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Led by Thomas E. Starzl, the era of liver transplantation began in 1963 at the University of Colorado, and by 1967, the first patient transplanted by this group survived more than a year [1]. However, not until further advances of knowledge, experience, and surgical technique in the field of split-liver technique allowed the transplantation of one donor graft into two recipients [2], was living donor liver transplantation (LDLT) attempted. First successfully performed in 1989 by Broelsch et al. [3] at the University of Chicago, a young girl born with biliary atresia was the recipient of her mother's left lobe of liver. Since that time, experience in the field has grown to include adult-to-adult living liver transplantation.

As the wait list for liver transplants far exceeds the availability of cadaver donors, the use and widespread acceptance of LDLT have increased. However, the need to protect the donor from unacceptable risk is of paramount concern. In one case series, hospital mortality from hepatic resection was 3% [4]. Fortunately, the worldwide experience for LDLT has demonstrated a much lower mortality rate of 0.4–0.6% [5] for living liver donation, yet an order of magnitude higher than the risk for renal donation [6]. It is therefore imperative that a potential liver donor is

thoroughly investigated and screened to optimize the safety of the procedure.

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## Preoperative Evaluation

In 2000, the Live Organ Donor Group published a consensus statement, providing a guideline how to screen prospective liver donors [7]. Variations of this guideline exist from center to center as to which evaluation or procedure is performed during which phase of the screening process.

## First Evaluation Phase

The first evaluation phase involves prescreening the prospective donor, usually performed by a registered nurse to confirm that a potential donor meets the following criteria [8]: The prospective donor should be of legal age and have sufficient intellectual ability to understand the procedure and the associated risks. There should be evidence of an emotional relationship between the prospective donor and recipient, and potential donors who are believed or known to have been coerced into the process must be excluded. It is paramount to safeguard the donor and ensure that their welfare supersedes all other concerns including those of the recipient. The potential donor must also have the ability and willingness to comply with long-term follow-up. ABO incompatible grafts are known to have a poorer long-term outcome, and thus, ABO compatibility is

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**Table 26.1** Laboratory investigations during first phase of evaluation

Laboratory investigations [11]		
Amylase	Serology for	HBV
		HCV
Lipase		HIV
Glucose		CMV
Protein		EBV
Protein electrophoresis		HSV
Triglycerides		
Cholesterol		
TSH		
C-reactive protein		Protein C
Ferritin	Protein S	
Transferring saturation	Antithrombin III	
Alpha-1-antitrypsin	Factor V Leiden mutations	
Ceruloplasmin	Prothrombin mutations	
Antinuclear antibodies	Homocysteine	
Coagulation profile	Factor VIII	
Urinalysis	Cardiolipin	
	Antiphospholipid antibodies	

considered a prerequisite for donation [8]. The donor should be negative for hepatitis B surface antigen and hepatitis C antibody. Some centers may accept hepatitis B core antibody positive. As these donors have been exposed to hepatitis B at some point in the past, it is prudent to perform a liver biopsy if the candidate is to be further considered. About 18–34% of potential candidates are rejected in this first phase without utilizing significant resources or undergoing invasive testing [9, 10].

## Second Evaluation Phase

The second phase requires a thorough medical, laboratory (Table 26.1), and psychological evaluation. The potential donor is presented to the transplant team, and a decision is made whether to proceed to comprehensive donor evaluation. The patient's overall health status is assessed, and specifically, the absence of diabetes, severe or uncontrolled hypertension, and any hepatic, cardiac, renal, or pulmonary disease is confirmed (Table 26.2) [11]. A thorough preoperative anesthetic evaluation should be done at this time as well.

A transplant psychologist and/or a social worker will conduct the psychosocial evaluation. The goal is to educate the potential donor about the psychosocial impact of donor surgery and recovery, identify potential psychological or psychiatric issues that preclude donation, and ensure donor is able to consent without coercion by recipient, recipient's family, or transplant team.

## Third Evaluation Phase: Graft Feasibility Determination

The tests listed in Table 26.3 will aid in determining graft suitability; however, not all of these tests are routinely performed in all centers. It is important to ascertain hepatic volumetric data, delineate hepatic anatomy including hepatic artery, portal vein, hepatic veins, and assess the degree of steatosis [7]. The degree of steatosis can be assessed using imaging techniques [12]. The percentage of steatosis is subtracted from the estimated liver volume, thus yielding a corrected liver volume [13]. If deemed necessary, percutaneous liver biopsy can also be performed. It is center-specific whether a candidate with significant steatosis is accepted.

**Table 26.2** Noninvasive investigations during the second phase of evaluation

Noninvasive investigations [11]	
Electrocardiography	Doppler ultrasound of carotid arteries
Chest roentgenogram	Abdominal ultrasound
Pulmonary function test	Echocardiography

**Table 26.3** Tests to determine graft feasibility during the third phase of evaluation

Volumetric CT or MRI scan of liver
Splanchnic arteriography
Endoscopic retrograde cholangiopancreatography
Liver biopsy

The three phases of the evaluation of the potential liver donor are listed in Table 26.4.

## Ethical Considerations

In 2006, The Transplantation Society issued an ethics statement with respect to the living lung, liver, pancreas, and intestinal (extra-renal) donor. (Care of the live kidney donor was addressed 2 years earlier at the International Forum on the Care of the Live Kidney Donor held in Amsterdam.) The Transplantation Society concluded:

The Ethics Committee of TTS recommends that live lung, liver, pancreas and intestine donation should only be performed when the aggregate benefits to the donor–recipient pair (survival, quality of life, psychological, and social well-being) outweigh the risks to the donor–recipient pair (death, medical, psychological, and social morbidities) [14].

The committee defined essential ethical elements that need to be followed by the transplant center.

The responsibility of the transplant team performing live donation includes:

- Involvement of health-care professionals exclusively responsible to the donor
- Repetition of the information
- Psychosocial evaluation
- Provide a reflection period after medical acceptance and decision to donate
- Assess donor retention of information and understanding

- External review committees

Informed consent needs to include:

- Cognitive capacity
- Voluntary decision
- Donor understanding
- Disclosure, including recipient conditions which may impact the decision to donate with recipient's permission
- Expected transplant outcomes (favorable and unfavorable) for the recipient
- Information on alternative types of treatments for the recipient, including deceased organ transplantation
- Donor registries

Donor autonomy needs to be assured including the freedom to withdraw from the donation process at any time, with reasons for not proceeding kept confidential.

Donor selection should include:

- Legally incompetent or those who lack the capacity for autonomous decision making should be excluded from donation.
- Rarely an independent advocate for the donor needs to be appointed.
- In the event that nondirected or distant acquaintance live organ donation is considered, special considerations to prevent donor exploitation should be made.
- Centers should regard long-term access to health care after the procedure as a prerequisite for donation.
- The donation process and follow-up should be cost neutral for the donor.

## Contraindications to Donation [5]

A calculated remnant liver less than 30% of original liver volume with complete venous drainage puts the donor at risk of too-small-for-size syndrome. Preoperative volumetric imaging may actually overestimate actual liver volume by 10%. Similarly, an estimated graft liver volume to recipient body weight ratio (GWBWR) of <0.8% is a contraindication for donation. Other contraindications are:

- ABO incompatibility except in special circumstances, such as infants <1 year of age

**Table 26.4** Living donor evaluation criteria

Phase I	Phase I	Phase II	Phase II	Phase II	Phase III
Age	Relationship	Psychosocial support	Medical evaluation	Laboratory evaluation	Graft assessment
18–60	Emotionally related to recipient; ABO compatible; negative serology for hepatitis and HIV viruses	Adequate psychosocial support systems as determined by pediatric transplant team, psychiatry, and social services	Comprehensive history and physical examination negative for acute or chronic illness affecting operative risk	Hematologic, serum chemistry, liver, and kidney function normal; normal EKG and CXR*; negative serology for hepatitis and HIV viruses	Volumetric MR* scan excludes occult mass lesions, documents adequate liver volume; graft represents at least 50% of expected recipient liver mass; arteriography documents arterial supply for anticipated graft (for adult LRT* only)

\*EKG electrocardiogram; CXR chest X-ray; MR magnetic resonance; LRT living-related donor transplant. Reprinted with permission from [8]

without presence of isoagglutinins, and in emergencies where a cadaveric transplantation is not possible

- Portal or sinusoidal fibrosis
- Nonalcoholic steatohepatitis (NASH)
- Steatosis >20% (only for right liver)
- Portal inflammation and necrotic-inflammatory changes
- HIV, HCV, or HBV (HBsAg+) positive

A BMI >30 kg/m [2] is a relative contraindication to donation as these candidates usually have hepatic steatosis. Another concern is the presence of patent foramen ovale (PFO) in the donor, as the risk of paradoxical air embolism during the resection is increased [15]. It has even been advocated that the preoperative evaluation should include echocardiography to rule-out PFO [16].

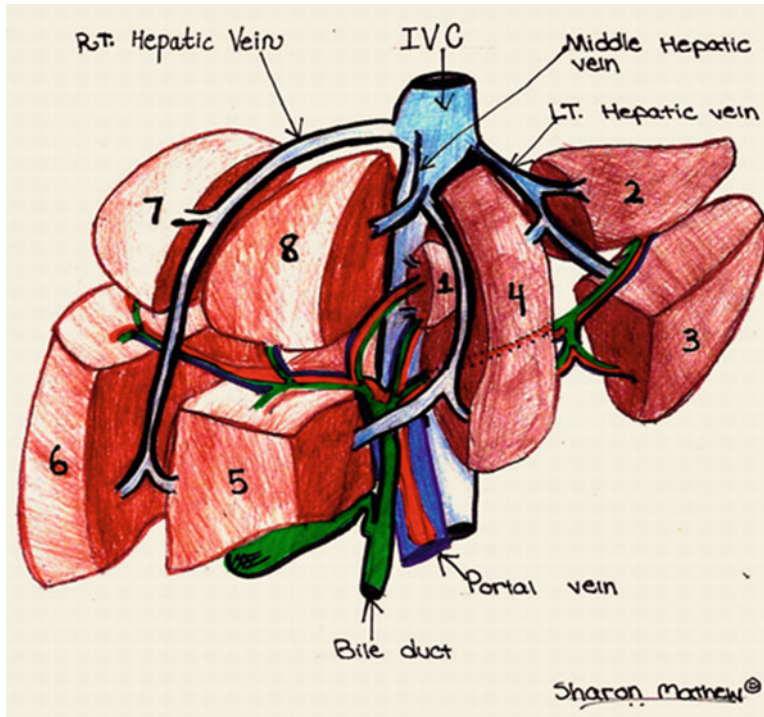
## Surgical Technique

In 1957, Claude Couinaud, a French surgeon, published his seminal work *Le Foie: Études anatomiques et chirurgicales* [17]. By delineating the segmental anatomy of the liver (Fig. 26.1), hepatectomy surgery became possible.

Four anatomic allografts are classically described for LDLT [18, 19]. The entire right

liver lobe (Couinaud segments V–VIII) is most commonly transplanted, comprising more than 60% of the donor's total liver mass. Normal liver volume is 1,294–1,502 mL in women and 1,796–1,956 mL in men [20]. The entire left liver lobe (Couinaud segments II–IV) is approximately 35% of the total liver volume, yielding 300–500 cc allografts that are ideally suited for recipients weighing approximately 50 kg. The left lateral segment (Couinaud segments II–III) yields 20% of total liver volume, a 200–300 cc allograft, and is used in large donor-to-recipient size disparity, and the recipient weight for a left lateral segment graft is usually restricted to less than 40 kg. Extended right liver (Couinaud segments IV–VIII) hepatectomy is the least commonly utilized graft and provides greater than 70% of standard liver volume (SLV) and is suitable for a small donor to large recipient situation. Risks to the donor by removal of such a large portion of the liver make this technique unjustifiable in most situations (Table 26.5).

Options for pediatric LDLT include entire left liver lobe, left lateral segment, and left lateral segment with a part of segment IV [19]. To assess graft size adequacy, a graft weight to recipient body weight ratio (GWBWR) is calculated [21]. Alternately, the percentage of the calculated SLV can be used [22, 23]. The graft size is considered



**Fig. 26.1** Couinaud's segmental anatomy of the liver

**Table 26.5** Extent of liver resection, involved Couinaud's segments and percentage/weight of liver removed.

Allograft	Couinaud's segments	Percentage liver removed (%)	Volume yield (cc)
Entire right lobe	V–VIII	60	600–900
Entire left lobe	II–IV	35	300–500
Left lateral segment	II–III	20	200–300
Extended right liver	IV–VIII	70	800–1,000

adequate if the GWBWR is within 1–3% [19]. A ratio of 0.8% is considered the minimum to prevent small-for-size syndrome in the recipient; however, experience at our center has shown successful grafting with graft ratios of as low as 0.49%. Recipients with severe portal hypertension or decompensated disease will require a larger graft, irrespective of calculated GWBWR. In general, left lobe will be used for recipient with a body weight 20–40 kg and left lateral segment or left lateral segment plus portion of segment IV for recipients with a body weight <40 kg [19]. In instances where a graft larger than left lobe is necessary, left half of caudate lobe can be added [24].

For pediatric LDLT, laparoscopic left lateral segmentectomy to resect segments II and III and

removal through a Pfannenstiel incision has been reported [25]. Laparoscopic right hepatectomy has also been described for adult living donor transplantation and is now routinely employed at our center [26]. However, classically, a right or bilateral subcostal incision with midline extension is performed for live liver organ donation.

## Anesthetic Management

Due to the potential for large volume blood loss during the hepatectomy, central venous catheterization is recommended to allow for rapid volume replacement and monitoring of central venous pressure (CVP). A low CVP (2–4 mmHg) is

desirable in order to minimize blood loss [4]. Pringle's maneuver, the surgical technique of intermittently occluding inflow, is routinely used to minimize blood loss in hepatectomy surgery; however, the risk of ischemic injury to the graft has in the past precluded its use in living donor hepatectomy. Recent evidence shows that this procedure can be safe for the graft, provides a cleaner surgical field, and results in a lower incidence of biliary complications [27, 28]. Techniques utilizing Trendelenburg position, volume restriction, nitroglycerine infusion, and furosemide administration may all be useful maneuvers to reduce CVP [29]. In addition to reducing CVP, Trendelenburg position of 15° is advocated to reduce the risk of venous air embolism.

The anesthesiologist must also be cognizant to minimize possible insult to the resected graft [30]. Firstly, hepatotoxic drugs, such as halothane, should be avoided. Halothane has a rate of metabolism of 20% and a risk of autoimmune hepatitis greater than that any of the other available inhaled anesthetics. Secondly, perfusion to the liver should be optimized. Hepatic blood flow is decreased by the nitrous oxide, by an elevated CVP, and as a consequence of a reflex vasoconstriction of the hepatic arterial and portal venous system in response to elevated pressures in the hepatic sinusoids. Lastly, graft edema must be minimized to reduce the risk of graft thrombosis, and the administration of mannitol to the living donor may aid in reducing graft edema [30]. Ultimately, LDLT has the advantage of minimizing cold ischemic time to 1 h or less as compared to the 4 up to 12 h of cold ischemic time with deceased donor transplantation. As a consequence, inflammatory markers after reperfusion are lower in LDLT and may improve graft survival [17].

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## Postoperative Management

At the conclusion of the operation, muscle relaxation is adequately reversed, and the vast majority of patients can be safely extubated in the operating room. At our institution, intensive care admission is routine and with an uneventful

recovery transferred to the surgical floor on postoperative day 1 and discharged from hospital postoperative days 7 to 10.

As living donors are generally healthy and unacquainted with chronic disease, postoperative complaints of pain are often greater than in patients who underwent hepatic resection of tumor [31, 32]. Preoperative epidural catheter placement may be an excellent option for postoperative analgesia [33] with the additional benefits of a shorter duration of postoperative ileus, attenuated stress response, fewer pulmonary complications, and early ambulation [34]. However, some centers avoid epidural analgesia as significant postoperative derangements of the coagulation profile can occur, and these may complicate the removal of the epidural catheter at a time when the patient is getting ready for discharge home [35].

In addition to the risk of postoperative coagulopathy due to lower hepatic volume, heparin administration to prevent graft thrombosis at the end of liver parenchymal dissection may further prevent anesthesiologists to place an epidural catheter [35, 36]. It is recommended that heparin administration be delayed 1 h after catheter placement and catheter removal delayed 2–4 h after the last dose of heparin and not until the aPTT is checked [37], and fortunately, the average time of heparin administration from epidural catheter placement is usually greater than 4 h [35].

Patient-controlled analgesia (PCA) is another mode of analgesia commonly used in many centers [30, 36]. Our center uses preoperative intrathecal morphine (ITM 0.3–0.5 mg) in combination with postoperative PCA, a regimen that is superior to PCA use alone [38]. A mild self-limiting pruritus is the most common adverse effect of ITM [38]. Preoperative ITM is not inferior to epidural catheter use as determined by the visual analog scale, but intravenous opioid use and incidence of pruritus are greater [39].

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## Complications

The altruistic nature of living donor hepatectomy for transplantation necessitates that all precautions to protect the donor must be taken. Deep

**Table 26.6** Clinical and biological outcome of living liver donation

	RH mean $\pm$ SD	LH mean $\pm$ SD	LL mean $\pm$ SD
<i>Clinical</i>			
Hospital stay (days)	7 $\pm$ 2.5	5.9 $\pm$ 1.3	6.66 $\pm$ 1.5
Anesthesia time (min)	528 $\pm$ 108	453 $\pm$ 73	340 $\pm$ 39
Estimated blood (mL)	583 $\pm$ 277	400 $\pm$ 175	294 $\pm$ 145
<i>Biological</i>			
INR peak	1.75 $\pm$ 0.3	1.37 $\pm$ 0.2	1.27 $\pm$ 0.2
TBili peak (mg/dL)	3.05 $\pm$ 1.4	2.6 $\pm$ 1	1.5 $\pm$ 1.3
AST peak (IU/L)	348 $\pm$ 260	239 $\pm$ 225	289 $\pm$ 226

Reprinted and adapted with permission from [6]. *RH* Right hepatectomy, *LH* Left hepatectomy, *LL* Left lateral hepatectomy, *INR* International normalized ratio, *TBili* Total bilirubin, *AST* Aspartate aminotransferase

vein thrombosis (DVT) leading to pulmonary embolism is a potentially catastrophic postoperative complication that can result in donor morbidity and/or mortality [40]. The use of graduated compression stockings and intermittent pneumatic compression intra- and postoperatively has been well validated in reducing the incidence of DVT [41]. Additionally, the prophylactic administration of subcutaneous heparin can reduce the risk of DVT by 50–70% [42]

Blood loss depends on the hepatectomy performed. A right hepatectomy (RH) is a more lengthy and challenging procedure and, as can be expected, associated with a longer anesthesia time, larger blood loss, greater derangements of the coagulation profile occur and significantly longer hospital stay compared to a left hepatectomy (LH) or left lateral hepatectomy (LL) [6] (Table 26.6). An early report of 100 consecutive hepatic resections reported that 59 of these patients received exogenous blood products [4]. A common strategy to minimize exogenous blood product administration is the use of intraoperative blood salvage, washed in a Cell-Saver™ (Haemonetics Laboratories, Boston, MA), and retransfusion of the red blood cells at the conclusion of the hepatectomy [16]. Preoperative autologous blood donation, erythropoietin administration, and isovolumetric hemodilution are other possible strategies variably employed.

Postoperative recovery and regeneration of the remnant liver begin immediately after resection. Transaminase enzymes peak within 48 h, and bilirubin usually peaks on approximately day 3 [16]. Small-for-size syndrome, usually described

as a transplanted graft that is inadequate in size and function, may also occur in the donor if the remaining volume is too low. A too small liver remnant can present with prolonged cholestasis, transaminitis, and synthetic function derangements [16]. The care for small-for-size syndrome is mainly supportive; however, various strategies have been proposed, including octreotide or vasopressin therapy to reduce portal pressure and intraportal glucose and insulin infusions to hasten remnant liver regeneration [16]. One case of liver failure in the donor requiring liver transplantation has been reported [43].

Biliary leaks are the most common serious complication after donor hepatectomy [43]. One case series reported biliary leaks in 13% of donors. Twenty percent of these cases resolved with external drainage via the original Jackson-Pratt drain, half required additional percutaneous drainage and 30% required endoscopic nasobiliary drainage. The source of the leak is commonly the cut surface, but may also be at the stump of the right hepatic duct [44]. A lower rate of 5–10% biliary leaks was observed with left lateral segmentectomy [19]. Biliary strictures occur less often; the same case series reported this complication in 1.5% of all donors [44]. Biliary strictures will more frequently require invasive interventions with temporary endoscopic retrograde biliary stenting and one donor required hepaticojejunostomy 20 months after surgery.

The most common reason for reoperation in the living donor is to repair an incisional hernia [45]. The occurrence of hernia is more frequent in

the obese population (BMI > 30) [46]; however, obesity is only a relative contraindication and does not necessarily preclude donation. A bilateral incision with midline extension has a higher risk of incisional hernia, as compared to a right subcostal incision with midline extension [19].

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