Segmental Grafts in Adult and Pediatric Liver Transplantation
Improving Outcomes by Minimizing Vascular Complications

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IMPORTANCE The use of technically variant segmental grafts are key in offering transplantation to increase organ availability.

OBJECTIVE To describe the use of segmental allograft in the current era of donor scarcity, minimizing vascular complications using innovative surgical techniques.

DESIGN, SETTING, AND PARTICIPANTS Retrospective study from August 2007 to August 2012 at a university hospital. A total of 218 consecutive liver transplant patients were reviewed, and 69 patients (31.6%; 38 males and 31 females; mean age, 22.5 years) received segmental grafts from living donors or split/reduced-size grafts from deceased donors.

MAIN OUTCOMES AND MEASURES Graft type, vascular and biliary complications, and patient and graft survival.

RESULTS Of 69 segmental transplants, 47 were living donor liver transplants: 13 grafts (27.7%) were right lobes, 22 (46.8%) were left lobes, and 12 (25.5%) were left lateral segments. Twenty-two patients received deceased donor segmental grafts; of these, 11 (50.0%) were extended right lobes, 9 (40.9%) were left lateral segments, 1 (4.5%) was a right lobe, and 1 (4.5%) was a left lobe. Arterial anastomoses were done using 8-0 monofilament sutures in an interrupted fashion for living donor graft recipients and for pediatric patients. Most patients received a prophylactic dose of low-molecular-weight heparin for a week and aspirin indefinitely. There was no incidence of hepatic artery or portal vein thrombosis. Two patients developed hepatic artery stenosis and were treated with balloon angioplasty by radiology. Graft and patient survivals were 96% and 98%, respectively.

CONCLUSIONS AND RELEVANCE Use of segmental allografts is essential to offer timely transplantation and decrease waiting list mortality. Living donor liver transplants and segmental grafts from deceased donors are complementary. It is possible to have excellent outcomes combining a multidisciplinary team approach, technical expertise, routine use of anticoagulation, and strict patient and donor selection.

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According to the national data, there are more than 16,000 patients awaiting liver transplantation (LT) in the United States. Every year, only one-third of the waiting list patients undergo transplantation. The overall waiting list mortality rate including those who die waiting or are too sick to undergo transplantation is consistently higher than 18%. Strategies proposed to increase the pool of organs include the use of organs from donors after cardiac death, extended criteria, high-risk donors, and segmental grafts from deceased donors and living donor LT (LDLT).

Living donor LT was first introduced in the pediatric setting and subsequently expanded to the adult population. This procedure has been plagued by concerns over donor safety, relatively higher rates of posttransplant vascular complications, particularly hepatic artery thrombosis (HAT), and biliary complications in recipients as compared with full grafts. To minimize vascular complications, mainly in small-diameter arterial anastomoses, various techniques including the use of microvascular surgery have been described. Use of split liver grafts allows a single organ from a deceased donor to be shared by 2 recipients. This technique was first described almost simultaneously in independent reports by Pichlmayr et al and Bismuth et al and later by others. However, despite meticulous selection of donor organs and advanced surgical expertise for splitting, split liver grafts are still considered extended-criteria allografts based on their outcomes, especially in adult recipients.

Our center is in a United Network for Organ Sharing region where availability of donor organs is scarce. As a result, we rely heavily on the use of segmental allografts. During the study period, more than 30% of all our transplants were segmental grafts, and this increased to nearly 50% in 2012. In this article, we describe our center’s strategy for the use of deceased and living donor segmental allograft in both adult and pediatric recipients. We present our focus on preoperative evaluation, size matching of graft and recipient, surgical techniques, and postoperative outcomes.

Methods

After obtaining approval from our institutional review board, we reviewed our database of all LTs performed during the 5-year period from August 2007 to August 2012 at the Yale-New Haven Transplantation Center. Owing to the retrospective nature of the study, we obtained a consent exemption from our institutional review board. Data on recipient demographic characteristics, the causes of liver failure, donor and graft types, operative techniques, postoperative management, vascular, biliary, and infectious complications, and graft and patient outcomes were retrieved and analyzed.

Preoperative Evaluation

Our living donor selection criteria have been described previously. For split LT (SLT), we prefer to use deceased donors meeting standard criteria. Those criteria have been previously described and include the following: donor age younger than 50 years, intensive care unit stay less than 3 days, last serum sodium level less than 150 mEq/L (to convert to millimoles per liter, multiply by 1.0), alanine aminotransferase level up to 2 to 3 times the reference range, hemodynamic stability, no vasopressor support, and dopamine administration less than 10 μg/kg/min. During split liver procurement, when available at the donor hospital, we use N-acetylcysteine (150-mg intravenous infusion 2 hours prior to procurement) as an oxygen free radical scavenger.

For adult recipients, we prefer a Model for End-Stage Liver Disease score lower than 30. Other criteria for decision to accept segmental grafts include graft weight to recipient weight ratio, body mass index (calculated as weight in kilograms divided by height in meters squared), cause of liver failure, and severity of portal hypertension.

Surgical Techniques

For SLT, 2 principal techniques have been described for splitting a single liver allograft. In situ splitting is performed prior to cold perfusion, and ex situ splitting is done after cold perfusion on the back bench. Although we used ex situ splitting in our early cases, in situ splitting is our currently preferred method. Advantages of in situ splitting include shorter cold ischemia time, which facilitates intercenter sharing, better evaluation of segment viability, and less blood loss on reperfusion. Because in situ splitting requires a lengthy dissection, we plan early and communicate clearly with other procurement teams to facilitate the safe allocation of all recovered organs. The recipient surgery is started only after the graft is determined to be adequate and cold perfusion has taken place.

For LDLT, donor and recipient operations are performed in an overlapping fashion, in adjacent operating rooms by 2 surgical teams. The donor surgery is started first, except in cases of a hepatic malignant neoplasm, where the recipient is explored initially for evidence of unexpected extrahepatic metastasis. An intraoperative cholangiogram is performed on the donor. When the graft is found to be anatomically suitable, the recipient hepatectomy is begun, minimizing cold ischemia time.

For anastomosis, the upper cava anastomosis is performed using the largest diameter possible for outflow while avoiding anastomotic twisting or kinking. For right lobe grafts with multiple hepatic veins, we prefer not to perform complex back-table venoplasty to create a common outflow vessel; instead, our technique is to drain segmental veins directly into the vena cava using interposition grafts. This reconstruction is crucial for venous drainage of segments 5 and 8. (Figure 1) For left lobe grafts, the middle and left hepatic vein orifices are combined and then anastomosed to the recipient cava using 5-0 polypropylene sutures (Figure 2). For infants receiving left lateral segment grafts, the left hepatic vein orifices are combined and then anastomosed to the recipient cava using 5-0 polypropylene sutures (Figure 2).

In adults, the portal vein is sutured with 6-0 running polypropylene sutures with a growth factor. In children, especially infants, the portal vein is anastomosed using 7-0 running sutures for the posterior wall and interrupted sutures for the anterior wall to accommodate the child’s growth.
Hepatic artery anastomoses were done with surgical loupes (magnification ×3.5-4.5). We typically use microsurgical instruments and 8-0 polypropylene sutures in an interrupted fashion. Gentle handling of vascular structures and avoiding redundancy, kinking, and tension are the key elements of our surgical technique.

Biliary reconstruction is done using 6-0 monofilament sutures in continuous fashion. For most of the left lateral segment grafts, we do Roux-en-Y hepaticojejunostomy. For extended right lobe, left lobe, and right lobe grafts, duct to duct anastomosis is preferred. We do not use T-tubes or internal stents for anastomosis.

Immediately after abdominal closure, Doppler ultrasonography is performed in all cases as a baseline study to ensure the patency of vascular structures. Doppler ultrasonography is repeated daily for the first 3 days postoperatively. A low threshold for reexploration is maintained if there is any suspicion of obstruction to the flow. If there are high resistive indices or difficulty visualizing the intrahepatic arterial flow, we routinely use a single 10-mg dose of nifedipine administered intravenously to relieve vasospasm, and we repeat the study.31

Immunosuppression

Our primary immunosuppression protocol for pediatric patients includes interleukin 2 receptor blocker, mycophenolate mofetil, and corticosteroids with delayed start of tacrolimus on postoperative day 3 or 4. Mycophenolate mofetil is withdrawn when the serum concentration of tacrolimus reaches therapeutic level of 10 to 12 mg/dL. Except in autoimmune diseases, corticosteroids are withdrawn at 6 months following transplantation.

For our adult patients, we follow a parallel protocol without the use of mycophenolate mofetil. In adult patients with abnormal renal function or simultaneous liver and kidney transplantation, mycophenolate mofetil is used. Adults and teenagers get a repeated dose of interleukin 2 receptor blocker on postoperative day 4.

Postoperative Management

Recipients of pediatric LDLT and SLT receive low-molecular-weight heparin (enoxaparin sodium) for systemic anticoagulation, once the international normalized ratio is 2.0 or lower, for 7 days. Simultaneously, all the patients receive oral aspirin, 81 mg in adults and 40.5 mg in young children, when the platelet count is higher than 30 × 10^3/μL (to convert to ×10^9 per liter, multiply by 1.0) and there is no evidence of bleeding. For pain management, the dosage of morphine is adjusted according to the weight of the liver graft.

Statistical Analysis

Kaplan-Meier survival curves were used to calculate 1-, 3-, and 5-year patient and graft survival. Data distribution is expressed as mean, median, range, and standard deviation. We used t test or χ² test to make comparisons. All calculations were made using SPSS version 22 statistical software (IBM Corp).

Results

From 218 consecutive LT patients during the study period, 69 (31.6%) received segmental grafts. Demographic characteristics of recipients and donors are shown in Table 1. The indications for LT in pediatric and adult patients are shown in Table 2. Donor and graft types used, ischemia times, and complications are shown in Table 3.

In our series, we had no HAT or portal vein thrombosis. Two patients (2.8%) developed hepatic artery stenosis; one was at the anastomosis, and the other was at the celiac axis level. Both were treated with balloon angioplasty (Figure 3 and Figure 4). The mean (SD) packed red blood cell use was 2.43 (3.28) units. Fourteen patients (20.3%) had 18 biliary complications (26.0%). Among them, 9 (13.0%) had early bile leaks (6 cut surface, 3 anastomotic leaks) and 8 (11.6%) developed late biliary strictures. One patient developed early bile duct obstruction secondary to technical complication and required surgical exploration. Two patients with early anastomotic bile leak also required surgical repair. The rest were managed by interventional radiology. Our surgical site infection rate was 4.0%. No patients died of infectious complications.
The mean calculated Model for End-Stage Liver Disease score was 17 (range, 6-34). Eight patients were listed and transplanted as status 1A and 2 were listed as status 1B, and these patients had no statistically significant difference in graft and patient survival outcomes or complications.

Our patient survival rates in pediatric and adult patients were 100% and 98%, respectively, and their graft survival rates were 100% and 96%, respectively. The Kaplan-Meier survival curves are shown in Figure 5. We lost 2 grafts; both patients underwent retransplantation with deceased donor whole liver grafts. However, 1 patient eventually died of ischemic brain injury and severe rejection.

Discussion

Driven by organ scarcity, development of segmental LT from both deceased and living donors has evolved owing to advancement of surgical techniques, better understanding of intrahepatic anatomy, concept of graft weight to recipient weight ratio, and better postoperative management. Disparity between the number of patients added to the waiting list and the number undergoing LT has been recently discussed by Dienstag and Cosimi.22 A generation ago, Bismuth, Pichlmayr, Broelsch, and colleagues set the stage with their pioneering work in cadaveric split liver grafts and living donor transplantation. Although this is not a new concept for the field of LT, there continues to be skepticism that segmental LT may be less than perfect. This is further complicated by the advent of concepts such as donor-recipient matching using donor risk index and other donor selection characteristics,33 while mortality increases on the waiting list. In this article, we demonstrate the important role of minimizing vascular complications in SLT and LDLT, by refined surgical techniques and anticoagulation protocols with excellent graft and patient survivals. More significantly, segmental grafts can enable timely LT to patients, and with proper donor and recipient selection, outcomes can actually be better than the national average using whole liver allograft.

Both LDLT and SLT require technical expertise and logistical considerations with a perfectly coordinated team effort. Decision making regarding suitability of donor liver for splitting is crucial. In this regard, an experienced procurement surgeon should be involved for both evaluating and performing the in situ splitting procedure. In classic SLT, liver parenchyma is divided to create a left lateral segment graft and an extended right lobe graft (Figure 6). Each technique of splitting the donor liver (in situ and ex situ) has its advantages and disadvantages. Some authors have advocated use of the ex situ splitting technique with survival outcomes and complications comparable to in situ splitting,34 and others have disputed this and shown better outcomes with in situ splitting.35,36 Although in situ splitting is superior to ex situ splitting, for centers with limited manpower, it may be very difficult to perform in situ splitting. We believe having a dedicated in situ splitting team trusted by all centers in the region could be an important strategy to increase the number of high-quality transplantable organs. Ischemia and reperfusion injury is another important factor in determining the complications and outcomes.
Decreasing the allograft ischemia time is an important logistical consideration to minimize ischemia and reperfusion injury and related graft failure. In the LDLT setting, it is possible to control or minimize ischemia time by performing donor and recipient procedures simultaneously or in an overlapping fashion by 2 surgical teams. Indeed, it has been our policy to pay attention to these logistics. As a result, we have achieved a mean (SD) total ischemia time of 75 (21.71) minutes (mean [SD] cold ischemia time, 41 [18.03] minutes; mean [SD] warm ischemia time, 34 [8.65] minutes) in our series.

Prevention and treatment of vascular complications are challenges in segmental LT. In the A2ALL consortium, Othloff et al reported that vascular complications are the most important cause of graft loss in LDLT. Previous large series have revealed a HAT rate of 4% to 15%, the proportion even higher in the pediatric population. Yersiz et al have reported a vascular complication rate of 7% in SLT. Salvalaggio et al have reported that rates of HAT can vary from 2.9% to 16.7% and are potentially related to center volume. Hepatic artery stenosis rates are not commonly reported in the literature but range from 4% to 10%. Recipients with vascular complications are often listed for retransplantation with high priority and may undergo retransplantation with a whole cadaveric organ. This effectively negates the effect of expanding the donor pool.

Our current strategy to minimize these vascular complications relies on implementing principles of microvascular sur-

Table 3. Graft Types, Outcomes, and Complications

<table>
<thead>
<tr>
<th>Variable</th>
<th>Living Donor</th>
<th>Deceased Donor Segmental Graft</th>
<th>Total, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Graft type, No.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ERL</td>
<td>0</td>
<td>11</td>
<td>11 (15.9)</td>
</tr>
<tr>
<td>LLS</td>
<td>12</td>
<td>9</td>
<td>21 (30.4)</td>
</tr>
<tr>
<td>RL</td>
<td>13</td>
<td>1</td>
<td>14 (20.2)</td>
</tr>
<tr>
<td>LL</td>
<td>22</td>
<td>1</td>
<td>23 (33.3)</td>
</tr>
<tr>
<td><strong>Outcome, mean (SD), min</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIT</td>
<td>41 (18.03)</td>
<td>455 (103.86)</td>
<td></td>
</tr>
<tr>
<td>WIT</td>
<td>34 (8.65)</td>
<td>35 (7.41)</td>
<td></td>
</tr>
<tr>
<td>TIT</td>
<td>75 (21.71)</td>
<td>490 (99.71)</td>
<td></td>
</tr>
<tr>
<td><strong>Complications, No.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAS</td>
<td>1</td>
<td>1</td>
<td>2 (2.8)</td>
</tr>
<tr>
<td>HAT</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HVCs</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PVCs</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Biliarya</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biliary strictures</td>
<td>6</td>
<td>2</td>
<td>8 (11.6)</td>
</tr>
<tr>
<td>Cut-surface bile leaks</td>
<td>5</td>
<td>1</td>
<td>6 (8.7)</td>
</tr>
<tr>
<td>Anastomotic bile leaks</td>
<td>2</td>
<td>1</td>
<td>3 (4.3)</td>
</tr>
<tr>
<td>Bile duct obstruction</td>
<td>1</td>
<td>0</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>4</td>
<td>18 (26.0)</td>
</tr>
</tbody>
</table>

Abbreviations: CIT, cold ischemia time; ERL, extended right lobe; HAS, hepatic artery stenosis; HAT, hepatic artery thrombosis; HVCs, hepatic venous complications; LLS, left lateral segment; PVCs, portal venous complications; RL, right lobe; TIT, total ischemia time; WIT, warm ischemia time.

a A total of 14 patients (20.3%) had 18 biliary complications (26.0%).
surgery, such as using microsurgical instruments and magnifying loupes, and following a refined postoperative anticoagulation protocol. As mentioned earlier, gentle handling of vessels during the preparation, using fine sutures in an interrupted fashion via microsurgical instruments, and avoiding tension kinking and twisting are the key elements of creating a perfect anastomosis. Using this technique in 69 consecutive segmental grafts, there were no cases of HAT. Only 2 patients developed hepatic artery stenosis, one of whom received a right lobe graft from LDLT. Another patient received an extended right lobe graft from in situ splitting and developed stricture at the hepatic artery but not at the anastomosis; this was related to ischemic changes in segment 4. Both cases of hepatic artery stenosis presented with cholangiopathy. Balloon dilatation by interventional radiology without stent placement was sufficient to restore normal hemodynamics and both grafts are functioning well, more than a year since their intervention. Other than the use of a segmental graft, there was no common risk factor between these 2 recipients.

Although rare, the risk of portal vein complications, both stenosis and thrombosis, is reported to be greater in segmental LDLT and SLT. Ueda et al\(^4\) in a larger series of pediatric LDLT reported an incidence rate of 8% and Buell et al\(^5\) have reported an incidence rate as high as 30%. This is owing to the technical difficulty in anastomosis of a short portal pedicle of the donor to the recipient portal vein and the mismatch in vein caliber, often requiring an interposition graft. Portal vein complications presenting during the early postoperative period (<3 months) have worse outcomes compared with the late-presenting cases. Early diagnosis is possible with a high index of suspicion, Doppler ultrasonography, and, if required, magnetic resonance angiography. Management with balloon

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**Figure 5. Kaplan-Meier Survival Curves for Grafts and Patients**

A, Graft survival. B, Patient survival.

**Figure 6. Illustration Showing the Different Graft Types**

Right lobe

Left lobe

Extended right lobe

Left lateral segment
Biliary complications are regarded as the “Achilles heel” in LT and are important causes of graft loss, morbidity, and mortality. It is reported to occur in 10% to 30% of cases following whole LT and 15% to 60% of cases following SLT and LDLT.\(^{46-48}\) In our series, the overall rate of biliary complications was 26.0%, including leaks and strictures (Table 3). Prevention and management of these complications remain the most challenging aspects of segmental LT. Multiple risk factors are involved for the development of biliary complications.\(^{47,49}\) We follow an aggressive and multidisciplinary approach to prevent and manage these complications. By shortening the cold and warm ischemia times as described earlier, we reduce the preservation injury. We believe that avoiding dissection around the periductal parenchyma, eliminating redundant length of the recipient bile duct, and ensuring ductal vascularity before anastomosis are the key factors for minimizing the bile duct problems. Reducing vascular complications also prevents biliary complications as the duct depends on hepatic artery circulation for its blood supply.\(^{50}\) We do not use T-tubes or internal stents for anastomosis and thus avoid problems associated with them. We closely follow up our patients and have a low threshold for intervention because timely intervention minimizes intra-abdominal infections including bile peritonitis and sepsis. Mycotic aneurysms of the hepatic artery, and graft loss. When leaks or bilomas are detected, we immediately start diagnostic workup with percutaneous transhepatic cholangiography or endoscopic retrograde cholangiopancreatography with dilatation and/or stent placement. Early percutaneous drainage of abdominal collection is done; when it is difficult to treat by nonsurgical methods, we do not hesitate to do operative intervention. Accordingly, 3 of our patients underwent surgical reexploration and repair. Appropriate antibiotic coverage is also started immediately. Because of these strategies, we had no graft or patient loss due to biliary complications, although we have had the previously mentioned biliary complication rate.

Two grafts were lost in our series. Both patients initially received living donor left lobe grafts with graft weight to recipient weight ratios of 0.94% and 0.68%, and they had a combination of aggressive antibody-mediated rejection (de novo donor-specific antibody) and concurrent small-for-size syndrome. There were no technical complications for the loss of the grafts as evaluated by the surgical team; the grafts were soft, and after reperfusion there was no overall segmental congestion and bile production was excellent. Both patients underwent retransplantation with whole liver grafts. We prefer to use left lobe grafts in LDLT owing to concerns of mental congestion and bile production was excellent. Both patients underwent retransplantation with whole liver grafts. We prefer to use left lobe grafts in LDLT owing to concerns of donor safety. We prevent the occurrence of small-for-size syndrome by preoperative volumetric estimation by computed tomography, perioperative monitoring of hepatic vein pressure gradient, and using octreotide in our protocol to control portal hypertension.

To summarize, in this series of 69 segmental graft LTs, we have achieved absence of HAT, portal vein complications, and hepatic vein complications. The use of segmental allograft provides an excellent resource in this era of donor scarcity and regional disparity. Although the surgical risks to the donor are quite different, LDLT and SLT are complementary and pose similar technical demands on the transplant surgeon. Careful patient selection, meticulous surgical technique, and anticoagulation protocols are key features of this success.


