The International Liver Transplantation Society Guidelines on Living Liver Donation

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Abstract: The following guideline represents the position of the International Liver Transplantation Society (ILTS) on key preoperative, operative, and postoperative aspects surrounding living liver donation. These recommendations were developed from experts in the field from around the world. The authors conducted an analysis of the National Library of Medicine indexed literature on “living donor liver transplantation” [Medline search] using Grading of Recommendations Assessment, Development and Evaluation methodology. Writing was guided by the ILTS Policy on the Development and Use of Practice Guidelines (www ila.org). ILTS members, and many more nonmembers, were invited to comment. Recommendations have been based on information available at the time of final submission (March 2016). The lack of randomized controlled trials in this field to date is acknowledged and is reflected in the grading of evidence. Intended for use by physicians, these recommendations support specific approaches to the diagnostic, therapeutic, and preventive aspects of care.

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PREAMBLE AND METHODS

The following guideline has been approved by the International Liver Transplantation Society (ILTS) and represents the position of the Society. Review of evidence was based on relevant clinical questions and outcomes of importance to patients, proposed by the ILTS-designated writing group chair and approved by the ILTS Guidelines Committee and Council. Acknowledged experts from around the world were recruited to address these questions after obtaining appropriate disclosures to exclude any conflict of interest. Recommendations were developed from analysis of National Library of Medicine indexed literature on “living donor liver transplantation” [Medline search] using Grading of Recommendations Assessment, Development and Evaluation methodology. Writing was guided by the ILTS Policy on the Development and Use of Practice Guidelines (www.ila.org). ILTS members, and many more nonmembers, were invited to comment. Recommendations have been based on information available at the time of final submission (March 2016). The lack of randomized controlled trials in this field to date is acknowledged and is reflected in the grading of evidence. Intended for use by physicians, these recommendations support specific approaches to the diagnostic, therapeutic, and preventive aspects of care.

Drafts of a full-length version (>20 000 words) were freely accessible for review and comment on the ILTSEducation.org website from June 2014 and were presented for discussion at the ILTS Annual Congress the same year. Presentations were also posted online, and over 900 ILTS members and many more nonmembers were invited to comment until submission of an abridged version to Transplantation in December 2015. All comments were taken into account by the writing group chair. Formal external peer review was then undertaken by the journal, reviewers also having declared no conflict of interest. Final drafts were approved by the ILTS Council.

Recommendations have been based on information available at the time of final submission (March 2016). The lack of randomized controlled trials in this field to date is acknowledged and is reflected in the grading of evidence. Each recommendation (Table 1) has been classified as strong or conditional,1,2 depending on quality of evidence, balance of benefit versus harm, importance to patients, and cost-effectiveness. The quality of supporting evidence was rated as high, moderate, or low (A, B, or C) according to Grading of Recommendations Assessment, Development and Evaluation criteria. Intended for use by physicians, these recommendations support specific approaches to the diagnostic, therapeutic, and preventive aspects of care (Table 1). However, they do not necessarily represent standards of care and should be applied only according to the best judgment of the treating team after full consideration of the circumstances relating to an individual patient.
Donors must be evaluated for potential recipients with good functional status and minimal portal hypertension. Donors must be evaluated for potential chronic liver disease. Macrovesicular steatosis greater than 10% is concerning; greater than 30% is an absolute contraindication for donation and increases the risks of graft failure in the recipient. Patients with predisposing factors for fatty liver (obesity, diabetes, dyslipidemia) and/or imaging findings consistent with fatty liver should undergo biopsy during pretransplant evaluation to clearly assess the extent of macrovesicular steatosis.

Any past or present condition which attributes a significant risk for perioperative complications in the donor is a contraindication for living donation, unless correctable. Therefore, the donor’s pretransplant work-up should include an exhaustive cardiovascular assessment. Echocardiography should be routine. Additional investigations, such as stress echocardiography and/or coronary angiography, may be needed.

Transmissible disease is a contraindication for living donation. Appropriate blood tests should be used to systematically screen for asymptomatic inherited coagulation disorders involving liver synthesis (eg, Leiden factor V, protein C, protein S deficiency, antithrombin deficiency).

From a psychological viewpoint, living donation can be challenging. Donors are aware that extending the recipient’s life depends on his or her decision to donate, and they should also be aware that posttransplant outcomes cannot be assured. Further, donors must understand that donation itself carries a potential risk of mortality and complications. For these reasons, assessment of the donor’s psychological status and stability is essential.

Recommendations:

1. The objectives of the donor evaluation are to ensure: (a) that an adequate partial allograft can be safely procured, (b) that there is no risk of disease transmission from donor to recipient, and (c) that the donor understands the process and would be able to overcome possible psychological consequences. Donors are generally between 18 and 60 years of age.

2. It is generally recommended that the recipient GRBWR is not lower than 0.8% (2C); however, lower GRBWR can be considered in selected cases. (2C)

3. Donor remnant liver volume should be no less than 30% to 35% of the initial volume of the whole liver. (1C)

4. If fatty liver is suspected, biopsy is needed: macrovesicular steatosis greater than 30% is an absolute contraindication, (1C)

5. Any disease transmittable from donor to recipient represents a contraindication for LDLT. (1C)

6. A multidisciplinary approach is needed for donor psychological assessment. (2C)

**Donor Consent**

The process of obtaining appropriate donor informed consent is summarized well by Gordon and includes: (1) assessment of donor competence to make decisions; (2) disclosure of information; (3) donor comprehension of the information; (4) a voluntary decision by the donor to donate, free from coercion; and finally, (5) donor agreement to undergo the procedure. Donor privacy should always be protected. In the United States, the United Network of Organ Sharing and the Centers for Medicare and Medicaid have provided oversight and important guidance for donor informed consent.
Particularly important is donor access to an independent donor advocate (IDA) and/or IDA team (IDAT). The IDAT must help ensure that the decision to donate is voluntary and without coercion, either self-imposed or the result of external pressures or manipulation. Importantly, separation must exist between the recipient transplant team and the donor team. The IDAT assures that the donor experience is safe and promotes the medical, psychological, and financial well-being of the donor.

Recommendations:
1. Informed consent must include full information on the potential surgical, medical, financial, and psychological risks (including death) of a hepatectomy. (1C)
2. The responsibility of the IDA/IDAT team is to assist the potential donor throughout the predonation and postdonation phases. (1C)
3. Potential outcomes for the recipient must be disclosed to the donor. (1C)

Donor Operations
The following sections describe the different living liver donor procedures each with their own balance of donor and recipient risk and various levels of technical complexity.

Right Lobe Without Middle Hepatic Vein
The issue of whether or not to include the middle hepatic vein (MHV) in right lobe liver grafts remains controversial. In western countries, the majority of the transplant programs tend to leave the MHV in the donor and to reconstruct V5 and V8 outflow on the back table. Published algorithms are designed to guide decision-making regarding inclusion of the MHV in the graft versus leaving it with the donor remnant. Multiple studies have demonstrated excellent recipient outcomes and comparable complication rates following right lobe LDLT without inclusion of the MHV, and some studies suggest that there is impaired regeneration of the donor remnant liver when the MHV is absent. Although it is clear that the presence of the MHV provides the ideal outflow for the donor liver remnant (or the graft when procured with the right lobe), the true functional consequences of an intact MHV remain unknown.

Magnetic resonance imaging or CT scanning accompanied by 3-dimensional reconstruction is optimal to ascertain accurate liver volumes and vascular and biliary anatomy. Three-dimensional renderings assist preoperative assessment of significant segment 5 and/or 8 venous branches that might require reconstruction in the recipient.

To improve venous outflow and compensate for the lack of the MHV on the graft, many groups have proposed back-bench reconstruction of significant segment 5 and/or 8 MHV tributaries. These studies suggest that segment 5 and/or 8 hepatic veins greater than 5 mm in diameter should be reconstructed. Others metrics for venous reconstruction include the proportion of the graft drained by V5 or V8; if this proportion represents greater than 10% of the total graft volume or if loss of this volume would reduce GRWR to an unacceptable level, venous reconstruction should be performed.

Recommendations:
1. Donor safety is improved with the lowest possible loss of hepatic parenchyma (1C) and retention of the MHV in the remnant. (2C)
2. Regeneration of hepatic parenchyma may be enhanced in left lobe remnants that retain the MHV. (1C)
3. Reconstruction of venous branches greater than 5 mm in diameter when present in segments 6, 5, and 8 of the right lobe graft lessens graft congestion, decreases graft dysfunction, and improves recipient outcomes. (1C)

Laparoscopically Assisted Right Lobe Hepatectomy Without MHV
Laparoscopically assisted living donor right hepatectomy is practiced in several large centers that report outcomes similar to those reported for traditional open procedures with regard to graft quality, ability to retain the MHV with the donor remnant, and overall donor safety. Improved outcomes have been reported in postdonation length of stay, postoperative pain, donor quality of life, and concerns about body image. All reports emphasize the need for advanced laparoscopic skills and strong experience in complex hepatobiliary surgery in individuals planning to undertake laparoscopically assisted living donor right hepatectomy.

Recommendations:
1. Laparoscopically assisted living donor right hepatectomy should only be performed by individuals with sufficient experience in both laparoscopic procedures and complex hepatobiliary surgery. (1C)
2. Laparoscopically assisted living donor right hepatectomy produces donor and recipient results equivalent to those performed with an open standard technique. (2C)
3. Laparoscopically assisted living donor right hepatectomy may improve donor outcomes with regard to postoperative pain, reduced length of stay, and quality of life/body image. (2C)

Right Lobe With MHV
The major concern for including the MHV in a right liver graft is donor safety. The benefit resides in the recipient where it facilitates achieving optimal venous outflow of the graft. Studies have demonstrated that in experienced hands, inclusion of the MHV does not increase living donor risk, provided the liver remnant is more than 30% of the donor’s standard liver volume, and there is no significant fatty change. Although some groups routinely include the MHV in right liver grafts, other centers have adopted a strategy of selective inclusion based on graft size, liver remnant size, venous anatomy, and recipient conditions.

Recommendations:
1. A right liver graft with MHV has optimal venous drainage and could provide a better recipient outcome, especially in recipients with significant portal hypertension or for those whose graft size is relatively small. (2B)
2. Inclusion of the MHV in a right liver graft does not seem to increase the risks for a living donor. (2B)
3. Preservation of the segment 4b hepatic vein will reduce congestion in the donor liver remnant. (1C)

Left Lobe
Due to the higher morbidity associated with right living donor hepatectomy and improved knowledge regarding how to prevent SFSS, left liver (Couinaud segments II to
IV or I to IV) procurement has gained an important place in the field of living liver donation and should be explored whenever possible.\textsuperscript{40-44} This procedure is almost always performed through an open approach, although recent reports demonstrate that it also can be done laparoscopically.\textsuperscript{35} The left lobe graft always contains the MHV. When present, both left or left and middle hepatic arteries should be preserved. Usually, it suffices to anastomose 1 artery in the recipient; the necessity to perform both arterial anastomoses depends on the arterial back-flow after rearterialization.\textsuperscript{42} The back-table work may require hepatic vein plasty to optimize venous outflow of the allograft.\textsuperscript{46-49}

Recommendations:
1. Adult living donor liver transplantation using a left liver allograft has become a validated and safe transplant procedure. (2C)
2. Outcomes for left liver living donor transplantation may be improved by graft inflow modulation. (2B)
3. Laparoscopic left liver living donor procurement requires further study and evaluation. (2C)
4. The usefulness of including the caudate lobe in left liver procurement to increase the liver mass needs further study. (2C)

Left Lateral Segment

Left lateral segment transplantation is performed from an adult to a pediatric recipient and has 4 major advantages over cadaveric split liver transplantation: (1) the graft quality is excellent, (2) the procedure is relatively low risk, (3) nearly always the procedure is performed in a parent to child relationship and therefore in an ethically justified environment, (4) the procedure is performed in an elective setting.\textsuperscript{50,51} The surgical technique of a left lateral segment (segments II and III) has been standardized for open approach and may become more popular in the future using the laparoscopic approach.\textsuperscript{37,52,53}

Recommendations:
1. Left lobe (segment II and II) living donation is a safe, well accepted and successful procedure alleviating pediatric organ shortage. (1C)
2. Laparoscopic left lobe hepatectomy represents a valid alternative to the open living donor procedure. (2C)

Right Posterior Sector Graft

The procurement of a right posterior sector (RPS) graft, though a rarely performed procedure, can be a good alternative to a full right-liver graft when it satisfies the minimum volume requirement for the recipient (40% of the recipient’s standard liver volume)\textsuperscript{34,55} and is larger in volume than the left liver.\textsuperscript{15,56} The final decision regarding procurement of a RPS graft should be made by comparing the sizes of the RPS and left lobe. Only when the RPS appears definitely larger than the left lobe plus the caudate lobe (S1) is the RPS graft selected.

As for donor outcomes with a RPS graft, the Tokyo group reported that the postoperative course is usually uneventful for most donors. On the recipient side, however, high biliary complication rates (45% to 50%), including leakage and stenosis, were reported.\textsuperscript{57-59} More stringent donor selection criteria for procurement of a RPS graft might be necessary in order to reduce potentially life-threatening complications in recipients.

It should be noted that the procurement of a RPS graft is extremely demanding from a technical stand point.

Recommendations:
1. The RPS graft can be used to expand the living liver donor pool and to minimize the donor morbidity rate occurring with the right lobe graft. (2B)
2. When the portal vein, hepatic artery, and bile duct to RPS are branching off extrahepatically, the procurement of RPS graft accompanies minimum morbidity in both donor and recipient. (2B)

Aftercare and Follow-Up of Living Donors

Living liver donation carries a significant estimated donor mortality at 0.1% and 0.5% for left and right liver donors, respectively.\textsuperscript{15,60} A morbidity rate of 20% to 35% is also expected.\textsuperscript{15,34,60,61} Complications, such as pulmonary embolism, myocardial infarction, peptic ulcer disease, and liver failure,\textsuperscript{62,63} have resulted in donor deaths. Hence, intensive monitoring and early identification of postoperative complications without delay is crucial. Most living donors will return to a previous level of physical performance and psychological status over a 1-year period.\textsuperscript{64,65} With only 2 and a half decades of experience, the long-term consequences of living donation have yet to be fully understood. In light of the potential for adverse psychological outcomes among donors, it is essential for transplant programs to conduct regular follow-up monitoring for all living liver donors. This will allow early identification of complications and adverse events and help achieve prompt restoration of donors’ health.

Recommendations:
1. Immediately after surgery, all donors should receive effective prophylaxis against deep vein thrombosis and stress peptic ulcer. (1C)
2. Upon discharge from the hospital, all donors should have regular clinical monitoring and follow-up for at least 2 years and preferably for life. (2C)
3. Laboratory tests for liver function and platelet counts should be checked at follow-up for at least 1 year. (2C)
4. All donors should be advised to have lifetime annual primary care examinations for health maintenance. (1C)

How Institutions Should Prepare for the Death of a Living Donor Patient

Living donor liver transplantation is associated with a well-documented risk of donor morbidity and mortality. No institution engaged in this high-risk clinical activity is immune from this risk. Studies in the field of crisis management show that preparing for a catastrophic event is imperative, both to respond appropriately and for prevention.\textsuperscript{66} The key phrase is “when, not if”.

Recommendations:
1. Hospital and teams involved in LDLT should create a framework on how to respond to a potential living donor crisis.
REFERENCES


