the best procedure available and should be the method of choice despite the high success of SLT. Any method safely enlarging the pool of donors has to be utilized, especially in view of the possible future application for adults. The procedures should be initially performed and tested in centres specialized in liver transplantation and liver surgery, with the aim of making the techniques more widely available in the future. High ethical standards are required to perform LRT. In the short term, SLT and LRT are the methods more apt to increase the organ pool and thus decrease pre-transplant mortality both in children and adults.

Liver transplantation has evolved from an experimental procedure to become the standard treatment for terminal liver failure in a period of 30 years. Its success has led to its use in a broadened spectrum of indications and, as a result, to an increased demand for the procedure itself.

Despite the employment of standard resources as the acceptance of marginal livers and the application of social and legislative measures, the number of donor organs available has reached a plateau worldwide. In some regions, like Germany, it has even decreased in the last few years. The limit on the use and expansion of liver transplantation is now the availability of organs.

Since the early 1980s, the resulting mortality of patients on waiting lists has led our group to develop segmental liver transplantation: a number of techniques which foresee the size reduction of the liver. This is attainable thanks to the regenerative potential of hepatic tissue apt to autoregulate itself and grow or shrink in the recipient to meet the needs of the patient. This is particularly important in children. Indeed, paediatric liver transplantation has been the driving force to develop these innovative techniques because, in children, the shortage of organs has been more critical. These techniques have already started to benefit the adult population with split liver transplantation (SLT). They could be further successfully applied in adult patients where they have the potential to strongly impact on the future of liver transplantation.
Liver splitting and living donor techniques

Segmental liver grafts

According to Coinaud, the liver can be divided into eight segments. The anatomical knowledge and the practice of resectional liver surgery have led the way in the use of liver segments as grafts: a whole liver can be reduced to smaller functional units by means of anatomical hepatectomies.

Not every single segment can be transplanted separately, since, in order to be used as a graft, a segment requires: an independent blood inflow (portal vein and hepatic artery) and outflow (hepatic veins), as well as a usable biliary drainage and sufficient parenchyma providing adequate function to support life. The grafts commonly used are the full right graft (segments V, VI, VII, VIII ± I), the full left graft (segments II, III, IV ± I), the left lateral lobe graft (segments II, III) and the right extended graft (segments I, IV, V, VI, VII, VIII) as summarised in Table 1.

There are some guidelines for selecting the donor-recipient size match to meet organ size discrepancy between donor and recipient, despite a high variability of relative size within liver segments. The constitution of donor and recipient, as well as the presence of ascites in the recipient are important determinants. The type of graft chosen, however, depends mostly on the size disparity between donor and recipient. For an extended right or a full right graft standard liver transplantation, size matching guidelines can be followed. A full right graft can fit in a recipient up to half the size of the donor. For a full left liver graft, a size disparity up to 4 to 1 is possible. With a left lateral lobe, a disparity of 10 to 1, and sometimes more, can be managed. The type and size of the segment should, however, be decided on an individual basis, after visualization of the donor liver and the recipient’s hepatic fossa, since the relative size of the individual segments can be very variable.

A left lateral lobectomy can procure grafts for patients up to 25-30 kg, according to the individual case. Transplantation of larger recipients requires a larger liver mass which can be provided by left or right hemihepatectomies. Once the graft volume is known, as in LRT, safe recommendations are a graft/recipient body weight ratio of 1/100, or 1%.

A limit to the full exploitation of segmental liver transplantation is the use of small grafts in large size recipients, adults for instance, since small grafts can provide a limited function until their regeneration occurs.

Segmental grafts can be obtained from these surgical techniques: reduced-size cadaveric liver transplantation (RLT), split liver transplantation (SLT) and living related liver transplantation (LRLT). The first two modalities utilize livers from cadaveric donors, while in LRLT the graft is obtained from a living donor. Yet the only techniques which can save, or increase, the number of grafts are LRLT and SLT.
Table 1 Different types of reduced size liver allografts

<table>
<thead>
<tr>
<th>Type of graft</th>
<th>Liver segments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full right</td>
<td>V VI VII VIII+I</td>
</tr>
<tr>
<td>Full left</td>
<td>II III IV+I</td>
</tr>
<tr>
<td>Left lateral</td>
<td>II III</td>
</tr>
<tr>
<td>Right extended</td>
<td>I IV V VI VII VIII</td>
</tr>
</tbody>
</table>

In RLT, in fact, since the non-used part of the liver is discarded, usually the larger right side, organs are only shifted from the adult to the paediatric population, without actual increase of the organ pool.

The first size reduction of a liver for a RLT was performed at New York Hospital in 1989\textsuperscript{3} and then reproposed almost simultaneously by Bismuth and Broelsch in 1984\textsuperscript{4}. RLT has since been used in children with results comparable to full liver transplantation and has demonstrated the feasibility and safety of segmental grafting\textsuperscript{6}.

Nowadays, RLT should be considered obsolete and be reserved for livers not amenable to splitting: marginal and average quality organs, traumatized donor livers and small paediatric donor livers to be used for very small recipients.

Living related liver transplantation (LRLT)

In LRLT, a segmental graft is obtained by means of a partial hepatectomy from a living donor, usually a parent or relative. The first LRLTs were performed in Brazil and Australia in 1989\textsuperscript{7,8}. In the same year, our group, then at the University of Chicago, started the first series with an appropriate ethical approach\textsuperscript{9,10}. After the successful accomplishment of RLT and the proof of the possibility to split a liver in two, LRLT was a consequent logical step in overcoming organ shortage. Again the trigger for the development of LRLT was the lack of donors in a paediatric setting.

In the beginning, harsh criticism of the ethical issues involved and technical difficulties hampered the spread of this excellent procedure. Nevertheless, LRLT has now been accepted and is an established transplant modality.

More than 700 LRLTs have been performed in about 50 centres around the world. Approximately half of these have been performed in countries without brain death law\textsuperscript{11}.

Ethical issues are of utmost importance because of the involvement of a healthy donor. Donation has to be non coerced and spontaneous, especially when no alternative for the recipient is available, as in high
Liver splitting and living donor techniques

urgency settings and in countries without cadaveric donation. The donor is well informed about alternatives and a voluntary consent is obtained twice, at different times.

The donor work-up is directed to the evaluation of the operative and psychological risk and the assessment of the suitability of the donor graft for a given recipient. The safety of the donor is the main concern in LRLT.

Pre-operative liver volumetric measurement has been classically carried out with computed tomography. Angiography is still the gold standard for vessel assessment. It seems that magnetic resonance imaging has the potential to provide volumetric information, show more detailed liver anatomy and eventually demonstrate bile duct anatomy and probably accurate vascular supply, all noninvasively. Accessory or multiple hepatic arteries and benign tumors, like FNH or hemangiomas, are not an absolute contra-indication to living donation.

In our programme at the University Hospital Eppendorf, 64 LRLTs have been performed using a selection pool of 192 donors. The definite risk of a liver living donor procedure is quantifiable from two postoperative deaths worldwide. The advantages are mainly the possibility of a planned, elective operation, the superior organ quality, the relief of the waiting list and the economical advantage in comparison to cadaveric liver transplantation, quantifiable to a 20–30% cost reduction in our hospital. Secondary advantages are relief of stress for the waiting family, organizational and logistic facility with respect to RLT or SLT and possibly a long term immunological advantage.

Implantation follows standard techniques with minimal modifications. Today, the use of interposition grafts for the vessels is avoidable: in our series, direct portal vein and arterial end to end anastomoses could be performed in all the last 34 cases. Immunosuppression follows a triple regimen with low dose cyclosporin A, steroids, and azathioprine.

According to the Hamburg International Living Donor Liver Transplantation Registry, the most frequent procedure is a left lateral heptectomy, including segments II and III, which has been performed in 76% of the cases. A left heptectomy has been carried out in 20% and atypical procedures in the rest of the cases. A left lateral lobectomy was mostly selected, since the recipients are small children and because of the decreased chance of complications in the donor, postoperative liver insufficiency being the most feared. Two right living donor heptectomies have been done: one in Kyoto and one in Hamburg. Recently a larger series has been performed in Hong Kong. Safe guidelines should leave 45–50% of the total liver mass in donors with optimal liver function.

The results of LRLT are excellent in elective population with survival rates of 80–90%, . The overall 1 year survival according to the ILDLR
is 73%. In our programme, it is 72% and it has achieved 96% in the last 2 years, also thanks to a better patient selection allowed by SLT.

**Split liver transplantation (SLT)**

In SLT, two separate grafts for two different recipients are obtained from one single cadaveric donor liver. After the success of RLT, in 1988 Pichlmayr first \(^{17}\), and soon after Bismuth \(^{18}\), performed the first SLT. Our group at the University of Chicago published the first large series in 1990 \(^{19}\).

Classically, a full right and a left lateral lobe allograft can be obtained performing a bench hemihepatectomy just to the left of the line of Cantilie; segment IV is discarded and, in order to obtain a left lateral segment allograft, the further parenchymal partition is carried to the right of the falciform ligament. Alternatively, the liver partition border can be at the line of Cantilie producing a full left and a full right liver allograft, retaining segment IV on the left side.

Initially, this technique, due to multiply the number of available organs, was plagued with complications, such as primary non function, bleeding and biliary fistulas. Suboptimal results were also due to its use in critically ill urgent patients. Moreover, a major problem was identified in the long ischaemic times again particularly on the right side, the larger graft commonly used for adults. All these problems have retarded the acceptance and the application of SLT, particularly in the adult population.

Our group lately has further improved technique and strategy with the "in situ" split, modifying: (i) the line of partition of the liver which was moved to the left at the falciform ligament line so to obtain a right extended and a left lateral grafts; and (ii) the procedure was performed in the heart beating cadaveric donor to decrease cold ischaemic times and carry out a more anatomical dissection trying to preserve the artery of segment IV \(^{20}\).

Thanks to these technical refinements, a better patient selection and the learning curve required because of the technical complexity of the procedure, SLT has reached results comparable to standard full organ \(^{21-23}\). SLT is now gaining popularity as a tool to be used both in paediatric and adult liver transplantation. To date, it is still used for a child and an adult and its potential, *i.e.* the application in adults, has not yet been fully exploited.
Future perspective

In the absence of new treatments to decrease the incidence of diseases causing end stage liver failure, the demand for liver transplantation and, thus, the organ shortage are expected to increase further in the future. As demonstrated in our programme, correct utilization of SLT and LRLT can presently almost annihilate the mortality in the paediatric population\textsuperscript{24}. In adult liver transplantation, which accounts for approximately three-quarters of the consumption of organs, the pre-transplant candidate mortality instead is still an acute problem: last year, in our programme, it reached 12%, despite the use of SLT and LRLT.

In the present steady state of the donor pool, the solutions are limited and more investigation is needed to solve the donor–recipient gap. Major advances are needed to have xenotransplantation\textsuperscript{25} and hepatocellular transplantation\textsuperscript{26} available in the clinics in the near future.

The application of SLT in adults can help in solving this problem. A limitation in the use of LRLT or liver splitting in adults is the employment of the smaller grafts, the left side. The minimal amount of liver transplantable is not really known, but it seems that a safe estimation is around 50% of the theoretical liver volume, even though sporadic smaller size fitting has been performed\textsuperscript{27,28}.

Our aim is to use ‘small for size’ segmental grafts from SLT and LRLT donors in adults. Technical improvements are being directed towards increasing the quantity, \textit{i.e.} the liver mass to be transplanted, and the function of the segmental grafts. Induction of early regeneration, avoidance of rejection, ischaemic or hyperperfusion injuries will also be addressed. One possibility is to adapt the technique to use left lateral grafts for smaller adults, or to apply technical modifications, such as turning again to the line of Cantilie for splitting, to yield a larger left graft suitable for adults, at the price of possible complications, as in the early SLT experience. Lo and Fan succeeded in transplanting ‘right extended grafts’ from living donors at the price of some donor complications\textsuperscript{29}. Due to this extra risk for the donor, right lobe living donor transplantation has to be used judiciously in the western world.

Strategic changes are also possibly needed. The bioartificial liver\textsuperscript{29}, or a type of liver replacement, should be definitely investigated not only for acute liver failure, numerically a relatively minor problem, but as temporary support for segmental grafting. The liver substitute could be used \textit{ad interim} in the critical immediate postoperative period when detoxification can favour recovery of the graft. Function can be maintained until regeneration of the transplanted segment has occurred at a significant degree to sustain life.

Auxiliary liver transplantation in acute liver failure is already a reality and should be further implemented\textsuperscript{30}. The use of auxiliary grafts in
cirrhosis could be considered eventually, but only after other measures fail to solve the organ shortage problem.

All these methods could help fill the shortfall between organ availability and recipients' needs, waiting for the advent of clinical xenotransplantation.

References

6. Orte JB, de Ville J, Sokal E et al. Size reduction of the donor liver is a safe way to alleviate the shortage of size matched organs in pediatric liver transplantation. *Ann Surg* 1990; 211: 146–57
11. The International Living Donor Liver Transplantation Registry. UKE, Hamburg, Germany; 1997
Liver splitting and living donor techniques


26 Dixit V. Transplantation of isolated hepatocytes and their role in extrahepatic life support. Scand J Gastroenterol 1995; 208 Suppl: 101-10


