Innovative surgical techniques in liver transplantation

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ABSTRACT

Liver transplantation is the only effective treatment for end stage liver disease. This fact has been accepted since the beginning of the 1980s. Organ scarcity has been a limiting factor to apply this method on all patients with end stage liver disease. The situation is even worse for the pediatric age group due to difficulty in getting size matching grafts. Innovative techniques in the form of reduced size, split-liver and living related liver grafting have been effective tools to reduce the mortality on the pediatric waiting list. The use of reduced-size grafts has become obsolete due to the fact that it shifts organs from the adult age group into the pediatric age group. Both split-liver and living related grafting are the ultimate solutions to organ scarcity. Until other solutions are available for clinical use in liver transplantation, these techniques have to be applied with great efficacy by the transplant centers.

Keywords: Liver transplant, split living related transplantation.


Since the performance of the first liver transplantation in a child in 1967,\textsuperscript{1,2} this procedure has developed to be the standard treatment of children with acute or chronic terminal liver disease. Liver transplantation has also become an established treatment for liver-based metabolic diseases.\textsuperscript{3,4,5}

Despite the continuously improving results, the progression of pediatric liver transplantation was hampered by the lack of size matched donors.\textsuperscript{6,7} While most children needing liver transplantation are below 15 kg of weight, only a few donors are found in this weight class.\textsuperscript{1}

This problem was solved in 1984, and after, by the use of reduced-size liver grafts (RLT). Several more efficient techniques were developed from this technique: Split-liver transplantation, living related liver transplantation and auxiliary liver transplantation.\textsuperscript{6,9,10,11,12}

Two major events in liver transplantation history have been of great support for the development of these new techniques. The development of the University of Wisconsin solution as a more efficient conservation solution, allowing for longer cold ischemia and the introduction of Cyclosporin A, which virtually tripled the patient and graft survival after liver transplantation.\textsuperscript{1,4,5}

Reduced-size cadaveric liver transplantation. In this technique, a liver resection is performed on the procured organ on the back table in order to obtain a transplantable but smaller graft which matches the small size recipient.

In 1984, Bismuth reported his experience with reduced-size liver graft and its use in liver transplantation.\textsuperscript{10} This example was taken over by the groups of Hannover, Brussels and Chicago who gained experience and further improved the procedure. These groups have shown a decline in the mortality of pediatric waiting lists.\textsuperscript{7,10}

Different types of grafts can be obtained by graft reduction. A left lateral lobe graft, consisting of segment II and III allowed transplantation with...
Table 1 - Types of reduced size liver allografts

<table>
<thead>
<tr>
<th>Types of graft</th>
<th>Liver segments</th>
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<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>
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donor/recipient weight ratio up to 10/1 (seldomly even more). A left liver graft (segments I, II, III, IV) can be used with a ratio up to 5/1 and a right liver graft (segments V, VI, VII, VIII) with a ratio of up to 2/1 (Table 1). 8,38

Several groups in Europe and the United States have shown that this technique is a safe way to alleviate the mortality on the pediatric waiting list. Graft survival, surgical complications and patient survival are relatively similar to full size organ transplants (29.2% graft loss of the full organ compared to 37.5% for the reduced size). 3

Reduced size grafting, however, causes a shift of organs from the adult donor pool towards the children. In addition, it wastes a substantial volume of functional hepatocytes. Therefore, it was logical to develop a technique in which the other side of the liver can also be used for transplantation. Split-liver technique was first developed by R. Pichlmayer in Hanover in 1988.

In view of the ever improving results of split liver grafting, there is no indication for RSLT any more except for: (1) Traumatized donor livers; (2) Pediatric donor livers.

**Technique of liver reduction.** Liver reduction is performed by doing the appropriate liver resection on the graft on the back table, so that a suitable size matching liver graft is obtained.

The procedure should be performed while the liver is emerged in the iced cooled UW solution so that the liver is not warmed up during the procedure, which may extend up to 2 hours.

The hilum of the liver is usually enclosed with the graft, so that long vessels as well as bile duct are available for the anastomosis. The use of interposition grafts is rarely needed.

For a left lateral graft the inferior vena cava is usually removed. This is optional for a full left graft as the IVC can be removed or included. Its diameter may need to be reduced using a vascular stapler. With a right graft the IVC is usually maintained.

Bleeding from the cut section is usually troublesome in RSL grafts. Its control should be carried out at the time of cutting the liver down by selectively ligating the vessels using fine suture material or surgical clips, the final control of the bleeding is usually done after reperfusion.

**Split liver transplantation (in-situ, ex-situ).** The idea of using one organ as a graft for 2 recipients (one adult and one pediatric, or 2 adults) came as a result from the pressure of organ scarcity especially for the pediatric age group. 12,14,15

The improving knowledge of the liver anatomy, as well as the increasing experience from reduced size transplants has been contributing much in the development of split liver transplantations. Pichlmayer performed the first splitting of a liver in Hannover in 1988. The right graft was given to a 63 year old woman with primary biliary cirrhosis, while, the left graft was transplanted into a 2 year old child with biliary atresia. 12

The first series of split liver transplantations came from the University of Chicago. The reported results were disappointing with a graft survival of 55% and a patient survival of 67% in the first 10 months. 5 The biliary complications were 27%. These results were much inferior to the results from full organ transplantation.

This early bad experience with the split liver technique resulted mainly from the combination of using it only in emergency cases, and in the fact that it was the beginning of the experience. These results reduced the interest in this technique for some years. The continuing organ shortage forced a renewed interest in split-liver transplant action by different groups in Europe.

The European experience with the split technique for the period between March 1993 and October 1996, as presented at the split-liver registry in Brussels, May 1996, showed that in 140 grafts the 6 month patient survival was 84%, with graft survival of 80%. These results were as good as those from whole organ transplantations' (DeVilla de Goyet, split-liver transplantation Europe 1988 to 1995). 16

The classical liver splitting usually yields a full right and a left lateral lobe allograft which can be obtained by performing a bench hemihepatectomy just to the left of the line of Cantlie, segment IV is discarded. In order to obtain a left lateral segment allograft, the further parenchymal partition is carried to the right of the falciform ligament. 7

Alternatively, a full left and a full right liver allograft can be obtained by placing the line of division at the line of Cantlie and retaining segment IV on the left side. This technique is unfortunately accompanied by complications such as bleeding and biliary fistulas. 17,18

Based on the experiences from the living related liver transplantations, the first splitting of a liver in the heart beating cadaveric donor was performed in Hamburg, May 1995. 19 This technique aims to avoid prolonged cold ischemia time, and to insure the anatomic integrity of segment IV vascularity before implantation.

The early experience with the procedure as reported by the Hamburg group, 7 in-situ splittings
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(patients survival of 92.8% and graft survival of 85.7% in 6 month follow-up). The biliary complications and primary non function which were previously reported in the ex-situ split liver technique were absent.

**Surgical procedure: (in-situ splitting).** The operation starts with a sternolaparotomy and evaluation of the liver. The infrarenal aorta and vena cava are freed and controlled so that rapid perfusion is possible in case of donor instability. The left lateral lobe (segments II, III) is then mobilized. The left hepatic artery and, if large and long enough, the specific artery to the left lateral lobe are identified and prepared. The same procedure is performed with the left portal vein.

The right border of the round ligament is next dissected. All the branches to segment IV are ligated and divided in order to get the line of parenchymal division clear of portal triads. The left hepatic vein is next dissected free from the cava extra-parenchymally. Using the clamp crush technique or Harmonic ultrasound disector, the parenchyma is progressively transected on the line just to the left of the round ligament (no vascular exclusion is performed till now). Hemostasis is insured on both sides of the section plane. At this stage the 2 parts of the liver are completely separated from each other and independently perfused. After clamping the vessels of the left lateral lobe, the graft is then removed and perfused with the UW solution. It is then packed while completely emerged in the iced cooled preservation fluid.

The implantation of the graft is usually performed using standard technique. The use of vascular interposition is usually not necessary.

Our policy at present, is that any liver offered to our center with reasonably good parameters is considered for splitting procedure. The recipients on our waiting list are consented from the beginning to receive a full organ or a split graft.

During the period from first January, 1994 until October 1996, 48 split liver transplantsations have been performed in our unit at the University Hospital Eppendorf, Hamburg, 25 of them were in-situ and 23 were ex-situ technique.

The in-situ splitting produced 13 left lateral grafts and 12 right grafts. The patients age ranged between 0, 33-63 with a mean age of 22 years. The weight ranged between 5-90 kg with a mean weight of 37 kg.

The overall patient survival is 88% (21/24). The graft survival is 76% (19/25). The graft survival rate varies between 92% for the right graft and 54% for the left sided graft. The patient survival in case of the right graft is 92%, which is comparably better than that for the left liver graft (83%).

The major advantages of this procedure over the ex-situ split is to reduce the rate of biliary complications as well as the occurrence of primary dysfunction of the graft. In our series, we have seen one case of biliary complications and 2 cases of PNF. No case of primary poor function was observed.

In-situ splitting of the liver provides 2 organs with optimal quality for liver transplantation. In combination with living donor liver transplantsations, it is hoped that these techniques will ultimately expand the donor pool by surgical innovations.

**Living related liver transplantations (LRLT).** The concept of living related liver transplantsations (LRLT) has now evolved into reality, but this was only possible by the recent advances in hepatic surgery: the improved understanding of liver anatomy, the very remote operative risks of partial heparectomy in non cirrhotic patients and the widespread success with reduced size and split liver transplantsations.

The remaining obstacle that had to be overcome before the program of LRLT could be initiated was the ethical dilemma of subjecting a healthy person to major hepatic resection to obtain the graft. The evidence for a substantially low risk to the donor has been derived from results of hepatic resections for benign liver disease in comparable cohorts of patients. The advanced surgical experience as well as the intensive care treatment render this operation with a calculable risk for the donor of less than 0.4%.

This operation was proposed as a theory by Smith in 1969. It was Raia et al in Brazil, 1988 who performed the first living related liver transplant. The operation was technically successful but the recipient died of a fatal transfusion reaction.

Subsequently, Strong et al in Australia reported a successful case of liver transplantation in a child by using the left lobe of the mother liver. However, the first center with the background of extensive experience in liver transplantation and of reduced size liver transplantation to establish a fully structured living related liver program was the University of Chicago group.

Up to now, more than 600 LRLT’s have been performed in 45 centers around the world (LRLT registry Hamburg, Germany). Approximately half of these have been performed in countries without an established brain death law.

The graft in LRLT is obtained by means of a partial heparectomy from a living donor, usually one of the parents. The operation should be safe and preserving sufficient tissue as well as liver function in the donor, at the same time providing an adequate graft for the recipient.

Safe size matching guidelines require a graft/recipient body weight ratio of 1/100. Even though the liver volume to BW ratio is not constant during the growth period, the relationship between the total liver volume and the body surface area in adult and pediatric population can be established, and should provide useful guidelines for the preoperative
estimation of standard liver volume in recipients. Some centers have used ratios of 0.6%-0.8% successfully.\textsuperscript{36,27}

Preoperative liver volumetric measurement has been classically carried out with CT scan. It seems that MRI has the potential to provide accurate information regarding liver volumetry, show more detailed liver anatomy and eventually the bile duct anatomy noninvasively.

An angiogram is recommended to determine the vascular anatomy of the donor liver, benign liver lesions such as hemangiomas, Follicular Nodular Hyperplasia (FNH) and the presence of accessory or multiple hepatic arteries are not an absolute contraindication for living donation.\textsuperscript{28}

In order to procure a graft of excellent quality, avoiding traumatic and ischemic injury, a hepatectomy without vascular exclusion is performed. The most frequent procedure is a left lateral hepatectomy including segments II and III. Since it carries lesser risks for the donor and provides adequate tissue mass for most of the pediatric recipients (patients up to 30 kg, according to the individual case).\textsuperscript{29}

**Donor operation.** The operation on the donor is performed through an upper abdominal "mercedes incision". Confirmation of the preoperative angiography on the vascular supply of the liver is carried out by dissection of the hepatoduodenal ligament. It is imperative to dissect only the left side of the ligament to avoid injuries to the right liver. The vessels should be freely dissected only to the bifurcation. A segment IV artery should be preserved if found to be arising from the right hepatic artery. The bile duct is not dissected at all.

Next, the dissection is carried out at the right side of the round ligament, at the recessus of Rex. The left hepatic vein is lastly dissected extraparenchymally. If the isolation of this vessel is difficult at this stage, it is advisable to perform it at the end of the parenchymal phase.

The bile duct is isolated and sharply divided at the hilar plate intraparenchymally during the hepatectomy. A sharp knife is usually used for this purpose.

The hepatectomy is performed a few millimeters to the right of the faliform ligament using the crush clamp technique or Harmonic scalpel (Ethicon) ultrasonic dissector. Vessel clamping and division is carried out at the end of the parenchymal phase.

**Recipient operation.** The recipient should be transplanted in an elective fashion. Implantation is similar to segment II and III reduced size liver transplantations,\textsuperscript{13} with preservation of the vena cava. The difficulties of the left lateral living related graft are the short outflow vein cuff as well as the short vessels and the bile duct at the cut section.

A key factor for the success of the operation is the hepatic vein positioning and reconstruction. The vein is anastomosed as proximal as possible on the vena cava either to the enlarged left-middle common vein orifice or to a new custom made vena cava orifice. The graft should be positioned so that the cut section faces the posterior right upper quadrant at the right of the vena cava.

All anastomosis are carried out with long term absorbable fine suture material and with the use of microsurgical loupes especially for the hepatic artery and the bile duct.

The bile duct anastomosis is an end to side Roux-en-Y hepaticejunostomy. Two bile ducts are present in one 3rd of the cases.

**Adult LRLT.** Transplantation of larger recipients requires a larger liver mass which can be provided by left or right hemi-hepatectomies. Careful donor evaluation and accurate liver volumetry are needed to avoid operative complications due to reduced liver mass, especially after right or full left hepatectomy. One should leave 45-50% of the total liver mass in donors with optimal liver function.\textsuperscript{29,30,31,32} The ethical discussion, in view of the potential risk for the donor is carried differently in countries with or without cadaveric liver donation.

The world experience on LRLT until December 1995, is summarized in Table 2.

From October 1991 until January 1997, 64 living-related liver transplantations were performed at the University Hospital Eppendorf, Hamburg, Germany.

LRLT is now a well established option in pediatric transplantations which yields superior results, the overall one year survival according to the ILD LR is 73%. In our program it is 72% and it has achieved a 96% in the last 2 years.

Conceptually, the real benefit of this procedure lies

<table>
<thead>
<tr>
<th>Rate %</th>
<th>No. LRLT</th>
<th>Survival</th>
</tr>
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<tbody>
<tr>
<td>1. Tanaka, Ozawa (Kyoto, Japan)</td>
<td>125</td>
<td>89%</td>
</tr>
<tr>
<td>2. Broelsch, Rogiers (Hamburg, Germany)</td>
<td>52</td>
<td>87%</td>
</tr>
<tr>
<td>3. Otte (Brussels, Belgium)</td>
<td>30</td>
<td>96.6%</td>
</tr>
<tr>
<td>4. Emond (UCSF, USA)</td>
<td>20</td>
<td>100%</td>
</tr>
<tr>
<td>5. Heffron (Omaha, Nebraska, USA)</td>
<td>26</td>
<td>87%</td>
</tr>
<tr>
<td>6. Hashimoto (Nagoya)</td>
<td>13</td>
<td>61.5%</td>
</tr>
<tr>
<td>7. Belghiti (Clichy)</td>
<td>11</td>
<td>90.9%</td>
</tr>
<tr>
<td>8. Lo (Hong-Kong)</td>
<td>9</td>
<td>89%</td>
</tr>
<tr>
<td>9. Katz (Houston)</td>
<td>9</td>
<td>88.9%</td>
</tr>
<tr>
<td>10. Lee (Seoul)</td>
<td>5</td>
<td>100%</td>
</tr>
</tbody>
</table>
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in the elective timing of the operation. It provides a
graft of excellent quality and permits the choice of
the optimal moment for the transplantation. LRLT
also drastically reduces the mortality on the pediatric
transplant waiting list, indirectly improves the results
of the cadaveric transplantation by shortening
waiting time and allowing transplantation earlier in
the course of the disease.33,34,35

LRLT is in synergy and not in competition with
cadaveric liver transplantation; it is the preferred
modality for elective cases since the start of the
successful split liver transplantation program in
Hamburg. In selected cases, it is a potential solution
for small size adult recipients, especially in critical
blood groups.

The question of living unrelated donation is a
problem of major ethical impact.6 In our view, only
emotionally related donation is acceptable. This
would then have to take place under excellent and
thorough psychological monitoring.

Auxiliary partial orthotopic liver transplantation.
This technique basically involves the placement of
hepatic allografts in a recipient in whom part of the
original liver (native as it is usually called) is left in-
situ; due to a space restriction this graft is usually a
segmental graft.

The graft can be placed either in an orthotopic
position after resecting the recipient left lateral lobe,
or it may be placed in a heterotopic position.
Orthotopic positioning of the graft is the recently
recommended technique.

The 2 commonly accepted indications for this
technique are acute hepatic failure and hepatic based
metabolic liver diseases (such as Criggler-Najjar
syndrome type I).11

The use of auxiliary liver transplantation in
Fulminant Hepatic Failure has been an attracting
option since a recovery of the failing liver is
expected in up to 70% of cases. Afterwards,
the transplanted segment can be removed surgically, or
the immunosuppression is dropped and the
transplanted segment is left to be rejected and
atrophied.

The use of this technique in case of metabolic liver
diseases is promising, since the liver in these patients
is only unable to produce a specific substance, which
can be provided by the transplanted segment.
Indications for which this has been tried are Criggler-
Najjar syndrome and OTC deficiency.

The possibility of taking the transplant segment
from a living donor is quite a new concept, which in
the present situation of organ scarcity is an attractive
option that is going to be an extra solution for the
organ shortage we are facing.

Auxiliary segmental transplantation in case of
metabolic liver diseases may also promote the
concept of gene therapy of the patient’s original
liver.

In our institution, 5 cases of Auxiliary liver
transplantation have been performed during the
period from May 1994 to September 1997. One of
these cases was a living donor graft. The indications
for the transplantation were idiopathic acute liver
failure in 2 cases, metabolic disease in 2 cases, one
case of paracetamol induced fulminant hepatic
failure.

All 5 patients are alive. From those performed on
metabolic disease, one graft was lost due to portal
vein steal syndrome and chronic rejection. The
patient was retransplanted with a full liver graft. In
the 2nd case, the graft is functioning well. Of the
three grafts performed for fulminant liver failure, 2
grafts are atrophied after stopping
immunosuppression because of native liver recovery.
The 3rd one is still functioning.

The main problems with this procedure are usually
the lack of room for the graft in the abdomen, the
difficulty of establishing a sufficient venous outflow
and finally the steal phenomenon which affects the
portal flow to the graft (majority of the blood goes to
the native larger size liver).

Until an effective solution for these technical
problems is well achieved, these techniques have to
be looked at as experimental trials.

In conclusion, with the extensive and very
enthusiastic work of surgeons on both sides of the
atlantic, end stage liver disease changed its concept
from a 100% mortality in a very short period, to a
disease that can be treated with a success rate
equivalent to that of liver transplantation.

This fact applies itself with greater truth to end
stage liver disease in the pediatric group. Only with
the use of those innovative techniques, the high
mortality in this age group on the waiting list could
be reduced from as high as 50% down to the reported
results from our group as well as other groups in
Europe and the United States of less than 3%.

The technique of reduced size liver transplantation
came as the earliest solution to this problem and was
popularized because of its safety as well as applicability to every pediatric liver transplant
program. The big draw back of the technique in
detouring the available organs from adult populations
to the pediatrics group was the main reason for it not
to continue its popularity and end up to be the
solution only for traumatized and pediatric donor
livers.

With the continuation of organ scarcity as a
serious problem, the Split-liver technique was in
theory the best solution for both age groups, since
one donor liver can serve 2 recipients equally.
Unfortunately, the technique at the beginning was
performed in the seriously ill patients; due to this fact
as well as due to its learning curve, the results of this
technique were much inferior than whole organ
transplant.

Only due to the enthusiasm of a few groups in
Europe continuing the work in refining the
technique, the Split technique improved its outcome and reduced the biliary and primary non function complications which accompanied its beginning.

Finally, the new idea of splitting the liver in the heart beating donor, using donor coagulation to control the bleeding from the cut section and saving the time of cold ischemia, this new technique which was invented and popularized by the Hamburg group, 18, 19 seems, from its preliminary results, to be very promising. Graft and patient survival rate is quite similar to whole organ transplantation. 20, 21

Living related liver transplantation has been taking its place and position as the superior technique by the fact that it reduces pressure on the waiting list without consuming organs from the organ pool, because of its superior timing, and because of organ quality. The outcome of the technique in view of graft and patient survival is superior to cadaveric transplantation. 22, 23, 34

The minimal risk to the donor which was proved after performing more than 600 LRLT's in the world, gave this technique a special acceptance especially in those countries with no brain death law.

The widening applications of living related liver transplantation into the adult age group, which, is being developed at several institutions in the world, 30, 31 has been facing the problem of calculating the size of the needed liver volume, 26, 27 and the possibility of exposing the donor to liver insufficiency. Extension of the procedure to transplant non related recipients from living donors has a special aspect of ethical concern that can hinder the procedure for a long time. 26

Auxiliary Liver Transplantation has been used mainly for Fulminant liver failure as well as metabolic liver diseases in children; the procedure has been also extended to use a living related liver graft as a bridging organ till the original organ recovers from failure.

It is only by the optimal use of the available innovative techniques that it is possible to substantially influence the waiting list mortality. Our group managed to reduce the mortality list from 18% in 1992 to 0% in 1995 and 1996. The future should show more frequent use of these techniques among the transplant centers worldwide and ultimately saving the lives of patients with end stage liver diseases.

References