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Left Hepatectomy Versus Right Hepatectomy for Living Donor Liver Transplantation: Shifting the Risk From the Donor to the Recipient

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Living donor liver transplantation (LDLT), originally used in children with left lateral segment grafts, has been expanded to adults who require larger grafts to support liver function. Most adult LDLT procedures have been performed with right lobe grafts, and this means a significant risk of morbidity for the donors. To minimize the donor risk for adults, there is renewed interest in smaller left lobe grafts. The smaller graft size increases the recipient risk in the form of small-for-size syndrome (SFSS) and essentially transfers the risk from the donor to the recipient. We review the donor and recipient risks of LDLT and pay particular attention to the different types of liver grafts and the use of graft inflow modification to ameliorate the risk of SFSS. Finally, a new metric is proposed for quantifying the recipient benefit in exchange for a specific donor risk. Liver Transpl 19:472–481, 2013. © 2013 AASLD.

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Early efforts in living donor liver transplantation (LDLT) focused on left lateral segment (LLS) grafts in pediatric recipients because they were initially disadvantaged on the waiting list. The LLS donor operation yields a graft with more than enough liver mass for an infant recipient. The relatively small size of LLS grafts can lead to liver dysfunction in adult recipients, so larger left lobe (LL) and right lobe (RL) grafts are commonly used. These larger grafts are associated with increased donor risk. There is a renewed interest in using smaller grafts to minimize donor risk. The use of smaller grafts, with their potential for lower donor risk but higher recipient risk, can be viewed as shifting risk from the donor back to the recipient. This review examines the tradeoff of donor and recipient risk associated with the donation and transplantation of smaller grafts, attempts to quantify that risk, and discusses ways to ameliorate it through graft inflow modification (GIM).

COMPETING RISKS

The recipient benefit from LDLT is well documented, with 83% survival 5 years after transplantation. Recipients with access to living donors have a shorter time to transplantation than patients awaiting cadaveric donors, and they have better outcomes when both the waiting-list mortality and posttransplant mortality are considered. The risk of death for a recipient of LDLT is 56% of the risk for a patient who does not have a living donor and either undergoes deceased donor liver transplantation (DDLT) or remains on the waiting list. For hepatocellular carcinoma (HCC) patients with a Model for End-Stage Liver Disease (MELD) score above 15, LDLT is generally preferred to DDLT. However, the use of smaller grafts in LDLT can be a viable option in patients with lower MELD scores, as long as the recipient risk is adequately quantified and managed.
(MELD) score > 15, the risk of death is 29% of the risk for a patient without a living donor. This benefit is not seen in HCC patients with a MELD score < 15. The benefit in this recipient population is moderated by the allocation preference that HCC patients receive, which likely results in the low number of LDLT procedures versus cadaveric transplants performed every year in the United States for patients with HCC.²

These results suggest that LDLT is most advantageous to patients on the waiting list who have the highest risk of death while waiting for transplantation and for whom the availability of donor organs is poor. The relationship between organ availability and LDLT use in the United States was demonstrated by the finding of much higher LDLT use in donor service areas in which the MELD score at the time of transplantation was high versus donor service areas in which the MELD score was low.³

The donor mortality risk with LDLT has been estimated to be on the order of 1/100 to 1/1000. The decision regarding the graft type involves balancing the donor risks of morbidity and mortality from the donor hepatectomy, which may be related to the remnant liver size, against the recipient risks of mortality and morbidity related to dysfunction from receiving a graft that is too small. In this sense, the risks and benefits of the 2 patients are competing with respect to the graft size. In 2001, Cronin et al.⁴ introduced the concept of double equipoise as an approach for evaluating the ethical acceptability of living donor organ transplantation. This concept is based on the assumption that the donor takes on risk to provide the recipient with benefits, and as a reward for taking the risk, the donor desires a successful outcome for the recipient. The recipient fears for the donor and wants to minimize the donor risk but also desires to have a successful transplant. Under these assumptions, a minimum recipient benefit and a maximum donor risk can be used to ascertain the theoretical ethical acceptability of LDLT.⁵ We will return to double equipoise and use it as a concept for selecting a liver graft after we discuss specific considerations regarding donors, recipients, and grafts.

DONOR SELECTION

The safety of the donor is paramount, so a potential living donor must meet certain criteria, which vary across centers. Typical criteria include ABO blood type compatibility with the recipient, an age between 18 and 60 years, the absence of any chronic illness or psychological disorder, a body mass index < 30 kg/m², adequate social support and medical insurance to ensure postoperative recovery. There must be no evidence of coercion or payment. If these criteria are met, the potential recipient undergoes an evaluation by an internal medicine physician, a transplant surgeon, and an independent donor advocate. Serological testing includes an evaluation for hepatitis, human immunodeficiency virus, syphilis, hypercholesterolemia, common causes of hypercoagulability, liver dysfunction, and diabetes. To assess the anatomic suitability for donation, a computed tomography or magnetic resonance imaging scan quantifies the LL and RL liver volumes, and computed tomography cholangiography or magnetic resonance cholangiopancreatography is used to define the biliary anatomy. For all men more than 35 years old and all women more than 45 years old with 1 or more cardiac risk factors, an echocardiogram and an exercise thallium scan are performed. Mammography, colonoscopy, pap smear, and prostate-specific antigen results must be up to date according to current routine health maintenance guidelines. A family history of primary biliary cirrhosis initiates an evaluation for anti-mitochondrial antibodies. Any history of smoking within 5 years requires an arterial blood gas measurement, and the donor must be free of nicotine for 6 weeks before donation. A urine toxicology screen must be negative for drugs of abuse, and the potential donor must abstain from alcohol before the operation. Generally, liver biopsy is performed selectively (eg, in a first-degree relative of a recipient with primary biliary cirrhosis, primary sclerosing cholangitis, or autoimmune hepatitis or if an ultrasound scan of the potential donor reveals a fatty liver).

DONOR MORTALITY

When the Vancouver Forum on living donation in 2006 summarized the global data for donors, the total number of deaths for LDLT donors at that time was 34, and only 4 were LL donors (1 of these was a suicide). The global donor mortality rate was 0.1% for LL donors and 0.5% for RL donors.⁶ In the United States specifically, there were 4 RL donor deaths and 1 LL donor death after left lateral segmentectomy (LLS).

In a recent worldwide survey reported at the 2011 International Liver Transplant Society Meeting,⁷ all liver transplant programs listed with the American Society of Transplant Surgeons, the Japanese Liver Transplant Society, and the European and Chinese liver registries were asked to complete a Web-based survey regarding their current clinical practices related to LDLT. Responses were received from 71 centers representing LDLT programs in North America, Europe, Asia, South America, Australia, New Zealand, and the Middle East. There were 23 donor deaths out of a total of 11,553 LDLT procedures. Eighteen of the deaths were reported directly in the survey, and another 5 deaths were reported by the Eurotransplant Registry for an overall mortality rate of 0.2%. There were no differences in the death rates between the hepatectomy types (18/8734 for right lobectomy (RL), 2/994 for left lobectomy (LL), and 3/2168 for LLS; P = 0.71 for RL versus LL, P = 0.71 for RL versus LLS, and P = 0.65 for LL versus LLS). Another 11 deaths after donor hepatectomy have been reported in the literature, but they were not captured in the survey.⁸–¹⁸ Twenty-four of the total 34 reported deaths occurred in RL donors.
Centers often have a predilection for either RL or LL donation, and some experts suggest centers experienced with a particular type of hepatectomy may, therefore, have lower mortality rates when they perform that particular procedure. Mortality from single reports is difficult to interpret because donor mortality is a rare event. Two large multicenter studies looked at the influence of center experience with a particular type of hepatectomy on donor mortality, and neither found any correlation.\textsuperscript{7,19}

**DONOR MORBIDITY IN ASIA AND NORTH AMERICA**

The world literature consists of mostly retrospective, single-center experiences strengthened by a few multicenter reviews. The applicability of the data is limited by poorly matched comparisons, small sample sizes, and learning curves.

**Donors Requiring Liver Transplantation**

The risk of donor hepatic insufficiency requiring retransplantation is difficult to estimate because it is founded on single-center reports and self-reported survey data. The world literature was reviewed in 2006,\textsuperscript{18} and according to that report and our review of the recent literature, there have been no described accounts of LL donors who required liver transplantation after donation, but there is a report of an RL donor who did,\textsuperscript{9} and there are more that have not been reported. According to a worldwide survey of near-miss events in liver donors,\textsuperscript{7} 5 RL liver donors required transplantation after donation; 4 required liver transplantation, and 1 required kidney transplantation (intravenous contrast–induced renal failure).

**Donor Morbidity**

Our review of the literature suggests that the morbidity risk generally increases as the hepatectomy mass increases from LLS donation to LL donation to RL donation and, finally, to extended RL donation. In a review of donor hepatectomies performed at 46 centers in Japan, the morbidity rates after 1680 donor operations were 8.2% for 753 LLS donors, 12.0% for 484 LL donors, and 19.0% for 443 RL donors (\textit{P} < 0.01).\textsuperscript{20} The biliary fistula rate was 10% in RL donors and 2% in LL donors. The length of the hospital stay was significantly shorter for LL donors. Subsequent studies confirmed lower complication rates for LL donors (20% versus 51% for RL donors) as well as a lower rate of Clavien II complications (4% versus 29% for RL donors; Table 1).\textsuperscript{21,22} Further supporting this direct relationship between the graft type and donor morbidity is a Japanese single-center, retrospective review of 335 lobectomies for adult-to-adult LDLT that reported morbidity for LL, RL, and extended RL donors (with odds ratios of 1.12, and 61, respectively).\textsuperscript{23}

Another single-center, retrospective study from Japan quantified the safety of LL versus RL; grafts were selected for adult-to-adult LDLT according to the ratio of the graft volume to the standard liver volume.\textsuperscript{24} On the basis of the concept that an LL graft is safer for the donor and should be the first choice when it is possible, they proposed a graft selection strategy that resulted in the use of LL grafts in two-thirds of their cases. For 137 LL grafts and 69 RL grafts, the donor morbidity rates were 29% and 43%, respectively (\textit{P} < 0.05), and the biliary complication rates were 2.9% and 10.1%, respectively (\textit{P} < 0.05). There was no significant difference in graft survival up to 5 years. Although the data were retrospectively gathered, logistic regression confirmed that in comparison with RLs, LLs were protective against biliary complications (odds ratio = 0.11, \textit{P} = 0.001).

A retrospective, multicenter report from the Japanese Liver Transplantation Society\textsuperscript{25} described 3565 adult-to-adult LDLT donors. Clavien class II to V complication rates were 3.5% for 1045 LLS donors, 8.7% for 1088 LL donors, and 9.7% for 1378 RL donors. Surprisingly, the LL and RL complication rates were similar, and this is one of the few reports to find this. It is possible that there was underreporting because this study was based on voluntarily reported retrospective data obtained by questionnaires from 38 of 55 centers (83%). The changes in institutional policy that took place over the study period, driven by the complications accumulating in this report, improved outcomes for RL donors, although LL complication rates were unchanged. This study is difficult to reconcile with the previous multicenter report and the single-center reports from Japan.

Another large, single-center, retrospective review from Japan examined complications for 500 RL and extended RL grafts and 762 LL grafts between 1990 and 2007.\textsuperscript{26} The grafts included 426 RL grafts that did not contain the middle hepatic vein and 74 that did, 493 LLS grafts, 180 LL grafts, 45 extended lateral segments, and 44 monosegment grafts. The rates of major complications (Clavien grade IIIa-V) were 44.2% for RL and extended RL donors and 18.8% for LL donors (\textit{P} < 0.05). Biliary complications, the most frequent major complications, were again more common after RL donation versus LL donation (12.2% versus 4.9%, \textit{P} < 0.05). Massive ascites was also more frequent after RL donation (1.0% versus 0.1%, \textit{P} < 0.05). The only donor death was attributed to hepatic failure after extended right hepatectomy in the setting of underlying nonalcoholic steatohepatitis. The authors concluded that morbidity (specifically biliary complications) was both more frequent and severe after RL and extended RL donation versus non-RL donation.

Similar findings were reported in a comprehensive report of 1508 cases at 5 centers in Asia from 1990 to 2001.\textsuperscript{27} The liver grafts included 605 LLS grafts, 334 LL grafts, and 561 RL or right lateral grafts with complication rates of 9.3%, 7.5%, and 28%, respectively. Complications were not only more frequent among RL donors but also more serious, and they included bile leaks (LLS, 5.5%; LL, 2.4%; and RL, 6.1%), cholestasis (LLS, 0.3%; LL, 0.0%; and RL, 7.3%), and
intra-abdominal fluid collection (LLS, 0.0%; LL, 0.0%; and RL, 3.6%).

A 2011 study described LDLT donor morbidity across 3 eras and highlighted the correlation between surgeon/center experience and donor outcomes. The overall Clavien complication rates were 42.9% for RL donors, 27.5% for LL donors, and 13.9% for LLS donors. The complication rates generally decreased from the earliest era to the most recent era (RL, 61.5% to 33.3% to 16.5%; LL, 25.0% to 38.9% to 14.3%; and LLS, 15.4% to 25% to 6.7%). Across all eras, Clavien class III or higher complications were more common in RL donors (26.8%) versus LL donors (10%) and LLS donors (8.3%).

A retrospective review of 500 LDLT cases from 2007 to 2011 at a single center in Turkey (where LDLT constitutes 85% of liver transplants) described donor complications. A majority of the grafts were RL grafts (RL, 91.2%; LL, 2.8%; and LLS, 6%). Complications were seen in 18.6% of the donors, and they were more common after LL (RL, 18.6%; LL, 36.7%; and LLS, 10.0%); this possibly reflects extensive surgeon experience with RL versus the procurement of left liver grafts. Biliary complications were again most frequent (10.8%). The likelihood of a donor requiring reoperation for any reason is 1% to 7%.

The North American literature is more difficult to interpret than the Asian studies because it consists mostly of single-center reports and the overall patient volumes are lower, particularly for LL donors. A relatively large North American case control analysis from 1996 to 2010 found no significant differences in complication rates for RL and LL donors, although a univariate analysis associated serious complications with RL donation (RL and extended RL), increases in the volume of liver removed, and peak bilirubin levels. A recent retrospective analysis of data from the United Network for Organ Sharing database describes an increasing trend in the yearly use of LL grafts from 5 (1998-2003) to 19 (2004-2010), which represents an increase from 2.3% to 7.2% of all LDLT procedures in this country. This study does not discuss donor complication rates.

The most comprehensive review of donor complications in the North American experience, the Adult-to-Adult Living Donor Liver Transplantation Cohort Study, describes an observational cohort of 760 living donors. Complications occurring at 9 centers from

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Examples</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>An alteration from the ideal postoperative course with complete recovery or one that can be easily controlled</td>
<td>Superficial wound infection, bile leak treated conservatively</td>
</tr>
<tr>
<td>II</td>
<td>Any complication that is potentially life-threatening or results in an ICU stay ≥ 5 days or a hospital stay ≥ 4 weeks but does not result in residual disability or persistent disease</td>
<td>Rejection requiring immunosuppression, transient creatinine rise for more than 1 week, infection requiring antibiotics</td>
</tr>
<tr>
<td>IIa</td>
<td>Complications requiring the use of only drug therapy or postoperative bleeding requiring &gt;3 U of blood</td>
<td>Primary graft dysfunction extending the ICU stay ≥ 5 days, postoperative bleeding requiring laparotomy, bile leak requiring endoscopy or surgery</td>
</tr>
<tr>
<td>IIb</td>
<td>Complications requiring invasive therapeutic treatments, readmission to the ICU, or prolongation of the ICU stay ≥ 5 days that do not result in residual disability</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Complications with residual or lasting functional disability or development of malignant disease (other than squamous or basocellular cutaneous malignancies)</td>
<td>De novo hepatitis C, nonprogressive chronic rejection, bile duct stricture not amenable to surgical or endoscopic treatment, cardiac arrest or myocardial infarction</td>
</tr>
<tr>
<td>IIIa</td>
<td>Complications with lasting disability that show no evidence of progression and have a relatively low risk of leading to graft failure and/or death</td>
<td>De novo hepatitis B, development of malignancy, persistent bile duct stricture not amenable to surgical or endoscopic treatment with progressive liver failure or recurrent cholangitis, progressive chronic rejection</td>
</tr>
<tr>
<td>IIIb</td>
<td>Complications with lasting disability that either are difficult to control or have a significant risk of leading to graft failure and/or death</td>
<td></td>
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<tr>
<td>IV</td>
<td>Complications that lead to retransplantation or death</td>
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<tr>
<td>IVa</td>
<td>Complications that lead to retransplantation</td>
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<tr>
<td>IVb</td>
<td>Complications that lead to death</td>
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NOTE: This table was adapted with permission from *Annals of Surgery*. Copyright 1994, Lippincott Williams & Wilkins.
1998 to early 2003 were analyzed retrospectively. Then, the retrospective cohort was followed through 2010, and new donors were tracked prospectively from 2003 to 2009 to obtain complication data with long-term follow-up to allow for an analysis of the resolution of complications. There were 707 RL donors and 33 LL donors and 20 donor operations were aborted. Forty percent of the donors experienced complications, although these complications were not classified by the type of lobectomy (right versus left). The vast majority of the complications were Clavien grade I or II, whereas 2.8% of the donors experienced grade III or IV complications. There were no donor deaths. Eighty percent of the complications were resolved within 3 months, and 95% were resolved within the first postoperative year. Psychological complications (3%) and incisional hernias (7%) appeared in patients after the first year of follow-up. Overall, the risk of donor complications in the Adult-to-Adult Living Donor Liver Transplantation Cohort Study was very similar to the risk in other recent North American reports, with the risk of residual disability, liver failure, or death estimated to be approximately 1%,33,34

In aggregate, the aforementioned studies offer convincing evidence that LL donation leads to a lower rate of donor complications than RL donation for LDLT. Specifically, Clavien class III to V complications, including biliary complications, are more frequent after RL donation. Therefore, when the success of the donor is considered and the recipient outcome is disregarded, LL donation is the operation of choice.

**EFFECT OF GRAFT VOLUME ON RECIPIENT OUTCOMES**

Because a well-functioning graft is important for achieving an acceptable recipient outcome, the effects of different grafts on recipient complications must be considered, especially when one is considering small grafts in recipients with portal hypertension. RL grafts have been most commonly used in adult recipients, but an awareness of donor risk has increased the number of LL grafts being transplanted.

**Recipient Complications Related to Graft Volume**

The concept of the standard liver volume was described in 1995 along with a formula for calculating it on the basis of the recipient’s height and weight.35 Previous literature has suggested that a graft weight/recipient weight (GW/RW) ratio ≥ 0.8% and a graft weight/standard liver volume (GW/SLV) ratio of 40% are the safe limits for donor graft size to avoid what has been termed small-for-size syndrome (SFSS).36–39

Although no consensus exists for a definition of SFSS, prolonged cholestasis with ascites without evidence of technical issues or rejection is the generally accepted clinical picture. After polling experts in the field in 2005, Dahm et al.40 defined small-for-size dysfunction as an undersized graft (GW/RW ratio < 0.8%) with 2 or more of the following findings on 3 consecutive days within the first week after transplantation: a bilirubin level > 100 μmol/L, an international normalized ratio > 2.0, and grade 3 to 4 encephalopathy. The authors defined small-for-size nonfunction as a small graft (GW/RW ratio < 0.8%) that required retransplantation or was the cause of a recipient’s death within the first week. For either of these diagnoses to be invoked, arterial and portal occlusion, outflow congestion, bile leaks, rejection, and infection could not be present. Other definitions have been used, and one problem with the literature regarding SFSS is differences in its definition.

Some literature suggests that grafts smaller than the GW/SLV cutoff of 40% can be used, but there is an increase in SFSS.41 The concept that there are thresholds at which the risk of SFSS becomes significant has been challenged.42,43 To evaluate the role of graft size in recipient outcomes, Ikegami et al.44 compared 33 patients who received grafts with GW/SLV ratios < 35% (mean ratio = 31.8) to 87 patients with GW/SLV ratios ≥ 35% (mean ratio = 42.5%). The 2 groups did not differ significantly with respect to 1- (80.7% versus 90.8%) or 5-year survival (64.2% versus 84.9%), prothrombin times, international normalized ratios, total bilirubin levels, daily ascites production, or hospital stay length. Although the differences were not statistically significant, the small sample sizes may have obscured clinically relevant differences. Further studies support the idea that the GW/RW ratio is not a predictor of outcomes.43,45 These 2 studies compared recipients with GW/RW ratios ≥ 0.8% to recipients with GW/RW ratios < 0.8%; however, they were again limited by small sample sizes, recipient portal hypertension was not quantified, and inflow modification was used more frequently in recipients with GW/RW ratios < 0.8%. Furthermore, one of these studies was based on recipients with relatively low MELD scores: 17.7 in the group with a GW/RW ratio ≥ 0.8% and 15.7 in the group with a GW/RW ratio < 0.8%.43 Therefore, although the studies to date are somewhat discordant, the consensus in the field is that a GW/RW ratio < 0.8% is a risk for SFSS. Although the GW/RW ratio is the most frequently cited risk for SFSS, recipients with GW/RW ratios > 0.8% are known to develop SFSS.46 Recipient factors such as portal hyperperfusion and splenomegaly contribute to allograft congestion after partial liver transplantation.47,48 and the degree of liver dysfunction at the time of transplantation is considered by some to contribute to the risk of SFSS.

Recent evidence suggests some risk of SFSS can be mitigated through surgeon experience. Chan et al.49 reported their center experience with 320 RL donors from 1996 to 2008 and divided their experience into the first 50 cases and the following 270 cases. In-hospital mortality decreased from 16.0% (8/50 patients) to 2.2% (6/270 patients, P = 0.00). The mortality rate with GW/SLV ratios < 40% was 50% (3/6) for the first group and 1.9% (1/52) for the second.
Graft Inflow Modification

In patients without cirrhosis who have liver tumors, right hepatectomy leaves approximately 30% to 40% of the liver volume. Prolonged hyperbilirubinemia is not common, and a very low 30-day mortality rate and a 1-year survival rate > 95% are expected. Supporting the rarity of hepatic insufficiency in patients without cirrhosis who undergo major hepatectomy, Hwang et al. reported no donors with persistent hyperbilirubinemia and no mortality among 578 RL donors. In contrast, SFSS occurs in LDLT recipients who receive a 30% to 40% standard liver volume graft, and this suggests that factors other than the transplanted parenchymal mass play a role in the syndrome. The consensus is that ischemia/reperfusion injury and recipient portal hypertension play key roles in the pathophysiology of SFSS.

After liver transplantation, a higher postoperative portal venous pressure (PVP) and portal hyperperfusion are associated with reduced graft survival and choleslasis. When the graft size was linked to the posttransplant portal pressure via PVP monitoring of LDLT recipients, PVP was elevated in patients with a GW/RW ratio < 0.8%, and patients with a mean PVP > 20 mm Hg had significantly worse 6-month survival than patients with a PVP < 20 mm Hg (84.5% versus 38.5%, P < 0.01).

Animal studies in pigs have shown that the risk of small liver grafts can be overcome with inflow modification. One study found a GW/RW ratio of 0.6% to be uniformly fatal in the control group, but all recipients were rescued when the flow was completely diverted through a mesocaval shunt and the upstream superior mesenteric vein was ligated. Further supporting this is another study in pigs in which grafts with a graft weight ratio of the recipient native liver weight of 25% were transplanted with or without a side-to-side portocaval shunt. Although the animals were followed for only 4 days, survival for the control animals was dismal (1/11), and it was much better for the animals with a portocaval shunt (8/11).

To prevent hyperperfusion in partial liver transplantation in humans, GIM via splenic artery ligation, splenectomy, or portocaval shunting has been performed, although specific indications for each method are not defined. To improve results with smaller grafts, Troisi et al. analyzed small-for-size grafts with a graft-to-recipient body ratio < 0.8 with and without GIM via a hemiportocaval shunt. The selective use of portocaval shunts significantly improved 1-year patient survival from 40% to 87.5% and graft survival from 20% to 75% in patients with small grafts. Some think that keeping the portal pressure < 15 mm Hg in the recipient is key for successful adult LDLT using smaller grafts. For example, Ogura et al. showed that 86 patients with a PVP < 15 mm Hg had better 2-year survival (93.0%) than 43 patients with a PVP ≥ 15 mm Hg (66.3%).

The bases for an intraoperative decision to perform GIM are not well understood. Currently, the surgeon’s decision to perform GIM is based on subjective variables (eg, graft size and consistency) combined with measures of PVP, portal venous flow (PVF) and hepatic artery flow. Controversy exists about the use of PVP or PVF. Although the expectation is that these will be strongly correlated if the resistance is fixed, clinical data suggest that this is not the case, and this suggests differences in inflow and resistance that are not well understood. Changes in the central venous pressure translate directly into changes in PVP, so the gradient from the portal system to the central venous pressure, the hepatic vein pressure gradient, should be used instead of the portal pressure alone. PVP must not be used individually to determine the need for GIM because graft hypoperfusion from the diversion of portal flow would result in up to 25% of cases.

The need for GIM has been suggested in recipients with graft hyperperfusion (PVP > 360 mL minute⁻¹ 100 g LW⁻¹), severe portal hypertension (hepatic vein pressure gradient ≥ 15 mm Hg), and low hepatic artery flow (< 100 mL minute⁻¹). The reduction in PVP produced by portocaval shunting can be too great and produce a portal steal phenomenon: this risks hepato-fugal flow, portal vein thrombosis, graft dysfunction, and encephalopathy.

A stepwise approach to GIM has been suggested with different methods. One method for GIM is splenic artery ligation. If portal hypertension is suspected and the PVF is not extremely elevated (360-500 mL minute⁻¹ 100 g LW⁻¹) and/or the GW/RW ratio is < 0.8%, the splenic artery should be test-clamped and ligated to reduce the hepatic vein pressure gradient. If the PVF is severely elevated (>500 mL minute⁻¹ 100 g LW⁻¹), then ligation is not likely to be effective, so a hemiportocaval shunt should be considered. Some centers have shifted to splenectomy as the primary means of GIM. In Japan, splenectomy in patients with a PVP ≥ 15 mm Hg increased the use of LL grafts (from 4.9% to 32.1%) and expanded graft selection criteria to include a GW/RW ratio > 0.7% (from 0.8%) while improving 1-year patient survival (87.9% versus 76.2%). A suggested benefit of splenectomy in patients with hepatitis C virus is a decrease in cytopenia in the posttransplant period, which allows more aggressive treatment of hepatitis C virus recurrence. Splenic artery embolization can be used as a minimally invasive treatment for SFSS in both delayed and early postoperative settings.

In conclusion, inflow modification is an important way to improve graft outcomes and should be considered when there is evidence of graft hyperperfusion. The elucidation of physiological differences of partial liver allografts has helped to prevent graft congestion and SFSS. SFSS is more common in grafts with low GW/RW ratios, but the size of the graft is only 1 factor in a complex situation involving multiple variables.

Revisiting Double Equipoise in Adult LDLT

Since the initial description of double equipoise, the concept has been applied to a range of living donor
situations (most recently the issue of transplantation for patients with HCC). Double equipoise describes the balance between the recipient’s survival benefit with or without LDLT and the probability risk of mortality for the donor. If the recipient benefits are too low or if the risk of donor mortality is too high, the living donor procedure will not be ethically defensible. Conversely, the optimal situation is one in which the recipient benefits are high and the risk of donor mortality is very low. The concept has been expanded to triple equipoise, which incorporates recipient need. Termed tripartite ethical equipoise, the balance of these 3 essential ethical dimensions—donor safety, expected recipient outcome, and recipient need—can be depicted with a vector-triangle diagram.

We now use the double-equipoise analysis to consider the following ethical issue: when the decision is made to perform LL or RL, which of the 2 parties—the donor or the recipient—should bear the greater relative mortality risk? On the basis of a review of the literature, we assume that LL is significantly safer than RL for donors. The recipient benefit depends on the size of the graft that is obtained and the risk for SFSS. When both left hemihepatectomy and right hepatectomy with a given donor can provide a GW/SLV ratio > 40%, we suggest that LL should be performed instead of RL (Fig. 1). However, we also assume that if a graft has a GW/SLV ratio < 40%, there is a probable decrease in recipient benefit. Therefore, the question with which we are most immediately concerned is what to do if RL would provide more than 40% volume but LL would provide less than 40% volume and put the potential recipient at increased risk for SFSS. Ethically, should the burden of risk be placed on the altruistic donor or on the recipient who will benefit from the donor’s altruism?

In order to aid our evaluation of the choice between potentially small-volume LL (GW/SLV ratio < 40%) and adequate-volume RL (GW/SLV ratio > 40%), we will employ the metric of recipient lives saved at 5 years per donor death (5-year RS/DD). This metric evaluates the effectiveness of LDLT and provides a measure of how much recipient benefit is obtained in exchange for donor risk. A perfect operation would have a recipient lives saved at 1 year per donor death (5-year RS/DD) value of infinity, so no donors would die and some recipients would be saved. Conversely, an unacceptable operation would have an 5-year RS/DD of 1; that is, on average, 1 donor would die for every recipient saved, so the donor’s life would effectively be traded for the recipient’s life. LDLT with a low 5-year RS/DD value would be ethically impermissible. By comparing RS/DD values for potentially small-volume LL LDLT and adequate-volume RL LDLT, we can assess which type of graft leads to a better dual outcome for the donor and the recipient.
To explore this question, we consider 2 scenarios. First, we consider a case in which the LL is small (20% < GW/SLV ratio < 40%) and the RL would yield an adequate-size graft (GW/SLV ratio > 40%; Fig. 2). We assume that the increased risk for SFSS with the small LL graft means that performing RL donation will increase the recipient benefit by a significant amount. However, the cost of this increase in recipient survival is a greater increase in the donor mortality risk. The adequate RL has an RS/DD ratio of 40, whereas the small LL has a ratio between 100 and 150. In other words, the RL exposes the donor to a risk out of proportion to the recipient benefit from that graft; therefore, the LL would be the operation of choice.

Because of uncertainty about the recipient benefit with small grafts and the range of reported donor mortality rates with RL and LL, we also consider a case in which the LL is very small (GW/SLV ratio < 20%) and the RL is adequate (GW/SLV ratio > 40%) at a center that specializes in RL donation, so the donor mortality rate may be reduced (Fig. 3). In this case, using the RL and paying the cost of a 100% increase in donor mortality yields the benefit of a 400% increase in recipient survival. Adequate RL donation has an RS/DD value of 100, and very small LL donation has an RS/DD value of 50. Therefore, in this scenario, adequate RL donation exposes the donor to more risk but efficiently converts that risk into increased recipient survival. Therefore, we believe that RL donation in a narrow range of cases achieves the proper balance of recipient benefit and donor risk.

CONCLUSION

LDLT is an effective treatment for end-stage liver disease. It can reduce the mortality burden for patients with long projected wait times, with high MELD scores, or in areas in which DDLT is not culturally acceptable. LDLT is unique because it requires balancing donor and recipient risk, for which the theory of double equipoise is a useful framework for discussion, with the most benefit experienced by patients with the highest risk of death while they are on the waiting list. The risk of donor death is low (0.2%-0.5%). Donor morbidity is decreasing as surgeon and center experience grows. Our review of the literature suggests that the rate of donor complications is 4- to 12-fold lower for LL donors,20,22,23,25-27 and when the Clavien complication system is used for analysis, the complications seem to be less severe. The use of LL grafts is a potential way of increasing the number of donor organs with lower donor risk, but these grafts risk SFSS in the recipient and shift the risk of living donation from the donor to the recipient. Although using smaller grafts from LL may decrease recipient benefit absolutely, our double-equipoise analysis suggests that LL is more efficient than RL in converting donor risk into recipient benefit.

Our analysis of this issue raises questions about how we should incorporate the preferences of donors and recipients into the surgical decision of what kind of donor operation should be performed. The shifting of preference toward LL is in accord with the history and tradition of LDLT, with the health and security of the living donor being paramount. As for small-volume LL versus adequate-volume RL, the surgeon, the donor, and the recipient should meet to discuss the risks and benefits of the 2 procedures. If either the donor or the recipient expresses a preference for smaller volume LL and the center is experienced in LL donation, then LL may be the operation that achieves the most appropriate balance. If both the donor and the recipient express a strong preference for larger volume RL and the center is experienced in RL donation and believes that the larger volume graft is required, then RL may achieve the most appropriate balance. However, in general, according to our double-equipoise analysis and the traditional rule of maximally protecting living organ donors, if the donor and recipient request guidance about which operation should be performed, we would recommend LL over RL.

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