The Current Status of Living Donor Liver Transplantation

Over the last 4 decades, liver transplantation has evolved into the treatment option of choice for a variety of patients with acute or chronic end-stage liver disease. Improvements in surgical techniques coupled with advances in intensive care practices and immunosuppressive therapy have resulted in 1-year patient survival rates of greater than 90% following liver transplantation. The rapid expansion in the number of centers providing liver transplantation, in conjunction with a previously unrecognized epidemic of liver disease, has placed an inordinate demand on liver transplant services in general. During the past decade, waiting times for liver transplantation and the rate of death on the transplant waiting list have increased by 10-fold. The synergy of these factors has resulted in a critical shortage of cadaveric or deceased donor organs for adults and children in need of liver transplantation.

The use of living donors for liver transplantation was introduced into surgical practice in the late 1980s. Since that time, the application of living donor liver transplantation (LDLT) has been widespread and rapid. Its early evolution was the result of a critical shortage of deceased donor organs of suitable size for infants, children, and small adults awaiting liver transplantation. With refinements in surgical techniques, transplantation of segments 2 and 3 (left lateral segment) from a living donor was associated with 1-year patient survival rates of 94% compared with 88% for patients who received deceased donor grafts. Moreover, donor morbidity and mortality rates were low.

The increased demand for liver transplantation experienced in the United States has been observed worldwide. It has been driven primarily by an epidemic of end-stage liver disease arising from chronic hepatitis C virus (HCV) infection and the dramatic increase in hepatocellular carcinoma (HCC) associated with HCV infection, also an indication for transplantation in selected patients. Despite efforts to expand the deceased donor pool, the demand for livers far exceeds the supply. Despite the increased application of novel surgical techniques such as
split-liver transplantation, auxiliary transplantation, and the use of non-heart-beating donors, the supply of organs has not kept pace with the demand.\textsuperscript{12-15}

Troubled by the ever increasing mortality rate for adults on the liver transplant waiting list, surgeons applied LDLT to adult liver failure patients in the United States in the late 1990s.\textsuperscript{16-20} The proliferation of this technique in the United States was such that the number of programs offering adult LDLT increased from 1 in 1997 to 38 in 2000. The result was a dramatic increase in the total number of living donor liver transplants (Fig 1).

### Historical Perspective

Although the first living donor liver transplants were performed in Brazil by Raia in 1988, the first successful transplant is credited to Strong of Australia and involved transplantation of the left hepatic lobe into a child.\textsuperscript{3,4} In the early 1990s, LDLT was developed extensively in Asia, particularly in Japan where cultural values inhibited cadaveric organ donation before the development of brain death criteria.\textsuperscript{21}

The early LDLT successes were seen in pediatric and other small recipients who received the whole left lobe or a portion thereof. Today, virtually all liver transplants performed in Asia are from living donors. In the United States, however, relatively few living donor liver transplants were performed before the mid-1990s. Between 1990 and 1996, donor procedures involving the left lobe and left lateral segment were popular-
ized at the University of Chicago by Broelsch and colleagues;\textsuperscript{5,6,22} however, this operation was reserved for children whose parents or other relatives served as donors. Although LDLT of the left lobe into adults was attempted in the United States, the procedure was virtually abandoned because the smaller left hepatic lobe provided insufficient hepatic mass for most adult recipients. Despite these limitations, the technique of LDLT flourished for children requiring liver transplant and, in many centers, became the procedure of choice for transplantation.

Until 1993, all living donor transplants were performed with the entire left hepatic lobe or some of its segments. The first adult-to-adult transplant of a right hepatic lobe was reported by Yamaoka and colleagues\textsuperscript{7,23} of Japan in 1993. Wachs and colleagues\textsuperscript{8} performed the first successful living donor right hepatic lobe transplant in the United States in 1997.

 Because the smaller left hepatic lobe provides less hepatocyte mass than the right, the efficacy of transplantation of the larger right hepatic lobe became apparent early in the experience. Consequently, by the dawn of the new millennium, the initial success of right lobe LDLT, in conjunction with the severe shortage of deceased donor organs, led to worldwide interest in this procedure.\textsuperscript{16,18,19,24,25}

Stratification of Patients with Chronic Liver Disease

The selection of candidates for liver transplantation has proven to be 1 of the least complex aspects of the process. In contrast, the allocation of deceased donor organs has become increasingly problematic. So that patient and transplant center equity is maintained, the process of organ allocation has been modified during the past 2 decades and continues to be evaluated by participating transplant centers as governed by the United Network for Organ Sharing (UNOS).

The stratification of patients with chronic liver disease has been 1 of the principal challenges of the last 30 years. Until recently, the classification described by Child and Turcotte,\textsuperscript{26} published in monograph form in 1964, was the basis of prognostic assessment of patients with cirrhosis. This system was based on 5 parameters (eg, serum albumin, bilirubin, presence of ascites, presence of encephalopathy, and nutritional status) to which 1 of 3 risk levels was attributed.

When the Child’s score was first utilized to stratify risk for patients with chronic liver disease, the system was criticized because of the subjective nature of most of its parameters (eg, ascites, nutritional status, and encephalopathy). Furthermore, the final result placed the patient in 1 of 3 classes rather than reflecting a spectrum of disease severity. Further
modification ensued in 1972 when Pugh and colleagues modified the Child-Turcotte classification, taking into account the aforementioned criticisms. The objective at that time was to develop an instrument to predict patient outcomes after surgical portal-systemic shunting. Pugh and colleagues introduced a points system for each element and replaced nutritional status with the prothrombin time. This modification has become the predominant measure of disease severity for patients with liver disease and has been applied to scenarios as diverse as the prediction of survival after variceal bleeding to the evolution of minimal listing criteria for orthotopic liver transplantation (Table 1).

In an attempt to limit the impact of subjectivity, several investigators have attempted to establish a system of assessing liver disease severity by developing mathematical models based on prospective data sets. Despite these efforts, it was not until 2002 that UNOS changed its organ allocation policy from one that conferred a value on accumulated waiting time plus Child-Pugh-Turcotte (CPT) score and medical urgency to a more objective allocation policy where waiting time and CPT score played no role. Before 2002, the UNOS liver allocation algorithm defined broad categories of urgency, often called UNOS statuses. Patients with cirrhosis and 7 Child’s points (Child’s class B cirrhosis) fulfilled minimal listing criteria and were designated status 3 on the liver transplant list. Patients with more than 10 points (Child’s class C cirrhosis) were designated status 2B and had higher priority on the transplant list. Finally, status 2A patients had Child’s class C cirrhosis but required in-hospital care in the intensive care unit and were given the second highest priority for organ allocation, with the highest priority given to patients with fulminant hepatic failure known as status 1.

Potentially, each transplant program could have many suitable candidates at a given UNOS status. The UNOS rules determined that

<table>
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<tr>
<th>TABLE 1. Calculation of Child’s-Pugh grade</th>
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<tr>
<td>Encephalopathy</td>
</tr>
<tr>
<td>Ascites Absent</td>
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<tr>
<td>Bilirubin mg/100 mL</td>
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<tr>
<td>Albumin g/100 mL</td>
</tr>
<tr>
<td>Prolongation of PT in seconds</td>
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<tr>
<td>INR</td>
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Scores are calculated based on points (1, 2, or 3) obtained for each of the 5 variables (Child’s class A < 6, B 7–9, C > 10).

PT, prothrombin time; INR, international normalized ratio.

Adapted from Pugh RN, Br J Surg 1973; 60:646-649.
accumulated waiting time broke the ties between competing candidates within the same UNOS status. As a result, this allocation scheme encouraged the placing of patients on the waiting list early so that they could accrue waiting time and advantage within the allocation system. The result was a bias against those patients with severe, chronic liver disease who were referred to the transplant center late in their disease courses.

Organ Allocation Policy and the MELD Score

In 1999, the federal government of the United States encouraged the establishment of policies that would allow deceased donor livers to be allocated according to uniform medical criteria. The new regulations replaced the CPT classification system as the basis for determining urgency for liver transplantation with the Model for End-stage Liver Disease (MELD) score, developed by clinicians at the Mayo Clinic.\(^{28}\) The MELD score was originally calculated to predict the outcome of trans-jugular porto-systemic shunt (TIPS) therapy for treatment of complications of portal hypertension (eg, variceal bleeding, ascites). Unlike the CPT classification, MELD was derived from prospectively gathered data rather than data constructed empirically.\(^ {28}\) Calculation of the MELD score is based on serum bilirubin, prothrombin time calculated as International Normalized Ratio (INR), and serum creatinine. The MELD score has many advantages when compared with the CPT score. First, it utilizes objective parameters. Second, its objective parameters are less subject to center-to-center variability. Third, the MELD score increases as the 3 constituent parameters deteriorate, as opposed to the CPT score in which the individual scoring elements remain fixed once a defined threshold has been reached.

The formula for the MELD score is

\[
3.8 \log_e(\text{bilirubin [mg/dL]}) + 11.2 \log_e(\text{INR}) + 9.6 \log_e(\text{creatinine [mg/dL]}) + 6.4 \times (\text{etiology}: 0 \text{ if cholestatic or alcoholic, } 1 \text{ otherwise})
\]

An on-line worksheet is available via the Internet at [www.mayo.edu/int-med/gi/model/mayomodl.htm](http://www.mayo.edu/int-med/gi/model/mayomodl.htm).

Kamath and colleagues\(^ {29}\) have prospectively validated the MELD score in 4 pretransplant populations. These groups included 1) patients hospitalized for decompensated liver disease, 2) ambulatory patients with noncholestatic cirrhosis, 3) patients with primary biliary cirrhosis, and 4) a group of unselected patients from the 1980s with cirrhosis. The data revealed that the MELD score was useful in determining the risk of death at 3 time intervals relevant to the decision to perform liver transplantation (eg, 1 week, 3 months, and 1 year). Moreover, the addition of clinical parameters often associated with decompensation and poor outcome such
as ascites, encephalopathy, variceal bleeding, or spontaneous bacterial peritonitis did not substantially improve the degree of fit between the MELD score and eventual outcome.29

**Implications of MELD Score on Liver Transplantation**

The use of MELD score in organ allocation has been as controversial as the system of organ distribution that it replaced. What is clear, however, is that “sicker” patients are being transplanted and that the proportion of deaths on the waiting list has fallen. The proportion of patients undergoing transplantation for end-stage liver disease in association with HCC has also increased. What is not taken into consideration when assessing recent waiting list mortality, however, is that the proportion of LDLT has increased over the same time period. In fact, the volume of LDLT has increased more than 6-fold over the last 4 years.30

The increase in patients with end-stage liver disease and concurrent HCC has occurred primarily as a result of assigning additional MELD points, thereby conveying a higher priority to patients with HCC compared with those without HCC who have the same degree of liver dysfunction. For a patient with HCC, the presence of either biopsy-proven HCC or rising alpha-fetoprotein levels in conjunction with appropriate imaging studies (eg, contrast-enhanced computed tomography [CT] or arteriography) results in the allocation of 20 MELD points. Every 3 months, 3 MELD points are added to the patient’s score until the patient either receives a liver graft or becomes ineligible for transplantation as a consequence of tumor burden (ie, tumor volume > 5 cm, or >3 lesions).11 Other exceptions to the MELD allocation scheme include the presence of confirmed hepatopulmonary syndrome, primary hyperoxaluria, or the presence of amyloidosis, all of which entitle potential transplant candidates to 24 MELD points. As with patients listed for the indication of HCC, 3 MELD points are added to the score every 3 months until either transplantation or death.

Although LDLT has been a successful procedure for most recipients, outcomes in patients who underwent transplantation as UNOS status 2As were marginal. A recent study addressed LDLT recipient outcomes relative to MELD score since such information would be useful in the selection of living donor recipients.31 At the University of Colorado, investigators retrospectively analyzed all right hepatic lobe adult-to-adult LDLT recipients between August 1997 and March 2002. Patients with fulminant hepatic failure were excluded. In the analysis, MELD scores at the time of LDLT correlated with 1-year patient and graft survival and
number of hospital days during the 90-day post-LDLT period. Of 62 recipients with greater than 6 months of follow-up who were transplanted for a variety of indications, the median MELD score was 13 (range, 6-40). One-year patient and graft survival rates were 95% and 84%, respectively, with no statistical difference between MELD scores of patients who died following transplantation and survivors (15 vs. 13). In addition, no difference was found in MELD scores between patients who underwent retransplantation and those who did not (16.5 vs. 13). Moreover, the median number of hospital days in the 90-day post-LDLT period was 16.0 days. However, LDLT recipients with a MELD score greater than 18 had significantly more hospital days than recipients with a MELD score of less than 18 (35.2 vs. 19.8 days). These data suggest that earlier consideration of LDLT results in shorter hospitalizations following the procedure.

**Indications for Liver Transplantation**

In considering indications for liver transplantation in adults, one must take into account 2 distinct groups of patients, those with acute liver failure and those with end-stage liver disease and subsequent cirrhosis. For patients with acute liver failure, several criteria have been defined to determine which patients require transplantation. The 2 methods that are most often utilized are the King’s College Hospital criteria and the Clichy criteria (Tables 2 and 3). Both methods offer specificity of 90% in predicting mortality from fulminant hepatic failure. Because of the donor organ shortage causing a delay between listing and the offer of a suitable

<table>
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<th>TABLE 2. Criteria adapted for identifying patients who are considered for transplantation, King’s College Hospital, London (King’s criteria)</th>
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| Acetaminophen  
  pH < 7.30 (regardless of encephalopathy grade after volume recussitation)  
  or  
  Prothrombin time > 100 seconds (INR > 6.5) + serum creatinine > 3.5 mg/dL if in grade III or IV coma |
| Nonacetaminophen  
  Prothrombin time > 100 seconds (INR > 6.5) (regardless of encephalopathy grade)  
  or  
  Any 3 of the following (regardless of encephalopathy grade)  
  1. Etiology (NANB/indeterminate hepatitis/halothane/drug reaction)  
  2. Age < 10 or > 40 years  
  3. Jaundice to encephalopathy interval > 7 days  
  4. Prothrombin time > 50 seconds (INR > 3.5)  
  5. Serum bilirubin > 34 mg/dL |

INR, international normalized ratio; NANB, non-A, non-B.
organ, it has been suggested that liver transplantation should be discussed with and offered to the families of all patients with grade III or IV encephalopathy; however the decision to proceed with transplantation should be deferred until an organ becomes available for the patient. An alternative method involves performing volumetric CT scans in patients in whom doubt exists and transplanting those with liver volumes of less than 700 mL. Those patients with hepatic volumes between 700 and 900 mL should undergo serial CT scanning and observation, and those with liver volumes greater than 900 mL are not offered transplantation. These aforementioned methods have not been subjected to rigorous prospective evaluation and, therefore, cannot be recommended for clinical application.

LDLT for patients with fulminant hepatic failure is the subject of considerable controversy. Performing a right hepatectomy in a healthy donor for an emergency transplant into a patient with fulminant hepatic failure raises serious ethical, medical, logistical, and economical concerns; however, for patients with chronic, end-stage liver disease and cirrhosis, LDLT should be considered. In general, patients should not be considered as candidates for LDLT unless they also fulfill listing criteria for deceased donor transplantation. This policy is controversial and many centers argue that LDLT provides an opportunity to extend the conventional indications for liver transplantation; however, recent data suggest that liver transplant survival benefit is greatest for patients with MELD scores greater than 15. According to the current Scientific Registry of Transplant Recipients (SRTR) database, patients with MELD scores of less than 15 derive no demonstrable benefit from transplantation.

### Donor Selection

In the United States, the first comprehensive report assessing the suitability of potential donors of right hepatic lobes was reported by Trotter and colleagues. Surprisingly, the proportion of liver transplant candidates with suitable donors was low. The study assessed the first 100 potential transplant recipients for LDLT at the University of Colorado Health Sciences Center, all of whom had first been listed for cadaveric transplantation and met the listing criteria of UNOS statuses 1, 2A, or 2B. Once listed, those patients deemed suitable for LDLT were given the option to approach potential donors.

| Age < 30 years | Confusion or coma + factor V level < 20% |
| Age > 30 years | Confusion or coma + factor V level < 30% |
Following administration of a preliminary screening questionnaire to recipients, a formal evaluation was planned. Of the 100 potential recipients evaluated, 51 were rejected based on recipient characteristics that included imminent cadaveric transplantation (8 patients); refusal of evaluation (4 patients); lack of financial approval (6 patients); and medical, psychosocial, or surgical problems (33 patients). Of the remaining 49 recipients who were considered to be ideal candidates for LDLT, 24 were unable to identify a suitable donor for evaluation. Although 26 donors were evaluated for the remaining 25 potential transplant recipients, almost one-half were rejected, 9 of those for medical reasons. Two potential donors declined to donate after being medically approved. The remaining 15 donor-recipient pairs underwent LDLT. Based on this prospective evaluation of the applicability of LDLT, only 15 of the original 100 recipients underwent transplantation. Recipient characteristics and donor availability will likely limit the widespread application of LDLT.18,36

In choosing appropriate recipients (both adult and pediatric) of living donor transplants, the transplant team must consider the advantages of the procedure as compared with cadaveric transplantation, primarily the reduction in waiting time and the ability to perform an elective procedure before disease progression and the recipient becomes too ill to transplant. Once a potential donor is evaluated and deemed suitable, LDLT may be scheduled as clinically appropriate. At 1 center, the median waiting time for transplant candidates for cadaveric livers was 354 days, whereas the median waiting time was 178 days for candidates for living-donor livers.37

When one considers the benefits of LDLT, the foremost advantage is that the procedure is scheduled electively. LDLT allows for optimal preoperative assessment and stabilization of recipients. A second advantage is that the cold ischemia time (the time between removal of the donor liver and its reperfusion in the recipient) is greatly reduced with LDLT. In cadaveric transplantation, this time typically measures 8 to 12 hours. With LDLT, the donor and recipient routinely undergo their procedures concurrently and in adjoining operating rooms, resulting frequently in cold-ischemia times of less than 1 hour. It is thought that a reduction in cold-ischemia time will limit allograft dysfunction and enhance immediate graft performance.38 Furthermore, living grafts have the advantage of being procured from healthy donors who have been extensively evaluated for comorbid diseases. In contrast, cadaveric organs are typically obtained from patients who have died after a critical injury, cerebrovascular accident, or critical illness. The function of organs from a deceased donor
may be compromised by the physiologic perturbations of brain death as well as the processes involved in ischemia-reperfusion injury.\textsuperscript{39}

The utilization of living donors for liver transplantation is associated with unique risks. Potential morbidity and mortality exist for a healthy person undergoing a procedure that has no benefit for the donor except the knowledge that they helped a loved one. In addition, data comparing long-term survival of living donor liver recipients to that of recipients of deceased donor livers is limited. Consequently, the incidence and extent of long-term complications and outcomes are less certain than with conventional transplantation. Moreover, there are few cost data analyses and no cost effectiveness data available. And last, as expected, the volume of the available liver mass to transplant is smaller with LDLT than with cadaveric transplantation. Despite this, it is rarely a cause of significant clinical problems due to preoperative screening, although there may be an increased incidence of mild delayed graft function. In all cases, the recipient of a potential transplant from a living donor should meet UNOS criteria for placement on the deceased donor liver transplant list. One must keep in mind that urgent cadaveric transplantation may be required if the graft from the living donor fails.

The transplant evaluation for potential liver transplant recipients is identical for both the deceased and living donor pools. Whether or not all patients listed for cadaveric transplantation are suitable for LDLT is controversial. Some would argue that the most appropriate candidates for LDLT are those patients in urgent need of transplantation, whereas other centers exclude those patients for LDLT based on concerns regarding donor coercion.

The majority of potential transplant recipients have decompensated, chronic liver disease. In addition, the recent changes in organ allocation using the MELD score rather than the traditional UNOS status has led to a shift in recipient characteristics to those who are more severely ill. Patients undergoing cadaveric transplant have a higher acuity of illness compared with those in the pre-MELD era. As a result, critically ill patients may be better candidates for expedited cadaveric transplantation than for living-donor liver transplantation. Nonetheless, there remains controversy as to whether patients with stable, chronic liver disease and lower MELD scores should be evaluated routinely for LDLT. Policies vary between transplant centers, with proponents of LDLT arguing that early transplant increases the chance of a favorable outcome. Ultimately, the decision to consider individual patients for LDLT rests with the multidisciplinary transplant team. Throughout the process, the potential
donor must be assigned advocates, and the team must base decisions on
the concept that donor safety is of utmost importance.

Once a potential recipient has been determined to be an acceptable
candidate for LDLT by the multidisciplinary transplant team, the patient
may submit the names of volunteer donors for evaluation. Donor
participation must be entirely voluntary, and it is the policy of transplant
centers to require that potential donors contact the transplant center
directly to initiate the assessment process. Solicitation of donors by the
transplant center is unethical and unacceptable. Potential donors range in
age from 18 to 60 years and are ABO blood group identical to or
compatible with that of the recipient. In addition, the potential donor
should have no medical comorbidities (eg, diabetes, hypertension, and so
on), and demonstrate a long-term, significant relationship with the
potential recipient (eg, spouse, other family member, or friend). There are
reports of anonymous, altruistic, living liver donors who have no
emotional bond with the recipient; however, the incidence is much less
frequent than that seen in the field of kidney transplantation. These
requirements alone will exclude approximately 50% of potential recipi-
ents from living donor consideration.18 Both adult and pediatric donors
are evaluated in a systematic fashion designed to exclude unsuitable
donors early in the evaluation process and before expensive medical
testing. Because many third party payors will only reimburse for the
complete evaluation of 1 potential donor, it is important to exclude
unsuitable donors as soon as possible.

The evaluation process at our own center involves the assignment of
independent teams to evaluate the recipient and donor to avoid any
perception of conflict of interest. This includes an independent transplant
nurse coordinator, social worker, hepatologist, surgeon, and psychologist.
Once the donor has contacted the transplant center, the initial evaluation
is performed by telephone and basic information is obtained (eg, age; sex;
height; weight; relationship to the recipient; blood type; current medica-
tions; and medical, psychiatric, and surgical history) to determine whether
the potential donor is suitable for further evaluation. The importance of
this initial phone interview cannot be overemphasized, since many
comorbidities may come to light during the phone interview that would
preclude further evaluation. Data seemingly as innocuous as height and
weight may be important in excluding a potential donor, since recent data
from Rinella and colleagues40 determined that 76% of potential donors
with a body-mass index (BMI) greater than 28 had substantial hepatic
steatosis, generally considered a contraindication to donation. In contrast,
no patient with a BMI of less than 25 had hepatic steatosis detected on
liver biopsy.\textsuperscript{40} Given that fatty livers function poorly after transplantation, potential donors with a BMI greater than 28 should be excluded from evaluation.

If the potential donor appears suitable after the initial telephone screening, a formal evaluation is scheduled with our hepatologist and psychologist. An independent survey of practice patterns among transplant programs in the United States recently reported that 90\% of donors were evaluated by a hepatologist, 95\% by a social worker, and 86\% by a psychologist or psychiatrist.\textsuperscript{25} Once cleared by the hepatologist and mental health professionals, the remaining phases of the assessment are scheduled. This typically includes additional invasive testing and a frank discussion regarding the risks and benefits of LDLT (Tables 4 and 5).

The types and frequencies of invasive diagnostic testing vary extensively between centers. Most programs do not require liver biopsy or arteriography except in selected cases.\textsuperscript{25} It is apparent that patients with a BMI of less than 25 can avoid biopsy completely, whereas potential donors with a BMI greater than 25 have at least a 25\% risk of having significant steatosis.\textsuperscript{40} Some centers utilize magnetic resonance imaging (MRI) or CT angiography as a noninvasive method of identifying aberrant arterial anatomy. Delineation of bile duct anatomy by using endoscopic retrograde cholangiopancreatography or magnetic resonance cholangiopancreatography is performed routinely in 85\% of centers in a recent survey, whereas 5\% of centers reported not using any imaging modality to examine the bile duct anatomy.\textsuperscript{25}

### Assessing Segmental Liver Volume

After a potential donor has cleared the medical and psychological screens, the most important step in determining donor suitability is an accurate assessment of the volume of liver available for transplantation. Traditionally, this has been determined by volumetric CT; however, MRI has gained in popularity recently.\textsuperscript{41} MRI has the advantage of assessing hepatic volume as well as providing images of arterial, portal venous, and biliary anatomy.\textsuperscript{42,43} The consequences of not resecting sufficient hepatic mass can be catastrophic, resulting in poor allograft function, graft failure, or death of the recipient.\textsuperscript{44}

An important issue in LDLT is the prevention of “small-for-size” syndrome. This can be avoided through an intensive evaluation of potential graft size before transplantation. The problems associated with small-for-size grafts were recently addressed in a report of 79 consecutive patients who underwent 80 living donor liver transplant procedures,
including 1 retransplant, at the University of Tokyo from 1996 to 2000. Patients were divided into 2 groups by graft size: graft weight/recipient standard liver volume ratio $\leq 40\%$ (n = 24) and $> 40\%$ (n = 56). Mean standard liver volume ratios were 37\% in the small graft group and 84\% in the large group. Survival rates were significantly lower in the small-for-size group (80\% vs. 96\%). The duration of hyperbilirubinemia and prothrombin time prolongation was significantly longer in the small-for-size graft group. These results suggest that an allograft weight ratio of $\leq 40\%$ confers a decreased survival rate after LDLT.

An alternative approach to the graft weight/recipient standard liver volume ratio is the concept of “graft-to-recipient weight ratio” (GRWR).
Using this approach, the volume of liver required to achieve an acceptable posttransplant outcome is 0.8% to 1% of the recipient’s total body weight. A recent report examined the interaction between the patient’s preoperative morbidity status and GRWR.46 Forty adults underwent liver transplantation using left (n = 10; mean graft weight, 481 ± 83 g) or right lobes (n = 30; mean graft weight, 845 ± 182 g). Small grafts were defined as GRWR of ≤0.85%, whereas large grafts were defined as GRWR greater than 0.85%. Among transplant recipients with normal liver preoperative hepatic synthetic function or Child’s class A cirrhosis, there was no significant difference with the use of small (n = 6) or large (n = 9) grafts, with graft survival rates of 83% and 88%, respectively. In

<table>
<thead>
<tr>
<th>TABLE 5. Potential risks for donors undergoing LDLT*</th>
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<tr>
<td>General risks</td>
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<tr>
<td>0.01% to 0.03% risk of procedure-related death for adult-to-child left lobe and left lateral segment donation.</td>
</tr>
<tr>
<td>0.1% to 0.3% risk of procedure related death for adult-to-adult right-lobe LDLT.</td>
</tr>
<tr>
<td>Acute liver failure or chronic hepatic dysfunction requiring urgent liver transplant, need for life-long immunosuppression, with its associated risks, complications, etc.</td>
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<tr>
<td>Anesthesia-related complications.</td>
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<tr>
<td>Blood-borne infection and other transfusion-related morbidity.</td>
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<tr>
<td>Risks associated with intensive care and hospital admission (methicillin-resistant <em>Staphylococcus aureus</em>, vancomycin-resistant <em>Enterococcus</em>, etc).</td>
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<tr>
<td>Infections and other complications related to intubation, mechanical ventilation, invasive monitoring, and catheter placement.</td>
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<tr>
<td>Preoperative risks</td>
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<tr>
<td>Risk of diagnosis of previously undiscovered disease.</td>
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<tr>
<td>Bleeding and other complications of liver biopsy.</td>
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<tr>
<td>Risk of pancreatitis with ERCP.</td>
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<tr>
<td>Allergic reaction to contrast media (MRI, CT, arteriography).</td>
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<tr>
<td>Postoperative risks</td>
</tr>
<tr>
<td>10% to 67% incidence of postoperative complications.25,54,77,78</td>
</tr>
<tr>
<td>Potential complications of any abdominal surgery.</td>
</tr>
<tr>
<td>Complications specific to liver resection (biliary leaks/strictures, bilomas, hepatic artery/portal vein thrombosis, Budd-Chiari syndrome, etc) with potential long-term sequelae from any of these adverse events.</td>
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<tr>
<td>Incisional pain and hernia.</td>
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<tr>
<td>Impairment in quality of life.</td>
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<tr>
<td>Compromise of success of future abdominal surgeries of the donor including transplant if required.</td>
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<tr>
<td>Potential for short-term or long-term disability that might affect employment status, interpersonal relationships and future issuance of health and life insurance.54</td>
</tr>
<tr>
<td>Financial hardship.</td>
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<tr>
<td>Deterioration in relationship between donor and recipient.</td>
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</tbody>
</table>

*Adapted from Schiano T, Kim-Schluger L, Gondolesi G, Miller C. Adult living donor liver transplantation: The hepatologist’s perspective. Hepatology 2001;33,1:3-9. ERCP, endoscopic retrograde cholangiopancreatography; MRI, magnetic resonance imaging; CT, computed tomography.
contrast, among patients with Child’s class B or class C cirrhosis, graft survival rates were 74% in recipients of large grafts (n = 19) and 33% in recipients of small grafts (n = 6; P = 0.023). Small-for-size syndrome developed in 5 of 6 patients with Child’s class B or class C cirrhosis who received small grafts. Of these, 2 patients died (1 patient after retransplantation) and 3 patients survived (2 patients after retransplantation). Graft function and survival are influenced not only by graft size, but also by pretransplant disease severity. Thus, GRWR as low as 0.6% can be used safely in patients without cirrhosis, with metabolic liver disease, or in patients with Child’s class A cirrhosis. Liver recipients with Child’s class B or C cirrhosis require a GRWR greater than 0.85% to avoid small-for-size syndrome and related complications.

In an early study, segmental liver size was determined by CT and was compared with the calculated volume actually obtained during donor hepatectomy. The volume of the left lateral segment (175 to 241 mL) and the left lobe (310 to 490 mL) varied markedly among the donors. The ratio of the left lobar to total liver volume varied widely between 23.2% and 35.9%. In other words, the donor’s size is not predictive of the dimensions of the left lobe.

**Informed Consent**

In light of recent reports of adverse outcomes for living liver donors, the importance of informed consent cannot be overemphasized. A full and frank discussion regarding LDLT and all its ramifications is critical in the assessment of potential donors. When the United States’ first pediatric living donor liver program was initiated at the University of Chicago, the procedures were performed under a protocol with the approval of the local ethics committee and utilization of a 2-stage consent to ensure volunteerism. In the United States, donor evaluation by an independent hepatologist is required by most programs. In some countries, such as the United Kingdom, a third physician independent of both the donor and recipient hepatologists and surgeons is required to assess the potential donor’s understanding of the impending surgery and its associated risks. Discussions regarding the risks associated with donation should be initiated early in the course of the evaluation. Potential donors should be aware of the limitations of transplantation as well as the risks of LDLT to the recipient (eg, graft failure, death, and so on). It is imperative that the donor is informed of all risks that they incur as a donor. The postoperative morbidity associated with liver donation ranges between 10% and 40%. The most common postoperative complications are bile leak, wound infection, and gastric/duodenal ulceration. In a review of 1000
living related liver donors, Lang and colleagues reported 3 deaths due to thromboembolic events or septic complications. Currently, there is no centralized database for the collection of adverse events associated with live liver donation; therefore, the incidence of death after the procedure is unknown. The risk of death from right hepatectomy for cancer is reported to be from 1% to 5%, and this range should be used as a point of reference during the informed consent process. The experience of the transplant team with surgery of this nature should also be discussed. In addition, it must be conveyed to the potential donor and their family that the evaluating physician is his or her advocate, primarily concerned with the donor’s mental and physical well-being and not focused on facilitating the rapid transplantation of a loved one.

Since the donor evaluation process may bring to light previously unknown disease processes in the potential donor, many programs, including our own, encourage the donor to obtain adequate life insurance coverage before embarking on the evaluation process. Abnormal tests identified during the process are reviewed at length with the prospective donor, and health care issues discovered as a consequence are followed up appropriately. Finally, if the donor is an appropriate candidate, the issues outlined in Table 5 should be reviewed again in private with the potential donor so that the possibility of coercion is avoided. At all points in the process, it is the responsibility of the transplant team to assure the donor that he or she has the right to withdraw from participation at any time and for any reason, and that the reason(s) for withdrawal will be protected under the confidential bond between the doctor and patient. The potential donor should always have the option of withdrawing under the guise of a medical disclaimer, thereby protecting the relationship between the donor, the recipient, and family members.

The Ethics of Donor Selection

The involvement of healthy living donors and the degree of technical difficulty associated with hepatectomy makes adult LDLT unlike any other surgical procedure. From the beginning, ethical issues have been at the top of the agenda of the liver transplant community, initially regarding the implications of donation of the left lobe or left lateral segment to children or small adults and then the implications of donation of the right lobe to adult recipients. Although the risk of death cited to prospective donors varies from center to center, a recent survey reported a 10-fold difference in the odds cited, varying from as low as 0.1% to more than 1%, reflecting doubt within the transplant community regarding the true risk. In the same study, the actual risk of death among 449
reported donors was 0.2%; however, a number of donor deaths were not reported in that study.

A recent assessment of morbidity associated with living liver donation from a donor perspective revealed no significant change in physical activity, social activity, or emotional stability following surgery and that 92% of donors resumed their predonation occupations. In addition, regardless of the ultimate outcome of the recipient, 100% of donors said that they would donate again or recommend donation to someone contemplating the procedure. All donors surveyed at that institution were satisfied with their donation decision, although morbidity in the first year after donation may be greater than previously appreciated.

A recent survey of 100 liver transplant surgeons assessed their views on the complex issues raised by LDLT. Data were collected at meetings devoted to LDLT and by electronic mail. Subjects provided the projected 1-year survival threshold that they would require for the recipient before they would consider performing LDLT. Interestingly, the accepted survival was 79%. A majority of surgeons agreed that transplant programs have a duty to their patients to offer LDLT, and that the increasing success of the procedure will expand indications for liver transplantation. Nonetheless, all felt that the risk to the donor was the basis for a moral dilemma. Whether or not transplantation from a deceased donor should be offered for failed LDLT that was performed for an extended indication also created a dilemma since this indication denies other deserving recipients access to organs for which they would have qualified. What was not in doubt in the survey was the ethical requirement to place the donor’s best interests first.

The ethical dilemmas associated with LDLT have also involved the media. Recently, a Canadian couple sought media help to find an altruistic donor who was willing to donate part of his or her liver to their infant son who suffered from biliary atresia. Although Canadian transplant programs do not perform transplants from donors who do not share an emotional bond with the recipient, many programs within the United States and Europe will proceed with these combinations. Consequently, ethicists have debated questions raised by media appeals for directed altruistic living donations of organs, including the liver. Despite the success of such pleas, Ross suggests that appeals of this nature raise ethical concerns regarding: 1) who has access to the media; 2) who will be successful in their media campaigns; and 3) how coercion and inducement by brokers (families or institutions) can be prevented. The same author has suggested that the media adopt a policy not to cover organ appeals by families, despite their human interest value. Moreover,
Ross\textsuperscript{55} argues that transplant centers develop a unified policy restricting directed living donations to those who have an emotional relationship with the recipient, but this stance is controversial.

An alternate approach to the ethical dilemma is the argument that the high risks assumed by live donors undergoing hemihepatectomy may be justified by the steadily increasing mortality rate for adult recipients waiting for transplantation. Using this argument, a comprehensive informed consent process forms the cornerstone of responsible decision-making for both donors and recipients.\textsuperscript{56} In addition, the autonomy of decision-making of donors and recipients may allow the extension of indications to patients not suitable to undergo transplantation with grafts from deceased donors. However, the predicament of what to do when living donor grafts fail in recipients who would not otherwise have been candidates for cadaveric transplantation is more problematic. It has been suggested by some centers that broadening of indications is appropriate only in centers with adequate experience and proven expertise in adult LDLT.\textsuperscript{56,57} It is the duty of transplant professionals and patients to ensure the proper application of adult LDLT.

**Cost of Living Donor Transplantation**

An important long-term consideration for LDLT is the expense of the procedure compared with deceased donor liver transplantation. To date, few data have been generated regarding the cost. LDLT, in general, is a more complex procedure than cadaveric transplantation, and the costs associated with donation including evaluation, the procedure, and post-operative care must be incorporated in any cost analysis. Indeed, many third party payors will only reimburse for the evaluation of 1 potential live donor, whereas other state and federally funded agencies will compensate for LDLT only when applied to pediatric recipients.

In a recent study from the University of Colorado, the comprehensive costs of LDLT were compared with those of cadaveric liver transplantation.\textsuperscript{58} In their analysis, all costs of medical services provided at the institution were recorded for 24 LDLT and 43 cadaveric recipients with more than 1 year follow-up who underwent transplantation between 1997 and 2000. Donor costs included all donor evaluations (including those who were rejected), right hepatectomy, and follow-up costs for 1 year. For recipients, LDLT and cadaveric recipient costs included medical care for a period of 90 days before transplantation, operative costs, and follow-up costs for 1 year. Cost was expressed as an arbitrary cost unit (CU) that was given a value between $500 and $1500. The total cost of LDLT was 162.7 CU, whereas the cost associated with deceased donor
livers was 134.5 CU. Although there was no statistical difference between the costs of living donor and deceased donor transplantation, the total comprehensive cost of LDLT was 21% higher than cadaveric transplantation.58

**Living Donor Hepatectomy for Adult Recipients**

**Introduction**

The techniques of donor right hepatectomy, extended right hepatectomy, and left hepatectomy are described below. The mutual principles of the procedures include dissection in the appropriate anatomic plane in the absence of portal occlusion, minimization of blood loss, and avoidance of injury to the remaining liver. It is also imperative to identify the relevant hepatic venous anatomy by intraoperative ultrasound (IOUS) and to preserve hepatic veins greater than 5 mm in diameter in the resected graft.

In general, the donor is prepared and positioned for operation in the same manner as a patient undergoing a major hepatic resecion for intrinsic liver disease. The donor may be offered the option of a thoracic epidural catheter for postoperative analgesia before being placed in the supine position. Central venous and arterial blood pressure lines should be placed. Because there have been donor deaths due to deep venous thrombosis, it is essential that prophylaxis is initiated before the induction of anesthesia with lower extremity sequential compression devices and then postoperatively with subcutaneous or low molecular weight heparin. The donor is also encouraged to bank 2 autologous units of blood before operation. In addition, isovolemic hemodilution can be used at the time of operation to limit the exposure to nonautologous blood. This process involves removing 2 units of blood from the donor and replacing the volume with crystalloid after anesthesia is induced.

**Right Donor Hepatectomy**

The technique of right donor hepatectomy outlined below was originally described by Marcos and colleagues and has been expanded by others,8,16 (Fig 2). A bilateral subcostal incision with midline extension to the xyphoid process is performed in all donors. The next step is cholecystectomy and intraoperative cholangiography to delineate hepatic ductal anatomy, particularly the variation in drainage of the right posterior segment duct. IOUS is facilitated by mobilization of the right lobe. Simple division of the attachments to the diaphragm is adequate at this point. The left lobe should not be mobilized so that “kinking” of the venous outflow due to twisting is avoided on removal of the right lobe.
This is an important technical consideration since a right lobe donor has required liver transplantation due to acquired Budd-Chiari syndrome due to this phenomenon.48

The avascular portion of the gastrohepatic ligament should be divided to prevent damage from retraction. IOUS defines the course and relationship of the middle hepatic vein (MHV) to the right hepatic vein (RHV) as they drain into the vena cava. The significance of identifying accessory veins that drain the right lobe cannot be overstated since those greater than 5 mm in diameter should be anastomosed directly to the recipient’s inferior vena cava (IVC). The superior surface of the liver is marked with the argon beam coagulator approximately 1 cm right of the MHV for later transection. The right hepatic artery (RHA) is identified usually as it
courses behind the common bile duct (CBD), and the attachments are divided carefully, minimizing dissection around the CBD. A vessel loop is placed around the artery for gentle traction and dissection proceeds into the liver, which also facilitates later dissection of the right portal vein (RPV). If the main arterial branch to segment 4 arises from the RHA, proximal dissection of the latter is performed only to the origin of this branch.

After the RHA has been isolated, the RPV is identified, mobilized, and encircled with a vessel loop. If the portal vein trifurcates, full mobilization of the portal vein is achieved after transaction of the parenchyma. If the portal vein branch supplying segment 4 arises from the RPV, then dissection is performed proximal to this branch. If it takes its origin from the left portal vein (LPV), dissection is performed beyond the bifurcation to assess the anatomy of the LPV, an essential maneuver before clamping the hepatic vasculature and removing the graft. Careful dissection of the RPV is then continued toward the liver. The right hepatic duct(s) are now visualized to orient the transection plane of the last one-third of the inferior surface of the liver. With this, mobilization of the right lobe is completed.

The next steps involve dissection of the retrohepatic IVC, preserving all significant accessory veins draining the right lobe. Veins of more than 5 mm in diameter or any others determined to be significant by IOUS evaluation are preserved. Dissection of the cava is continued until the RHV is encountered. Utilizing blunt dissection techniques, a right angle instrument is advanced between the MHV and RHV to the third digit of the opposite hand. Care must be taken to ensure that no lateral traction is placed on the liver during this maneuver. If the retrohepatic cava is significantly adherent, these maneuvers should not be attempted, and control should be achieved during the final steps of the parenchymal transection.

Once all vessels are isolated, the liver parenchyma can be transected with the aid of the Cavitron Ultra-sonic Aspirator (CUSA®), Harmonic scalpel® (Johnson & Johnson), standard electrocautery, or argon beam coagulation. All significant blood vessels and bile duct branches are ligated with permanent monofilament sutures on both the donor and the recipient side. Transection begins at the anterior edge of the liver and proceeds cranially and toward the hilar plate simultaneously. The last one-third of the line of the transection on the inferior surface of the liver is determined by the position of the right bile duct. If multiple ducts are present, the most superior one draining the right lobe defines the plane. When the transection reaches two-thirds of the distance between the
anterior edge and hilar plate, the right bile duct is sharply divided. Adequate length should be left on the distal side of the bile duct to avoid narrowing the common hepatic duct at closure. When multiple ducts to the RL are encountered, no attempt to obtain a single duct should be made by cutting the CBD. The bile duct is left to drain throughout the remainder of the case. An excellent way to trace the intraparenchymal course of the ducts, and thereby prevent injury during the remaining transection, is by probing with a metal dilator. Hepatic transection continues cranially and posteriorly until the RHV is mobilized at the level of the vena cava. The bridge of liver behind the portal vein is then transected, leaving the right lobe attached only by the main vessels.

Before dividing the vessels, 40 U/kg of heparin, 12 g of mannitol, and 20 mg of furosemide are administered. The vessels are clamped and divided only after adequate inflow to the remnant left lobe is absolutely confirmed. No adjustments should be made to accommodate the particular recipient needs. The RHA is clamped and divided, leaving adequate length for closure of the proximal end without compromising the common hepatic artery or branch to the remaining segment. The distal transected portion of the RHA is left open to back-bleed. Next, the RPV is clamped. The RPV continues in roughly the same direction as the main portal vein, whereas the LPV forms an acute angle with the main portal vein. Blood flow in the main and left portal veins is quickly assessed using a Doppler probe, and the clamp moved closer to the RL if there is any compromise in flow. Division of the RPV too close to the bifurcation can result in stenosis or occlusion of the main portal vein. Prior dissection past the bifurcation of the portal vein permits adequate visual assessment of the LPV before division. Again, the vessel must be divided leaving adequate length for closure without encroaching on the main and left portal veins. The RPV is left open, allowing the right lobe to back-bleed into the abdomen. A finger is placed in the portal orifice to avoid significant hemorrhage without promoting stagnation of blood in the lobe. The accessory hepatic veins are next clamped and divided. With upward retraction of the right lobe, the RHV is then clamped and divided. It is cumbersome to place the hepatic vein clamp unless the accessory veins are first divided. The right lobe is transferred off the operative field, perfused with cold University of Wisconsin solution via the portal vein, and weighed. Flushing via the artery is generally avoided to prevent intimal injury. The lumen of the bile duct is rinsed with Wisconsin solution.

The remaining hepatic vein stump and any accessory branches to the IVC are closed with monofilament vascular sutures, followed by closure
of the portal vein orifice. The hepatic artery stump is simply ligated. Doppler interrogation of the left lobe is repeated. Fibrin glue is applied over the entire cut edge of the liver and drains are placed in the liver bed and next to the cut surface before closure.

**Extended Right Donor Hepatectomy**

Lo and colleagues describe the extended right hepatic lobectomy that includes the donor’s right and middle hepatic veins and is utilized for donors with small right lobes to provide additional hepatic mass (Fig 3). This procedure is initiated with a bilateral subcostal incision with midline extension to the xyphoid process. IOUS examination is performed to identify and evaluate the major vascular structures of the liver. Special attention is paid to the anatomy of the junction of the middle and left hepatic veins and the possible existence of a right inferior hepatic vein. Cholecystectomy is performed with intraoperative cholangiography to delineate anomalous biliary anatomy. Dissection along the right side of the liver hilum exposes the RHA. The RHA is dissected free to the right side of the common bile duct only. The RPV is mobilized, and individual branches to the caudate lobe are divided between ligatures. The right lobe of the liver then is mobilized, and the RHV is isolated outside the liver. If present, the right inferior hepatic vein is isolated and preserved.

When compared with the right lobe graft, which drains via the RHV, the extended right lobe graft (segments V, VI, VII, and VIII, and a rim of segment IV) includes middle hepatic venous drainage as well. The line of parenchymal transection is marked on the surface of the liver along the line of demarcation produced by temporary occlusion of the right hepatic artery and portal vein. Parenchymal transection is performed on the left side of the middle hepatic vein using an ultrasonic dissector without vascular inflow occlusion for either side of the liver. The right hepatic duct is divided close to the cut surface of the liver without disturbing the surrounding Glissonian sheath. The middle hepatic vein is completely isolated at its junction with the left hepatic vein. Continuation of the parenchymal transection proceeds until the graft becomes completely detached, except for the RHA, RPV, right and middle hepatic veins, and in selected cases, any additional right inferior hepatic veins. The RPV, RHA, and hepatic veins are individually clamped and divided. The liver graft is flushed immediately with cold University of Wisconsin solution through the portal vein on the back table. The bile duct is rinsed; however, the hepatic artery is generally not cannulated, but the lumen is rinsed. Fibrin glue is applied to the cut surface of the remaining liver, the operative field is drained, and the donor is closed.
It is paramount to assure adequate residual liver volume for the donor. Grafts must be of sufficient mass to support the recipient, but not at the expense of leaving inadequate residual volume in the donor and risking liver failure. The remnant liver volume should be no less than 30% of the original estimated weight.25

**FIG 3.** (Top) Donor operation. (Bottom) Implantation of the graft. RHV = right hepatic vein, MHV = middle hepatic vein, LHV = left hepatic vein, MPV = main portal vein, RPV = right portal vein, LPV = left portal vein, RHA = right hepatic artery, RHD = right hepatic duct, CBD = common bile duct. (Used with permission from Lo CM, Fan ST, Liu CL, Wei WI, Lo RJ, Lai CL, et al, Ann Surg 1997;226:264.)
Left Donor Hepatectomy

If volumetric CT scanning demonstrates sufficient left hepatic mass to support the intended recipient, the left donor hepatectomy technique represents an option. Although the left hepatectomy is a safer option for living donors, its use is limited by recipient size (most are too large) as well as issues regarding difficulties encountered positioning the graft during implantation in an attempt to avoid torsion and subsequent venous outflow obstruction. The left donor hepatectomy technique outlined below was originally described by Takayama and colleagues and includes caudate resection, which increases graft volume by an average of 10%.59

A bilateral subcostal incision with midline extension to the xyphoid process is performed. After division of the left triangular and gastrohepatic ligaments, the suprahepatic vena cava and extrahepatic segments of the major hepatic veins are exposed. When the cranial side of the left caudate lobe is retracted caudally, the junction between the IVC and the main trunk of the left and middle hepatic veins is exposed. The main trunk is encircled extrahepatically with a vessel loop. The left hepatic artery is dissected free from the surrounding tissue. The IVC ligament is ligated and divided from the left side, and the short hepatic veins draining the left side of the caudate lobe into the IVC are also ligated and divided. Cholecystectomy and intraoperative cholangiography are then performed.

The middle and right hepatic arteries and the left and right main branches of the portal vein are dissected free and encircled with vessel loops. During dissection of the left and right branches of the portal vein, all portal venous branches feeding the left side of the caudate lobe are preserved. Hepatic parenchymal transection can be performed under intermittent occlusion of the right hepatic artery and RPV. The transection plane is placed approximately 1 cm to the right of the demarcation line between the right and left lobes at the liver surface and a few millimeters to the right of the middle hepatic vein, as far as the center of the anterior surface of the IVC. After parenchymal division, the transection point of the left hepatic duct is determined utilizing the aforementioned intraoperative cholangiogram. The appropriate blood vessels are clamped and divided as described above.

This technique is recommended for recipients in whom the donor left lobe is of adequate volume for support. Using serum bilirubin as a marker of liver dysfunction, the donor morbidity rate for right hepatectomy has been reported to be higher than that for left hepatectomy, although there is no difference in the recipient mortality rates (14% vs. 15%).60,61 Left hepatectomy donation remains a viable option if donor and recipient sizes are compatible.
Surgical Technique of Implantation: Adult

The technique of right hepatic graft implantation is described below. The incision and exposure proceeds as for the standard cadaveric liver transplant. A generous bilateral subcostal incision is made in all recipients, with extension to the xyphoid process optional. Xyphoid extension is required only for upper caval exposure and visualization if necessary due to the body habitus of the recipient. The recipient hepatectomy proceeds in the standard fashion with preservation of the IVC. Care must be taken to preserve enough length of the hepatic artery and portal vein for later reconstruction. Taking this into consideration, the artery, which is divided early in the hepatectomy to limit blood loss, is transected for some length distal to the bifurcation. The bile duct is transected next, leaving enough length on the recipient side to facilitate a duct-to-duct anastomosis if that is desired, although anastomosis of the donor duct to a Roux limb is standard. The IVC is surrounded by an umbilical tape to control bleeding, if necessary. The branches draining directly into the cava are ligated and divided sequentially, thus separating the liver from the vena cava. Eventually, the diseased liver is left on a pedicle of right, middle, and left hepatic veins.

On the arrival and examination of the graft in the recipient operating room, the portal vein is divided and the RHV is clamped with a small vascular clamp. If there are dual portal veins or hepatic arteries present in the donor liver, these should be reconstructed as needed before completion of recipient hepatectomy. A vascular stapling device may be used to divide the left and middle veins in tandem. If there is hemodynamic instability or loss of visualization due to bowel edema, a temporary portocaval shunt can be constructed.

The right hepatic vein of the graft is then anastomosed to the recipient right hepatic orifice or directly to the vena cava. Any accessory draining veins larger than 5 mm are anastomosed to the vena cava directly to facilitate venous drainage of the graft. Adequate hepatic venous drainage is paramount not only to immediate graft function but also long-term graft and patient survival. In the early surgical experience, a significant proportion of early graft loss was due to inadequate venous outflow. Before completion of the right hepatic venous anastomosis, the graft is flushed via the portal vein with an iced Ringer’s solution to remove the intrahepatic University of Wisconsin solution that contains a high concentration of potassium. The portal vein of the graft is then anastomosed to the recipient portal vein, and the clamps are removed to
reperfuse the graft with portal blood. Hemostasis is confirmed, and then attention is directed to the hepatic artery. The donor hepatic artery is anastomosed to the proper, right, or left hepatic artery depending on size matching, length, and projected positioning.

Biliary reconstruction follows by either creating a Roux-en-y hepatico-jejunostomy or by choledochocholedochotomy. Standard drains are placed after achieving hemostasis. Due to the implantation of a right hepatic graft into the normal anatomical position, the risk of graft torsion is minimal.

For transplantation of the left hepatic lobe, implantation proceeds in a similar fashion with the exception of 2 important caveats. The venous drainage of the left lobe graft includes the left and middle hepatic veins, often on a common pedicle. This common orifice can be implanted into the confluence of the middle and left hepatic vein orifice in the recipient vena cava (Fig 4). Second, to avoid compromising venous outflow from torsion of the graft, the graft should be resuspended to ligamentous remnants of the diaphragm medially as well as the anterior abdominal wall.

Recipient Outcome and Complications: Adult

The general consensus in the transplant surgery community concerning LDLT is that it represents an acceptable form of therapy for the management of end-stage liver disease, provided donor risk is minimized and recipient survival is at an acceptable level. Many investigators have reported equivalent short-term outcomes for patients receiving deceased donor and living donor liver transplants; however, these results may reflect healthier living donor recipients at the time of transplantation. In reviewing recent published series from large LDLT centers, outcomes vary. At the University of Essen, the overall 1-year patient and graft survival rates published in a recent review were 79.4% and 75.3%, respectively, including those patients transplanted for acute liver failure. The overall 3-year patient and graft survival rates were 71.0% and 64.3%, respectively. Retransplantation was required in 14.9% of these patients due to primary graft failure.

In the University of Colorado’s recent report, survival in the first 41 patients was 93% with less than 1-year follow-up. Four patients required retransplantation due to technical complications (9.8%), all 4 receiving their living donor transplants within the center’s initial 11 cases. In a recent publication, the main variables associated with immediate graft survival included medical condition of the recipient at the time of
transplant, retransplantation versus primary transplant, and increased age of the donor.  

Clearly there is a surgical learning curve for this procedure, and the majority of early graft loss is due to technical complications. Causes of early LDLT graft loss include hepatic artery thrombosis (HAT), venous outflow compromise or occlusion, and the aforementioned small-for-size issues. The most significant and common complications of LDLT are

biliary. The reported incidence of bile leak following transplantation ranges from 0% to 43%.\textsuperscript{16,64} It has been shown that biliary complications decrease with experience of the surgical team.\textsuperscript{65} By avoiding dissection around the right hepatic duct as it exits the hepatic parenchyma, exacerbation of duct ischemia can be avoided. Management of an early leak is difficult. Reoperation is preferred to avoid sepsis. At our center, we perform the biliary anastomosis over an internal stent. This carries particular benefit if reoperation is necessary since the ductal epithelium may be of such poor quality that primary repair is impossible. Wide drainage and control of sepsis is mandatory. Early biliary leaks are a contributing factor to late stricture, and it is not surprising that the reported incidence of late stricture is 15% to 20% in most centers. There are few reports in the literature on late biliary strictures after LDLT. Decompression by percutaneous biliary catheters is difficult due to a lack of biliary dilation even with obstruction.\textsuperscript{65} Operative intervention is warranted if other methods fail; however, these procedures are difficult.

\textit{Recurrence of Hepatitis C}

Chronic hepatitis C infection is the most common indication for liver transplantation. Some centers have reported that hepatitis C recurs earlier and more severely in the recipients of living donor transplants when compared with patients who receive livers from deceased donors.\textsuperscript{58} The incidence of graft loss has also been shown by some investigators to be higher. Several factors have been shown to contribute to this phenomenon. The degree of human leukocyte antigen (HLA) matching between donor and recipient is higher in LDLT, a factor thought to contribute to recurrence of hepatitis C. It is also thought that the smaller hepatic mass transplanted during LDLT results in reduced metabolism of immunosuppressant medications, thus rendering the recipient overimmunosuppressed, a factor known to facilitate hepatitis C recurrence. In addition, regeneration of living donor livers following transplantation may promote the uptake of hepatitis C viral particles into hepatocytes and enhance viral translation and replication. Hepatic regeneration of this intensity is not observed in livers obtained from deceased donors.

If future studies show that the outcome of LDLT for hepatitis C is truly suboptimal, then strategies to decrease the impact of recurrence should be adopted. These include dosing immunosuppressants appropriately, considering early treatment of hepatitis C with interferon and ribavirin, and utilizing the donor who shares less HLA homology with the recipient if more than 1 donor is available.
Left Lateral Segment Hepatectomy for Transplantation in Pediatric Recipients

Introduction

Pediatric patients of all ages with end-stage liver disease are best treated with liver transplantation. As with adult liver transplantation, there is a large discrepancy between the number of available cadaveric organs and recipients. The situation is further complicated in pediatric patients, especially in infants, where the number of size matched pediatric organ donors further limits the number of transplants. Pediatric liver transplant candidates suffered from prolonged waiting times resulting in a disproportionately high pretransplant mortality rate as well as elevated posttransplant morbidity and mortality rates. As a result, many pediatric liver transplant centers developed techniques of “reduced sized” liver transplantation based on the segmental anatomy of the liver. The experience with cadaveric reduced size liver transplantation evolved into utilizing partial liver grafts from living donors for transplantation into pediatric recipients. The first such living donor liver transplant was performed in 1988, and since then more than 1000 living donor liver transplants have been performed in pediatric patients.3,4,6

Donor Evaluation

In the case of living donors for pediatric recipients, the majority of the donors are either a parent or a close relative, although unrelated donors have been utilized as well. Regardless of relationship with the recipient, all donors should undergo the same evaluation process that was previously described in this report.

Surgical Technique

In the case of pediatric recipients, the left lateral segment (segments II & III) from an adult donor is primarily utilized for transplantation, although monosegment grafts (segment III) and left lobe grafts (segments II, III, and IV) are also utilized for neonates and older children, respectively. The incisions for living donor liver resection for the left lateral segment that are used include a Reynolds flap (a vertical midline incision from the xiphoid process to just above the umbilicus, which is then extended transversely to the right anterior axillary line at the level of the tip of the 12th rib) or the traditional bisubcostal chevron incision, with or without a vertical midline extension to the xiphoid process. The chevron may be advantageous in donors with a larger body habitus.

On initiation of the resection, the ligamentum teres is ligated and
divided, along with the falciform ligament as close to the anterior abdominal wall as possible. By preserving the width of the falciform ligament that is attached to the liver, it can be utilized as a biological covering for the cut surface of the remaining donor liver. The left triangular ligament and the gastrohepatic ligaments are then divided with electrocautery, thereby freeing the left hepatic lobe. Care must be exercised dividing the gastrohepatic ligament since there may be an accessory or replaced left hepatic artery, which must be preserved because it will provide the arterial inflow for the transplanted graft. After the left hepatic lobe is mobilized, intraoperative ultrasound is performed to delineate the hepatic venous anatomy and define the plane of parenchymal transection. The left hepatic vein is then isolated at the level of the hepatic vein-vena cava junction and is encircled with a vessel loop. Occasionally, segments II and III will have independent venous orifices on the vena cava that must be recognized to avoid inadvertent injury and may require reconstruction before implantation in the recipient. In addition, the middle and left hepatic veins may have a common insertion in the vena cava, which will require division of the parenchyma to identify the junction of the middle and left hepatic veins and preservation of the middle hepatic vein.

Hilar dissection begins by dividing the bridge of liver tissue between the ligamentum teres and the liver hilum. At the base of the ligamentum teres, the left hepatic artery followed by the left portal vein branch and left common hepatic duct are isolated. It is important to remain to the left of the ligamentum teres to prevent injury to the structures entering the right lobe. If only segments II and III are to be utilized for transplantation, then the left hepatic artery and left portal vein branches must be dissected distally as much as possible with preservation of any large arterial branches to segment IV. The portal vein branches to segment IV can be ligated and divided. The bile duct from segment IV must also be preserved in a left lateral segmentectomy. The bile ducts to segments II and III usually form a common channel and can be identified a couple of centimeters deep to the liver surface within the umbilical fissure. In 25% of the population, the segment II and III ducts fail to form a common channel before joining the segment IV duct to form the left hepatic duct.

Parenchymal division is initiated with scoring of the liver surface with electrocautery. The parenchyma is divided 1 cm to the left of the falciform ligament, for a left lateral segment graft. Bridging vessels and biliary radicals are ligated on both sides of the transection plane as the parenchymal dissection proceeds. Once the parenchymal transection is completed, heparin is administered systemically to prevent intrahepatic
clot formation, and the hepatic artery and portal vein are clamped and divided followed by the hepatic vein. The liver segment is placed in ice cold slush and perfused with University of Wisconsin solution through the portal vein and hepatic artery (hepatic artery perfusion is per the surgeon’s choice and great care must be taken to avoid intimal injury). The stumps of the hepatic vein and artery are closed in the standard fashion. The cut surface of the liver is inspected for hemostasis and bile leaks. Fibrin glue is again used as a sealant and closed suction drains are placed along the cut surface of the liver to monitor for postoperative bleeding or bile.

The expected hospital length of stay for liver donation is 5 to 10 days, with 6 to 8 weeks for complete recovery. The major complications of liver donation include death (0.1-1%), biliary leak or stricture (6%), need for reoperation (5%), nonautologous blood transfusion (5%), and serious postoperative infection (1%). Liver insufficiency after donation has been reported, including a donor undergoing cadaveric liver transplantation for fulminant hepatic failure following right hepatic lobe donation. Unlike right donor hepatectomy, no cases of liver failure or insufficiency have been reported following left lateral segment donation.48

**Surgical Technique of Implantation: Pediatric**

Implantation of the left lateral segment graft is described below. The incision and exposure proceeds as for the standard cadaveric liver transplant. A generous bilateral subcostal incision is made in all recipients with optional extension to the xyphoid process. In pediatric patients, the inverted T incision can be made as well. As in adult patients, removal of the diseased liver proceeds in the standard fashion, with the vena cava being preserved. Caval cross-clamping is usually well tolerated by pediatric recipients and can be accomplished after the graft has been inspected and any necessary extension grafts have been anastomosed to either the portal vein or hepatic artery.

Implantation proceeds with the hepatic vein of the graft being anastomosed to the recipient vena cava using a large, triangulated cavotomy in the upper cava. Extreme care must be taken to rotate the cut surface of the graft toward the cava such that the venous anastomosis will not kink and the graft will not rotate on completion. This maneuver ensures optimal venous outflow from the graft. Before completion of the caval anastomosis, the graft is flushed via the portal vein with iced Ringer’s solution to remove the University of Wisconsin solution. The portal venous anastomosis follows, taking care to avoid both rotation of the anastomosis and excessive length to avoid kinking. The clamps are removed, and the graft
is reperfused with portal blood. If the native recipient hepatic artery is too short, a saphenous vein graft from the donor or an ABO-compatible, cryopreserved conduit can be used to derive arterial inflow from the recipient’s aorta. Biliary reconstruction is accomplished by Roux-en-y hepaticojejunostomy. The standard drains are placed near the cut surface and the procedure is completed with abdominal closure. Early Doppler evaluation is mandatory because hepatic artery thrombosis is a frequent early postoperative complication.

**Recipient Outcome and Complications: Pediatric**

Living donor liver transplantation using the left lateral segment was initially developed for pediatric recipients to circumvent their high mortality rate on the cadaveric waiting list. It is currently a standard therapy for infants with end-stage liver disease because size-matched cadaveric organs are scare. In a recent report, the cumulative world experience was reviewed and currently exceeds 2000 cases, with a donor mortality rate in the range of 0.1%. Between 1993 and 2002, 235 children received a primary liver transplant, 135 from deceased donors and 100 from live donors. The 5-year recipient survival rates were 85% for standard liver transplantation and 92% for LDLT. The 5-year graft survival rates were 77% and 89%, respectively. In this report, there was no donor mortality. These results are similar to those reported elsewhere.

In general, pediatric recipients who receive a graft from a live donor have a survival that equals or exceeds that of cadaveric organ recipients. Complications do occur, the most common of which are hepatic artery thrombosis and bile leaks or thrombosis; however, living donor liver transplantation remains an excellent modality for the treatment of end-stage liver disease in children.

In pediatric recipients of living donor grafts, the incidence of hepatic arterial thrombosis has been reported to range from 7% to 20% and remains 1 of the most devastating complications in terms of morbidity and mortality. It is the most common cause of early graft loss. The presentation of early hepatic arterial thrombosis is acute graft dysfunction, and it represents an inciting event for biliary leak and sepsis. In 1 series, 50% of biliary leaks were a result of hepatic artery thrombosis. Although early Doppler evaluation of the allograft is useful to establish a baseline, it is operator dependent and clinical suspicion of hepatic artery thrombosis must be confirmed with angiography or re-exploration. Arterial thrombosis in the early postoperative period requires prompt reoperation. Early thrombectomy and reconstruction may salvage the graft; however, if there is biliary epithelial necrosis or hepatic necrosis,
retransplantation may be necessary. In 1 series, 40% of children with hepatic artery thrombosis survived without retransplantation with an 83% 1-year survival overall.68 There are factors associated with an increased risk of hepatic artery thrombosis in pediatric liver transplant recipients: small recipient size (<10 kg), graft type (living donor > cadaveric), arterial anastomotic type (ie, end-to-end > aortic conduit), and hypercoagulability in the recipient (either underlying or acquired via intraoperative fresh frozen plasma).10,68,72 Some centers now propose all arterial anastomoses in LDLT in children be performed with microscopic techniques to limit the incidence of thrombosis; however, this is not uniformly accepted.51,73 Biliary complications usually manifest as bile leak, obstruction, or late strictures. Reconstruction of the biliary tract of the graft during transplantation is most commonly via Roux-en-y hepaticojejunostomy. In a series from Taiwan, biliary complications occurred in 3 of 34 patients, including bile leakage from the Roux-en-y limb, a missed biliary radicle, and late strictures of unknown origin.73 The complications were managed with reoperation or interventional radiology techniques. Clearly, if a bile leak is identified early in the postoperative period, hepatic artery patency must be established. Operative intervention, however, should proceed expeditiously. Hepatic arterial flow should be reestablished if necessary. Leaks from the Roux should be repaired primarily or revised. We utilize internal biliary stents in all cases to assist in the primary anastomoses. If the bile leak occurs early, the stent can facilitate repair. If the leak occurs from the cut surface of the liver, biliary radicles can be controlled with monofilament sutures. Wide drainage is required to prevent or control sepsis. Obstruction of the biliary anastomosis is less common—4% in some series.70 In cases of internal biliary tract obstruction, interventional radiology techniques may be required. Stricture formation postransplant occurs as a result of several factors. Most late strictures occur within 6 months of graft implantation and respond to interventional radiology manipulation. Occasionally, biliary strictures and resulting cholangitis will necessitate retransplantation.73 The incidence of biliary complications is similar in living and deceased donor pediatric liver transplant recipients.70

**Future Directions**

For the foreseeable future, the organ donor shortage will remain the most significant problem facing transplant professionals. Reports of donor deaths have diminished the enthusiasm and rapid proliferation of living donor transplantation in the United States; however, as techniques...
improve and the learning curve is overcome, the number of living donor transplants will likely increase.

Patients with fulminant hepatic failure have been bridged to transplantation with liver assist devices. The successful application of these technologies would increase the donor deficit because those patients who would otherwise have died might survive until transplantation. The potential for hepatic assist devices to decrease the need for livers is limited to those specific patients with fulminant hepatic failure who recover while being supported.

The sole treatment of chronic, end-stage liver disease due to cirrhosis is liver transplantation. The use of livers from other species, also known as xenotransplantation, has been proposed; however, several barriers remain to be overcome. Although it is generally believed that pigs would serve as donors, the potential for disease transmission to humans (zoonosis) has produced substantial debate. Porcine endogenous retrovirus (PERV) is of particular concern to federal regulatory agencies in the United States. Whether a pig’s liver can synthesize the thousands of proteins necessary to support human life is unknown.

Summary

In response to the critical organ shortage, transplant professionals have utilized living donors in an attempt to decrease the mortality rate associated with waiting on the liver transplant list. Although the surgical techniques were first utilized clinically 15 years ago, application of LDLT has been somewhat limited by the steep learning curve associated with developing a program. Clinical success with LDLT in children was realized early in the experience and application of the techniques to the adult population has occurred more recently.

Although transplant centers embark on LDLT with enthusiasm, the safety of the donor must always be at the forefront of the process. Potential donors must come to the decision to donate without pressure from members of the family or transplant team. He/she should also be assigned advocates who constantly promote the donor’s best interest. Failure to adhere to strict donor evaluation protocols and standardized operative techniques could result in disastrous consequences.

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