

A Worldwide Survey of Live Liver Donor Selection Policies at 24 Centers With a Combined Experience of 19 009 Adult Living Donor Liver Transplants

Arvinder Singh Soin, FRCS, 1 Rohan Jagat Chaudhary, 1 Hirak Pahari, 1 and Elizabeth A. Pomfret2

Background. Although surgical technique in living donor liver transplantation (LDLT) has evolved with a focus on donor safety and recipient challenges, the donor selection criteria remain considerably disparate. Methods. A questionnaire on donor selection was sent to 41 centers worldwide. 24 centers with a combined experience of 19 009 LDLTs responded. Results. Centers were categorized into predominantly LDLT (18) or deceased donor liver transplantation (6), and high- (10) or low-volume (14) centers. At most centers, the minimum acceptable graft-to-recipient weight ratio was 0.7 or less (67%), and remnant was 30% (75%). The median upper limit of donor age was 60 years and body mass index of 33 kg/m². At 63% centers, age influenced the upper limit of body mass index inversely. Majority preferred aspartate transaminase and alanine transaminase less than 50 IU/mL. Most accepted donors with nondebilitating mild mental or physical disability and rejected donors with treated coronary artery disease, cerebrovascular accident and nonbrain, nonskin primary malignancies. Opinions were divided about previous psychiatric illness, substance abuse and abdominal surgery. Most performed selective liver biopsy, commonly for steatosis, raised transaminases and 1 or more features of metabolic syndrome. On biopsy, all considered macrovesicular and 50% considered microvesicular steatosis important. Nearly all (92%) rejected donors for early fibrosis, and minority for nonspecific granuloma or mild inflammation. Most anatomical anomalies except portal vein type D/E were acceptable at high-volume centers. There was no standard policy for preoperative or peroperative cholangiogram. Conclusions. This first large live liver donor survey provides insight into donor selection practices that may aid standardization between centers, with potential expansion of the donor pool without compromising safety.

(Transplantation 2019;103: e39-e47)

iving donor liver transplantation (LDLT) has evolved since its introduction in 1989¹ into a widely accepted, and an equally efficacious therapeutic option compared with

Received 18 March 2018. Revision received 28 September 2018. Accepted 1 October 2018.

The authors declare no funding or conflicts of interest.

A.S.S. participated in the conception of the work, data analysis, and interpretation, drafting the work, critical revision for important intellectual content and final approval of the version to be published. R.J.C. participated in the data acquisition, analysis and interpretation, drafting and final approval. H.P. participated in the data acquisition, analysis and interpretation, drafting and final approval. E.A.P. participated in the conception, critical revision and final approval of the version to be published.

Correspondence: Arvinder Singh Soin, FRCS, Medanta Institute of Liver Transplantation and Regenerative Medicine, Medanta-The Medicity, Gurgaon, Haryana 122001, India. (absoin@gmail.com, arvinder.soin@medanta.org).

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com).

Copyright © 2018 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0041-1337/19/10302-0e39

DOI: 10.1097/TP.00000000000002475

deceased donor liver transplantation (DDLT) for end-stage liver disease.² Surgical protocols at various centers converge on donor safety and biliary and vascular techniques. However, donor selection criteria remain considerably disparate across centers and are influenced by the proportion of DDLT versus LDLT performed by the center, the necessity of accepting the limited living donor options, by the longevity and disease patterns within the local population and by the chronology of development of DDLT and LDLT. With experience, the higher volume centers are willing to accept more donors with complex anatomy, posterior sector grafts and lower graft-to-recipient weight ratio (GRWR) than lower-volume centers.

Varying selection criteria for donor age,³ steatosis, preoperative liver biopsy, acceptable comorbid conditions, right versus left graft, type of right lobe graft (RLG), acceptable GRWR, among others prompted us to conduct this International Survey on donor selection practices.

MATERIALS AND METHODS

A survey questionnaire on donor selection policies was designed, keeping in mind the standard acceptance criteria and controversies. Institutional review board approval was obtained. The questionnaires were sent to 41 centers worldwide,

¹ Medanta Institute of Liver Transplantation, Haryana, India.

² Division of Transplantation, University of Colorado Anschutz Medical Campus, Aurora, CO.

with a mix of predominantly LDLT (pLDLT), predominantly DDLT (pDDLT), eastern, western, low- and high-volume centers. Most centers from the east were pLDLT, whereas all the western centers were pDDLT. All centers performed more than 20 LDLT a year. The list was compiled from available literature, the Scientific Registry of Transplant Recipients, the European Liver Transplant Registry, the Indian Society of Organ Transplantation, the Japanese Liver Transplant Society, the Hong Kong Society of Transplantation, the Korean Network for Organ Sharing, and the International Registry on Organ Donation and Transplantation. Email correspondence was used for survey completion. 4-15 After reviewing the responses, we labeled the centers high-volume or low-volume if they had performed more or less than 500 LDLT in total.

The questionnaire contained 33 questions (SDC, Materials and Methods 1, http://links.lww.com/TP/B642), mostly answered by yes or no or multiple choice objective answers. Descriptive answers were kept to a minimum to simplify analysis and to elicit a high response rate. The questions were on program demographics, donor age and body mass index (BMI), liver function tests, liver steatosis, indications for liver biopsy and histological findings, donor comorbidity, GRWR, remnant, anomalous anatomy and graft type. The survey was completed in 6 months from January 2016. This survey was not meant to be all inclusive, but reflected donor selection practices in a cross-section of LDLT centers across the globe.

Definitions

Modified RLG which has separate segment 5 and 8 hepatic veins; the middle hepatic vein (MHV) being retained with the remnant liver.

Right lobe with partial or subtotal MHV in which half or nearly the entire MHV is retrieved with the right lobe.

Standard RLG in which there is no anterior sector venous outflow reconstruction.

Mild mental subnormality: A person who is mentally slow but is able to give an informed consent.

Upper-extremity disability: Independent, but inability to fully use either or both upper limbs due to amputation, other injury, previous disease, or neurological weakness.

Lower-extremity disability: Independent but inability to fully use either or both lower limbs due to amputation, other injury, previous disease or neurological weakness.

Statistical Analysis

P value was calculated using the χ^2 test and Fisher exact test, where applicable. P values were expressed up to 2 decimal places and P value of 0.05 or less was considered as significant.

RESULTS

Twenty-four (59%) of 41 centers with a combined experience of 19 009 LDLTs responded to the survey.

The program demographics are outlined in SDC, Materials and Methods 2 (http://links.lww.com/TP/B642). There were 18 pLDLT, eastern centers (including 1 in Turkey) and 6 pDDLT, western centers. There were 10 high-volume centers and 14 low-volume centers. In describing the results, we have alluded to the differences in practice, if any, among different types of centers.

Most centers (20/24, 83%) performed adult and pediatric transplants, whereas the remaining performed only adult liver transplants.

Lowest Acceptable Donor Liver Remnant

For RLG, most centers (18/24, 75%) preferred at least 30% remnant, 3 preferred 35%, and 1 preferred 28%. The remaining 2 centers had age-specific criteria for remnant selection, with 1 center opting for 28% for donors younger than 35 years and 30% for those above 35 years, and the second, 28% and 30% for donors aged younger and older than 45 years, respectively.

Lower Limit of Recipient GRWR

To match the graft volume to the recipient, 21/24 centers used GRWR whereas 3 considered graft volume as a percentage of the standard liver volume (SLV) (Figure 1).

For RLG, the lower limit of GRWR was 0.7% at 7 centers, 0.5% to 0.65% at 7, 0.8% at 5, and 1% and 0.75% at 1 center each. Of those who measured % of SLV, 2 accepted a graft volume of 30% of SLV and 1, 40% of SLV (equivalent to GRWRs of 0.6% and 0.8% respectively).

Overall, 16 (67%) of 24 centers accepted RLG with a recipient GRWR between 0.5% and 0.7%, 7 with a GRWR of 0.8% or higher and 1 with a GRWR of 0.75%. Five of the 7

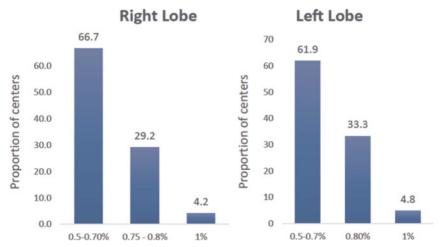


FIGURE 1. Lower limit of recipient graft-to-recipient weight ratio (standard liver volume translated into graft-to-recipient weight ratio).

© 2018 Wolters Kluwer Soin et al e41

TABLE 1.

Donor eligibility according to age

Criteria	No. centers	Proportion
Age (n = 24), y		_
Upper age limit		
50	3	12.5%
55	7	29.2%
60	7	29.2%
>60	5	20.8%
No defined age limits	2	8.3%
Lower age limit		
18	19	79.2%
20	3	12.5%
16	2	8.3%

centers preferring a graft with a higher GRWR were high-volume centers. Furthermore, high-volume centers tended to aim for a higher GRWR than low-volume centers (P = 0.05).

For left lobe grafts (LLG), 18 of the 21 that centers responded practiced a GRWR based policy. Seven opted for GRWR of at least 0.8%, 10 for 0.5% to 0.7%, and 1 for 1%. Of the remaining 3, 2 opted for 30% of SLV (equivalent of GRWR of 0.6%) and 1 for 35% of SLV (equivalent of GRWR of 0.7%). Overall, 13 (62%) of 21 responders accepted LLG with a GRWR between 0.5% and 0.7%.

The lower limit of GRWR for LLG was lower for the low-volume centers compared with high-volume centers (P = 0.04).

Donor Age and BMI

Table 1 shows the details of acceptable upper and lower limits of age among donors. More than half the centers (14/24, 58%) accepted donors aged 60 years or more. The lower limit of donor age was 18 years at most centers (19/24, 79%).

Figure 2 shows the acceptable upper limit of donor BMI. The median upper limits of BMI were 33 and 30, respectively, among high- and low-volume centers. Age influenced the upper cutoff for BMI inversely at 15 (63%) of 24 centers.

Nearly half (11/24) the centers set a lower limit of BMI at 16 to 20, whereas the others did not.

Procoagulant Workup

Half the centers (12/24) evaluate procoagulants as a part of donor evaluation. The practice was more common among pDDLT (5/6, 83%) than pLDLT centers (7/18, 39%).

Acceptable Transaminases

Eight (33%) of 24 programs accepted "normal" laboratory values for aspartate transaminase/alanine transaminase, and 6 (25%), 4 (17%) and 2 (8%) accepted donors with an aspartate transaminase/alanine transaminase up to 40, 50, and 45 IU/mL, respectively. One center each accepted twice the normal laboratory value, up to 30 IU/mL, up to 55 IU/mL, and up to 60 IU/mL, respectively.

Assessment of Donor Liver Steatosis

Computed tomography (CT) scan was the most commonly used noninvasive method (18/24, 75%; P < 0.01) followed by MRI (4) and ultrasound (2). Nine (37%) of 24 centers that performed MRI for steatosis (5 centers performed both MRI and CT scan), majority (6/9, 67%) were high-volume centers, and among them, MR spectroscopy was the preferred method. High-volume centers used MRI more often than low-volume centers (P = 0.05).

All centers considered macrovesicular steatosis to be significant, whereas only 50% (12/24) considered microvesicular steatosis (up to 10-50%) permissible. The acceptable upper limit of macrovesicular steatosis in RLG (Figure 3) was 30% at 6 (25%) of 24 centers, 20% at 7 (29%), 15% at 5 (21%), 10% at 3 (12%), 5% at 1, and no limit at 2 centers. For LLG, among the 21 of 24 who responded, the upper limit of macrosteatosis was 30%, 20%, 15%, 10%, and 40% at 7 (33%), 4 (19%), 3 (14%), 3 (14%), and 1 centers, respectively; 3 did not have an upper limit.

Eleven (46%) of 24 centers preferred to add macrovesicular and microvesicular steatosis to assess graft suitability, but the combined cutoff varied widely (10-80%). Nearly half (11/24, 46%) subtracted steatosis from GRWR and donor remnant volumes to arrive at the estimated actual volumes, whereas the others did not. Almost all the centers (21/24, 88%; P < 0.01) would treat potential donors with steatotic livers preoperatively and reevaluate them for suitability after weight loss. Among 21 centers treating potential donors with liver steatosis, 19 (90%) chose diet, 12 (57%) exercise,

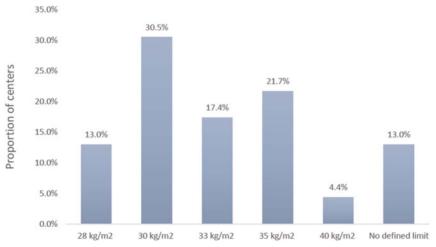


FIGURE 2. Upper limit of BMI.

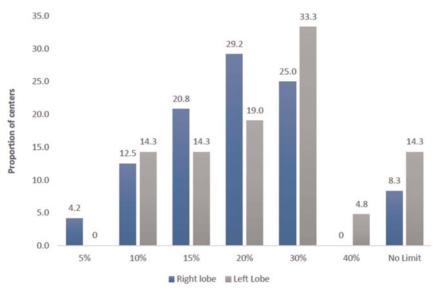


FIGURE 3. Upper limit of macrovesicular steatosis in the donor.

and 5 (24%) medications as treatment modalities with considerable overlap. The majority selected diet and exercise as the regimen of choice. There were no differences among various types of centers in their policies on steatosis.

Donor Liver Biopsy

All but 1 center (Asan Medical Center, Seoul, South Korea) (23/24) preferred selective preoperative biopsy on donors, with no differences among center types. Figure 4 depicts the indications for biopsy at various centers.

Among the 23 who did a biopsy for steatosis on imaging, CT scan (17), MRI (11, 9 of these were high-volume centers; P < 0.01), and ultrasound (8) formed the basis of their decision. Among the 11 centers that furnished details of their CT criteria for biopsy, 6, 4, and 1 centers based their decision on Liver Attenuation Index, liver attenuation to splenic attenuation ratio in Hounsfield units, and liver attenuation, respectively. Eleven centers performed biopsy for high BMI—the cutoff being greater than 28 and greater than 30 at 5 and 4 centers, respectively.

Significance of Donor Histology

Seven of 24 (29%) centers rejected donors for mild inflammation, 10 (42%) 24 nonspecific granuloma, and almost all (22/24; 92%) for early fibrosis (F1).

Abnormal Laboratory Tests and Donor Comorbidity as Exclusion Criteria

Hepatitis Core Antibody Status

All centers accepted hepatitis B core antibody (HBcAb) positivity among donors.

Abnormal Liver Function Tests

Three-fourths (18/24, 75%) of the centers did not reject donors for abnormal values of liver function test.

Minimal Acceptable Hemoglobin in the Donor

Fourteen (67%) of 24 preferred a hemoglobin (Hb) of 10 g/dL or greater, 7 accepted lower, whereas 3 centers did not have any criteria for Hb.

Comorbid conditions among donors: Active substance abuse or serious comorbidity was assumed to be a contraindication.

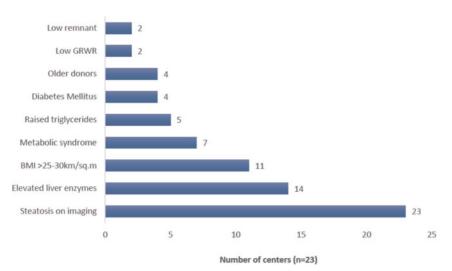


FIGURE 4. Indications of biopsy.

© 2018 Wolters Kluwer Soin et al e43

Fourteen (58%) of 24 centers accepted donors with a history of alcohol abuse and 10 centers (42%) accepted a history of drug abuse. About two-thirds of centers (15/24, 63%) did not exclude donors based on mild mental subnormality as long as they were competent to give informed consent. None of the centers accepted donors with an active psychiatric illness; however, if the psychiatric illness was in remission, half (12/24) accepted such donors. Most centers did not exclude donors with isolated upper- or lower-extremity disability (17/24, 71%; 18/24, 75%) (P = 0.04). Only 7 centers (7/24, 71%; 18/24, 75%)29%) rejected a donor with beta thalasemia minor. Almost all centers rejected donors with previously treated coronary artery disease (23/24, 96%) or cerebrovascular accidents (22/24, 92%). Most centers (21/24, 88%) excluded malignancies other than brain or skin primaries. Eleven (46%) of 24 centers also excluded donors with previously treated nonmelanoma skin cancer.

Previous Surgery

Fifteen (63%) of 24 centers accepted, 8 were selective, and 1 refused donors with previous abdominal surgery. Among the selective centers, 7 accepted previous laparoscopic cholecystectomy, and 2 also accepted other laparoscopic upper abdominal surgery. One center accepted donors after 3-dimensional CT liver evaluation in case of previous surgery for a benign condition. Overall, previous laparoscopic cholecystectomy was acceptable to 23 of 24 centers and other laparoscopic upper abdominal surgeries to 18 (75%) of 24 centers.

Donor Exclusion for Autoimmune/Hereditary Diseases

Most centers accepted donors who were first-degree relatives of recipients with Wilson disease (20/22, 91%; 2 did not respond), hemochromatosis (18/21, 86%), hemophilia (18/22, 82%), autoimmune disease (21/22, 95%), primary biliary cirrhosis (22/23, 96%), primary sclerosing cholangitis (22/23, 96%), and Maple Syrup Urine Disease (15/19, 79%).

Donor Vascular and Biliary Anatomy

Majority of centers (19/24, 79%) rejected portal vein anatomy Nakamura type D, E, or high take-off of right anterior portal vein from LPV for RLGs (Figure S1A, SDC, http://links.lww.com/TP/B642). Nine of 24 centers (38%, 4/18 pLDLT and 5/6 pDDLT) rejected grafts with 3 arteries. Half the centers rejected donors with 3 or more graft hepatic ducts, with a significant difference between western than eastern centers (5/6 [83%] vs 7/18 [39%]; P = 0.05), but not between the low and high-volume centers (8/14 [62%] vs 4/10 {40%]; P = 0.4). Most (20/24, 83%) did not reject donors on hepatic venous anatomy; the 4 that did were low-volume centers. Thirteen (54%) of 24 selectively accepted donors with left-sided gallbladder.

Cholangiogram

Eleven (46%) of 24, 6 (25%) of 24, and 5 (21%) of 24 centers preferred both intraoperative cholangiogram (IOC) and magnetic resonance cholangiopancreatography (MRCP), IOC alone, and MRCP alone, respectively. One selectively performed cholangiograms depending on graft type, whereas 1 center rarely performed cholangiograms.

Type of Graft

Majority of the centers preferred RLG (18/24, 75%) for adult to adult LDLT. Modified RLG (MHV left with the remnant) approach tailored to each case, partial or subtotal (part or most of MHV with the graft) and standard (no anterior sector reconstruction) RLGs were the preferred policy at 13, 8, 2, and 1 centers, respectively.

Based on volumetry and anatomy, 14 (58%) 24 centers would consider posterior sectoral graft in selected cases. Majority of them were eastern (13/14, 93%; P = 0.02) and high-volume (9/14,64%; P < 0.01) centers.

DISCUSSION

This study represents the largest published worldwide LDLT survey to provide insights into donor selection practices shaped by center experience and insufficient availability of deceased donors.

Most centers have evolved protocols for successful LDLT centered around donor safety. However, their policies vary considerably with respect to older donors, ¹⁶⁻¹⁸ type of graft, acceptable GRWR, acceptable donor comorbidities, steatosis, and liver biopsy.

Although earlier studies quoted an acceptable donor liver remnant as low as 25% to 28%, ^{19,20} most currently favor a minimum remnant of 30%. Two of the pLDLT centers considered age when defining the lower limit of the remnant, ²¹ perhaps owing to the lower regeneration potential after 50 years. ²²⁻²⁷

In contrast to the previously accepted lower limit of GRWR of 0.8% in right lobe LDLT, ^{28,29} the study showed that the majority of centers currently accept a GRWR of 0.7% or even lower in selected cases, with similar cutoffs in right and left lobe LDLT.

The survey revealed an apparently paradoxical finding of the lower limit of GRWR being lower in low volume compared to high-volume centers. This is possibly because pLDLT centers are likely to have a wider choice of donors and obtain a higher GRWR. Low-volume centers had less experience with RLGs and probably preferred LLGs, hence resulting in lower GRWRs.

The upper age limit of donors varied between 50 and older than 60 years, possibly due to geographic differences in life expectancy and availability of younger donors. Recent data suggest a significant impact of advanced donor age (>50 years) on the postoperative outcomes of the donor and long-term graft survival rates. 30-32

Nearly all centers rejected donors with a BMI of more than 35. An upper limit of 33 might be reasonable because heavier donors may have higher postoperative complications.³³

Although opinions were divided, it may be prudent to screen high-risk groups (BMI > 28, age > 50) for procoagulant disorders. 34-36

There was no consensus among centers on acceptable values of serum transaminases. Although higher values are acceptable in a deceased donor liver with sufficient graft volume, ³⁷ this is not the case in adult LDLT wherein even mild, self-limiting donor liver pathology may lead to remnant liver or graft dysfunction. With elevated transaminases, inflammation and/or necrosis must be ruled out on a liver biopsy as per the American Gastroenterological Association recommendations. ³⁸

Hepatic Steatosis

Hepatic steatosis is the commonest cause of rejection of otherwise medically fit donors. 39 Ultrasound, ratio (liver attenuation to splenic attenuation ratio in Hounsfield units) or the difference between of liver and splenic attenuation (liver attenuation index) in Hounsfield units on noncontrast CT scan, 40,41 and spectrophotometry or 3-point Dixon on MRI $^{42-44}$ are commonly used to assess steatosis. Histologically, microsteatosis represents 1- to 2-µm fat droplets not displacing the nucleus and occurring in alcoholic or drug-induced liver disease or a nonspecific finding. $^{45-47}$ Macrosteatosis typically represents droplets more than 20 µm that displace the nucleus and form either by coalescence of microsteatotic droplets as in alcoholic liver disease or by themselves in nonalcoholic fatty liver disease. 45 Although all agree that macrovesicular steatosis impacts graft function, 48 microsteatosis in a healthy liver graft of adequate volume can be ignored. 39,48

In a study of 9677 deceased donors in the United Network of Organ Sharing and European Liver Transplant Registry databases, 49 microsteatosis did not affect survival in any category of balance of risk scores, 50 whereas more than 30% macrosteatosis adversely effected survival with higher balance of risk scores. Others have reported similar findings, and that the steatosis is reversible. 51-54 Although some believe that mild steatosis does not impair hepatic regeneration, 55 others suggest ischemia-related dysfunction of the affected hepatocytes.⁵⁶ Not surprisingly, only half the centers subtracted the proportion of steatosis from the GRWR. The survey confirmed that (1) the accepted upper limit of macrovesicular steatosis for right and LLGs is 10% to 20%, (2) steatosis on noninvasive imaging should prompt a predonation liver biopsy for its quantification and presence of hepatitis, and (3) many potential donors with steatosis can become fit for donation with preoperative diet and exercise over 4 to 8 weeks.⁵⁷⁻⁵⁹

Indications and Interpretation of Predonation Liver Biopsy

Although a selective predonation liver biopsy is usual, ⁶⁰ its criteria remain controversial. Elevated triglycerides and/or metabolic syndrome have been linked to steatosis and steatohepatitis. ^{61,62} Regeneration potential reduces with age. ²³⁻²⁵ Hence, steatosis detected on noninvasive imaging, abnormal transaminases and 1 or more components of metabolic syndrome were the most common indications for liver biopsy, especially among older donors and with borderline remnant and graft volumes.

Inflammation and/or fibrosis (early fibrosis, F1 or higher)^{63,64} on biopsy are clearly not acceptable. The significance of nonspecific granulomas on histology⁶⁵⁻⁶⁷ is controversial, with only half the centers accepting such donors. In another study,⁶⁶ 21% had at least 1 histological finding precluding liver donation (steatosis in two thirds, and hepatitis, granulomatosis, schistosomiasis and cryptogenic fibrosis in the others).

Comorbidity in the Donor

Exclusion policies among donors based on coexisting morbidities varied between centers. HBcAb-positive donors were universally acceptable. In such cases, the long-term risk to recipients of transmission of hepatitis B seropositivity is 25% to 50%, ^{68,69} and conversion to hepatitis B virus DNA positive status 10% to 30%. ⁷⁰ Currently, posttransplant therapy with

nucleotide and nucleosides analogues (entecavir or tenofovir) is recommended for such recipients for 5 years. 71-73

The majority of centers accept donors with transient elevation of serum transaminases provided they normalize before donation, and the biopsy is normal.

The minimal acceptable Hb at majority of the centers was 10 g/dL, although some accepted less. Most agree that potential donors with beta thalassemia minor, and those with correctable anemia can be eligible after correction.

Although half of the centers accepted donors with a previous psychiatric illness in remission, caution is prudent in such donors since living donation is a significant psychological stress,⁷⁴ and there are reports of depression and even suicide among donors.⁷⁴⁻⁷⁶

Physical disability among donors that would not interfere with recovery to preoperative functional status was acceptable to the majority. Again, evidence that physical composite scores after donation normalize over 6 months,⁷⁷ lends support to this policy.

There was clear consensus to exclude those with previous history of coronary artery disease, stroke, nonskin extracranial malignancy, and previous drug abuse. However, only half of the centers would consider reformed alcoholics as donors even if they had a normal liver biopsy.

A prior history of laparoscopic cholecystectomy or other upper abdominal surgery was not considered a deterrent for donation. This supports data from Lo,⁷⁸ demonstrating that previous upper abdominal surgery did not lead to higher morbidity among donors.

Asymptomatic first-degree relatives of recipients with hereditary or autoimmune liver diseases, such as Wilson disease, hemochromatosis, hemophilia, and Maple Syrup Urine Disease, are not excluded, but may require predonation liver biopsy, enzyme, and/or genetic studies.^{79,80}

Anatomy and Graft Type

Complex anatomical anomalies were not considered an absolute contraindication in the majority of centers. A clear preoperative delineation of the anatomy by triple phase contrast imaging, 81 with or without 3-dimensional reconstruction, 82 remains invaluable in planning the operative approach to preserving venous outflow of the graft, without compromising the remnant outflow, especially in RLGs. 83,84 The more experienced LDLT centers would accept grafts with 3 or more arteries, especially if there are common areas of supply between arteries, and eventually, up to 2 arterial anastomoses are expected. 85 As for portal vein anomalies, the majority of centers would reject Nakamura types D and E (Figure S1A, SDC, http://links.lww.com/TP/B642). 86,87 We (at A.S.'s and E.P.'s centers) would accept intrahepatic take off of right anterior portal vein provided it is 10 mm or greater in caliber and can be reconstructed on the bench with a conduit. However, if the branch was small, yet supplying a significant part of the functional parenchyma, we would likely reject the donor.

Biliary complications are more common in LDLT compared to DDLT, with an incidence of up to 38% 88-90 due to the presence of multiple, small graft ducts requiring reconstruction. 88 Most centers performed MRCP and/or IOC, 91-94 and over half of them rejected donors with 3 or more graft ducts. High-volume and/or eastern centers (pLDLT centers) were more likely to accept complex biliary anatomy. For centers where biliary anatomy (Figure S1B,

© 2018 Wolters Kluwer Soin et al e45

SDC, http://links.lww.com/TP/B642)⁹⁵ is not a reason for donor rejection, IOC alone would be logical, 96,97 because it detects all biliary anomalies.⁹⁸

Although a few centers have previously described the use of LLGs for adults with good results, 99 75% of the centers use RLGs and more than half prefer modified RLG. Any acceptable approach must ensure good remnant outflow. 100,101

Posterior sector grafts (PSG) were used largely by eastern and/or high-volume centers, when the anatomy was favorable, the posterior sector volume was higher than the left lobe volume and the remnant volume was inadequate with a RLG. 102 Kokudo et al 103 have described 28 PSG grafts out of 437 LDLT with 90% graft survival, and 10% vascular and 33% biliary complications. Microscopic arterial reconstruction and avoidance of multiple hepatic ducts, as well as Huang A4 biliary anatomy (Figure S1B, SDC, http:// links.lww.com/TP/B642) may reduce the incidence of biliary complications in PSG. 101-104

A limiting factor of this survey was the fact that the questionnaire was new and simply structured, without descriptive details. However, the questions were intentionally designed to be simple and easy to answer. Although no formal pilot study was conducted to assess the quality of questions and responses before this survey, input from all the authors, and 14 other faculty members (7 surgeons, 4 hepatologists, 2 anesthesiologists, and 1 intensivist) in the first authors' institute were incorporated in the final questionnaire.

SUMMARY AND CONCLUSIONS

The results of the largest survey of its kind on live liver donor selection policies from different centers across the world with a collective experience of over 19 000 LDLTs are presented. The participants included the majority of highvolume centers, as well as a representative cross section of western/eastern/predominantly DDLT or LDLT centers.

There was general agreement on acceptable GRWR, remnant liver, macrosteatosis, nonroutine inclusion of MHV in RLG, selective liver biopsy, histological findings that preclude donation, accepting HBcAb-positive donors, accepting relatives of patients with familial or genetic diseases, and rejecting donors with a past history of significant comorbidity.

Views varied widely on donor age, microvesicular steatosis, volume correction for steatosis, acceptable value of serum transaminases, significance of nonspecific granulomas on histology, procoagulant workup and the mode of preoperative cholangiogram or IOC.

Increasing experience and the nonavailability of deceased donor options have resulted in evolution of policies on accepting low GRWR grafts and variant anatomy, the use of MRI in donor evaluation, and the use of posterior sector grafts.

There was no consensus on the acceptable lower limit of donor BMI, and the impact of age on acceptable percentage of donor steatosis.

This combined survey of predominantly DDLT and predominantly LDLT centers provides new insights into live liver donor selection criteria and may aid standardization across centers and registries.

ACKNOWLEDGMENTS

The authors are grateful to the centers and their lead/senior transplant clinicians who contributed to the survey, all of whom are listed (apart from the authors' centers) here. SG

Lee, Asan Medical Center, Seoul, Korea. S Gupta, Apollo Hospital, Delhi, India. JW Joh, Samsung Medical Center, Seoul, Korea. CL Chen, Kaohsiung Chang Gung Memorial Hospital, Taiwan. SC Chan, Queen Mary Hospital, Hong Kong. KS Suh, Seoul National University, Seoul, Korea. Y Tokat, Florence Nightingale Hospital, Istanbul, Turkey. LB Jeng, China Medical University Hospital, Taiwan. D Grant, Toronto General Hospital, Toronto, Canada. S Sudhindran, Amrita Institute of Medical Sciences, Kochi, India. M Rela, Global Hospital, Chennai, India. V Vij, Fortis Hospital, Noida, India. N Mehta, Sir Ganga Ram Hospital, Delhi, India. N Heaton, King's College Hospital, London, United Kingdom. V Pamecha, Institute of Liver and Biliary Sciences, Delhi, India. J Roberts, University of California San Franciso, CA. K Yamashita, Hokkaido University, Japan T Kiuchi, Nagoya University, Japan. V Kumaran, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India. D Azoulay, Hôpital Paul Brousse, Paris, France. J Lerut, Université Catholique de Louvain, Brussels, Belgium. H Egawa, Tokyo Women's Medical University, Japan.

REFERENCES

- 1. Strong RW, Lynch SV, Ong TH, et al. Successful liver transplantation from a living donor to her son. N Engl J Med. 1990;322:1505-1507.
- 2. Maluf DG, Stravitz RT, Cotterell AH, et al. Adult living donor versus deceased donor liver transplantation: a 6-year single center experience. Am J Transplant. 2005;5:149-156.
- 3. Fan ST, Lo CM, Liu CL, et al. Safety of donors in live donor liver transplantation using right lobe grafts. Arch Surg. 2000;135:336-340.
- 4. International Liver Transplantation Society. www.ilts.org.
- 5. https://www.tts.org/isodp/resources/organ-donation-societies (International Organ Donation Societies).
- The Scientific Registry of Transplant Recipients. https://srtr.transplant.
- 7. European Liver Transplant Registry. http://www.eltr.org/spip.php?page=
- 8. Indian Society of Organ Transplantation. http://isot.co.in/.
- 9. Japanese Liver Transpl Society. http://jlts.umin.ac.jp/english.html.
- 10. Hong Kong Society of Transplantation. http://www.hkst.org/.
- 11. The Canadian Association of Transplantation. www.cst-transplant.ca/en/.
- 12. http://www.odt.nhs.uk (United Kingdom: Organ Donation and Transplantation).
- 13. France: French Federation for Organ Donation. www.france-adot.org.
- 14. Turkey: Turkish Transplantation Society. www.tond.org.tr. 15. Konos Korean Network for Organ Sharing. www.konos.go.kr.
- 16. Kuramitsu K, Egawa H, Keeffe EB, et al. Impact of age older than 60 years in living donor liver transplantation. Transplantation. 2007;84:
- 17. Shah SA, Cattral MS, McGilvray ID, et al. Selective use of older adults in right lobe living donor liver transplantation. Am J Transplant. 2007:7:142-150.
- 18. Dayangac M, Taner CB, Yaprak O, et al. Utilization of elderly donors in living donor liver transplantation: when more is less?. Liver Transpl. 2011; 17:548-555
- 19. Nadalin S, Malagò M, Radtke A, et al. Current trends in live liver donation. Transpl Int. 2007;20:312-330.
- 20. Valentín-Gamazo C, Malagó M, Karliova M, et al. Experience after the evaluation of 700 potential donors for living donor liver transplantation in a single center. Liver Transpl. 2004;10:1087-1096.
- 21. Lee SG. A complete treatment of adult living donor liver transplantation: a review of surgical technique and current challenges to expand indication of patients. Am J Transplant. 2015;15:17–38.
- 22. Akamatsu N, Sugawara Y, Tamura S, et al. Impact of live donor age (>50) on liver transplantation. Transplant Proc. 2007;39:3189–3193.
- 23. Pomfret EA, Pomposelli JJ, Gordon FD, et al. Liver regeneration and surgical outcome in donors of right-lobe liver grafts. *Transplantation*. 2003:76:5-10.
- 24. Haga J, Shimazu M, Wakabayashi G, et al. Liver regeneration in donors and adult recipients after living donor liver transplantation. Liver Transpl. 2008:14:1718-1724
- 25. Klink T, Simon P, Knopp C, et al. Liver remnant regeneration in donors after living donor liver transplantation: long-term follow-up using CT and MR imaging. RoFo. 2014;186:598-605.

- Nadalin S, Testa G, Malago M, et al. Volumetric and functional recovery of the liver after right hepatectomy for living donation. *Liver Transpl.* 2004; 10:1024–1029.
- Olthoff KM, Emond JC, Shearon TH, et al. Liver regeneration after living donor transplantation: adult-to-adult living donor liver transplantation cohort study. *Liver Transpl.* 2015;21:79–88.
- Marcos A. Right lobe living donor liver transplantation: a review. Liver Transpl. 2000;6:3–20.
- Selzner M, Kashfi A, Cattral MS, et al. A graft to body weight ratio less than 0.8 does not exclude adult-to-adult right-lobe living donor liver transplantation. *Liver Transpl.* 2009;15:1776–1782.
- Tokodai K, Kawagishi N, Miyagi S, et al. Poor long-term outcomes of adult liver transplantation involving elderly living donors. *Transplant Proc.* 2016;48:1130–1133.
- Paterno F, Wima K, Hoehn RS, et al. Use of elderly allografts in liver transplantation. *Transplantation*. 2016;100:153–158.
- Kubota T, Hata K, Sozu T, et al. Impact of donor age on recipient survival in adult-to-adult living-donor liver transplantation. *Ann Surg.* 2018;267: 1126–1133.
- Moss J, Lapointe-Rudow D, Renz JF, et al. Select utilization of obese donors in living donor liver transplantation: implications for the donor pool. Am J Transplant. 2005;5:2974–2981.
- Morris-Stiff G, White A, Gomez D, et al. Thrombotic complications following liver resection for colorectal metastases are preventable. HPB. 2008;10:311–314.
- Durand F, Ettorre GM, Douard R, et al. Donor safety in living related liver transplantation: underestimation of the risks for deep vein thrombosis and pulmonary embolism. *Liver Transpl*. 2002;8:118–120.
- Bustelos R, Ayala R, Martinez J, et al. Living donor liver transplantation: usefulness of hemostatic and prothrombotic screening in potential donors. *Transplant Proc.* 2009;41:3791–3795.
- Fakhar N, Nikeghbalian S, Kazemi K, et al. Transplantation of deceased donor livers with elevated levels of serum transaminases at Shiraz transplant center. *Hepat Mon.* 2016;16:e40140.
- American Gastroenterological Association. American Gastroenterological Association medical position statement: evaluation of liver chemistry tests. Gastroenterology. 2002;1230:1364–1366.
- Patel S, Orloff M, Tsoulfas G, et al. Living-donor liver transplantation in the United States: identifying donors at risk for perioperative complications. Am J Transplant. 2007;7:2344–2349.
- Limanond P, Raman SS, Lassman C, et al. Macrovesicular hepatic steatosis in living related liver donors: correlation between CT and histologic findings. *Radiology*. 2004;230:276–280.
- Vohra S, Goyal N, Gupta S. Preoperative CT evaluation of potential donors in living donor liver transplantation. *Indian J Radiol Imaging*. 2014;24:350–359.
- 42. Krishan S, Baijal AA, Saraf N, et al. Accuracy of MR based calculation of hepatic fat fraction. *J Clin Exp Hepatol*. 2014;4:S83.
- Hwang I, Lee JM, Lee KB, et al. Hepatic Steatosis in living liver donor candidates: preoperative assessment by using breath-hold triple-echo MR imaging and 1H MR spectroscopy. *Radiology*. 2014;271:730–738.
- Joe E, Lee JM, Kim KW, et al. Quantification of hepatic macrosteatosis in living, related liver donors using T1-independent, T2*-corrected chemical shift MRI. J Magn Reson Imaging. 2012;36:1124–1130.
- Crawford JM, Burt AD. Anatomy, pathophysiology and basic mechanisms of disease. In eds Portmann A, Ferrell L. MacSween's Pathology of the Liver Churchill Livingstone Elsevier; 2012:1–77.
- Fraser JL, Antonioli DA, Chopra S, et al. Prevalence and non-specificity of microvesicular fatty change in the liver. Mod Pathol. 1995;8:65–70.
- 47. Hall A, Covelli C, Manuguerra R, et al. Transaminase abnormalities and adaptations of the liver lobule manifest at specific cut-offs of steatosis. *Sci Rep.* 2017;7:40977.
- Soejima Y, Shimada M, Suehiro T, et al. Use of steatotic graft in livingdonor liver transplantation. *Transplantation*. 2003;76:344–348.
- Dutkowski P, Schlegel A, Slankamenac K, et al. The use of fatty liver grafts in modern allocation systems risk assessment by the balance of risk (BAR) score. Ann Surg. 2012;256:861–869.
- Dutkowski P, Oberkofler CE, Slankamenac K, et al. Are there better guidelines for allocation in liver transplantation? A novel score targeting justice and utility in the model for end-stage liver disease era. *Ann Surg*. 2011;254:745–753.
- Marcos A, Ham JM, Fisher RA, et al. Single-center analysis of the first 40 adult-to-adult living donor liver transplants using the right lobe. *Liver Transpl.* 2000;6:296–301.
- Marcos A, Fisher RA, Ham JM, et al. Liver regeneration and function in donor and recipient after right lobe adult to adult living donor liver transplantation. *Transplantation*. 2000;69:1375–1379.

- de Graaf EL, Kench J, Dilworth P, et al. Grade of deceased donor liver macrovesicular steatosis impacts graft and recipient outcomes more than the donor risk index. *J Gastroenterol Hepatol*. 2012;27: 540–546.
- 54. Li J, Liu B, Yan LN, et al. Reversal of graft steatosis after liver transplantation: prospective study. *Transplant Proc.* 2009;41:3560–3563.
- Cho JY, Suh KS, Kwon CH, et al. The hepatic regeneration power of mild steatotic grafts is not impaired in living-donor liver transplantation. *Liver Transpl.* 2005;11:210–217.
- Zamboni F, Franchello A, David E, et al. Effect of macrovescicular steatosis and other donor and recipient characteristics on the outcome of liver transplantation. Clin Transpl. 2001;15:53.
- 57. Choudhary NS, Saraf N, Saigal S, et al. Estimation of normal values of serum transaminases based on liver histology in healthy Asian Indians. *J Gastroenterol Hepatol*. 2015;30:763–766.
- Choudhary NS, Saraf N, Saigal S, et al. Rapid reversal of liver steatosis with life style modification in highly motivated liver donors. *J Clin Exp Hepatol*. 2015;5:123–126.
- Jin YJ, Kim KM, Hwang S, et al. Exercise and diet modification in nonobese non-alcoholic fatty liver disease: analysis of biopsies of living liver donors. J Gastroenterol Hepatol. 2012;27:1341–1347.
- Simpson MA, Verbesey JE, Khettry U, et al. Successful algorithm for selective liver biopsy in the right hepatic lobe live donor (RHLD). Am J Transplant. 2008;8:832–838.
- Choudhary NS, Saraf N, Saigal S, et al. Prediction of nonalcoholic fatty liver in prospective liver donors. Clin Transplant. 2017;31: DOI:10.1111/ctr.12890.
- Duseja A, Singh SP, Saraswat VA, et al. Non-alcoholic fatty liver disease and metabolic syndrome—position paper of the Indian National Association for the study of the liver, Endocrine Society of India, Indian College of Cardiology and Indian Society of gastroenterology. J Clin Exp Hepatol. 2015;5:51–68.
- Kleiner DE, Brunt EM, Van Natta M, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology*. 2005;41:1313–1321.
- Brunt EM, Kleiner DE, Wilson LA, et al. The NAS and the Histopathologic diagnosis in NAFLD: distinct clinicopathologic meanings. *Hepatology*. 2011;53:810–820.
- Trotter JF. Selection of donors for living donor liver transplantation. Liver Transpl. 2003;9:S2–S7.
- Nadalin S, Malagó M, Valentin-Gamazo C, et al. Preoperative donor liver biopsy for adult living donor liver transplantation: risks and benefits. *Liver Transpl.* 2005;11:980–986.
- Rya CK, Johnson LA, Germin BI, et al. One hundred consecutive hepatic biopsies in the workup of living donors for right lobe liver transplantation. *Liver Transpl.* 2002;8:1114–1122.
- Huprikar S, Danziger-Isakov L, Ahn J, et al. Solid organ transplantation from hepatitis B virus-positive donors: consensus guidelines for recipient management. Am J Transplant. 2015;15:1162–1172.
- Celebi Kobak A, Karasu Z, Kilic M, et al. Living donor liver transplantation from hepatitis B core antibody positive donors. *Transplant Proc.* 2007;39:1488–1490.
- Loss GE Jr, Mason AL, Nair S, et al. Does lamivudine prophylaxis eradicate persistent HBV DNA from allografts derived from anti-HBc-positive donors?. Liver Transpl. 2003;9:1258–1264.
- Chotiyaputta W, Pelletier SJ, Fontana RJ, et al. Long-term efficacy of nucleoside monotherapy in preventing HBV infection in HBsAgnegative recipients of anti-HBc-positive donor livers. *Hepatol Int.* 2010;4: 707–715
- Perrillo R. Hepatitis B virus prevention strategies for antibody to hepatitis B core antigen-positive liver donation: a survey of north American, European, and Asian-pacific transplant programs. *Liver Transpl.* 2009:15:223–232.
- Papatheodoridis GV, Sevastianos V, Burroughs AK. Prevention of and treatment for hepatitis B virus infection after liver transplantation in the nucleoside analogues era. Am J Transplant. 2003;3:250–258.
- Trotter JF, Hill-Callahan MM, Gillespie BW, et al. Severe psychiatric problems in right hepatic lobe donors for living donor liver transplantation. *Transplantation*. 2007;83:1506.
- Parikh ND, Ladner D, Abecassis M, et al. Quality of life for donors after living donor liver transplantation: a review of the literature. *Liver Transpl.* 2010;16:1352–1358.
- Humphreville VR, Radosevich DM, Humar A, et al. Longterm health-related quality of life after living liver donation. Liver Transpl. 2016;22:53–62.
- Adcock L, Macleod C, Dubay D, et al. Adult living liver donors have excellent long-term medical outcomes: the University of Toronto liver transplant experience. Am J Transplant. 2010;10:364–371.

© 2018 Wolters Kluwer Soin et al e47

 Lo CM. Complications and long-term outcome of living liver donors: a survey of 1,508 cases in five Asian centers. *Transplantation*. 2003;75: S12–S15.

- Mohan N, Karkra S, Rastogi A, et al. Living donor liver transplantation in maple syrup urine disease—case series and world's youngest domino liver donor and recipient. *Pediatr Transplant*. 2016;20:395–400.
- 80. Kasahara M, Sakamoto S, Horikawa R, et al. Living donor liver transplantation for pediatric patients with metabolic disorders: the Japanese multicenter registry. *Pediatr Transplant*. 2014;18:6–15.
- Duran C, Uraz S, Kantarci M, et al. Hepatic arterial mapping by multidetector computed tomographic angiography in living donor liver transplantation. J Comput Assist Tomogr. 2009;33:618–625.
- 82. Sakai H, Okuda K, Yasunaga M, et al. Reliability of hepatic artery configuration in 3D CT angiography compared with conventional angiography—special reference to living-related liver transplant donors. *Transpl Int.* 2005;18:499.
- Soin AS, Mohanka R, Singla P, et al. Segment IV preserving middle hepatic vein retrieval in right lobe living donor liver transplantation. *J Am Coll Surg.* 2011;213:e5–e16.
- Suh KS, Suh SW, Lee JM, et al. Recent advancements in and views on the donor operation in living donor liver transplantation: a single-center study of 886 patients over 13 years. *Liver Transpl.* 2015;21:329–338.
- 85. Marcos A, Ham JM, Fisher RA, et al. Surgical management of anatomical variations of the right lobe in living donor liver transplantation. *Ann Surg.* 2000;231:824–831.
- Nakamura T, Tanaka K, Kiuchi T, et al. Anatomical variations and surgical strategies in right lobe living donor liver transplantation: lessons from 120 cases. *Transplantation*. 2002;73:1896–1903.
- 87. Cheng YF, Huang TL, Lee TY, et al. Variation of the intrahepatic portal vein; angiographic demonstration and application in living-related hepatic transplantation. *Transplant Proc.* 1996;28:1667–1668.
- 88. Soin AS, Kumaran V, Rastogi AN, et al. Evolution of a reliable biliary reconstructive technique in 400 consecutive living donor liver transplants. *J Am Coll Surg.* 2010;211:24–32.
- Soin AS. Smoothing the path: reducing biliary complications, addressing small-for-size syndrome, and making other adaptations to decrease the risk for living donor liver transplant recipients. *Liver Transpl.* 2012; 18(Suppl 2):S20–S24.
- Soin AS, Thiagarajan S. Liver transplant scene in India. MAMC J Med Sci. 2016;2:6–11.

- Song GW, Lee SG, Hwang S, et al. Preoperative evaluation of biliary anatomy of donor in living donor liver transplantation by conventional nonenhanced magnetic resonance cholangiography. *Transpl Int.* 2007;20:167–173.
- Macdonald DB, Haider MA, Khalili K, et al. Relationship between vascular and biliary anatomy in living liver donors. AJR Am J Roentgenol. 2005; 185:247–252.
- Kashyap R, Bozorgzadeh A, Abt P, et al. Stratifying risk of biliary complications in adult living donor liver transplantation by magnetic resonance cholangiography. *Transplantation*. 2008;85:1569–1572.
- 94. Cheng YF, Chen CL, Huang TL, et al. Single imaging modality evaluation of living donors in liver transplantation: magnetic resonance imaging. *Transplantation*. 2001;72:1527–1533.
- 95. Huang TL, Cheng YF, Chen CL, et al. Variants of the bile ducts: clinical application in the potential donor of living-related hepatic transplantation. *Transplant Proc.* 1996;28:1669–1670.
- Pagano D, Cintorino D, Li Petri S, et al. Intra-operative contrast Cholangiography in living donor liver transplantation: the ISMETT experience. *Transplant Proc.* 2015;47:2159–2160.
- Guba M, Adcock L, MacLeod C, et al. Intraoperative 'no go' donor hepatectomies in living donor liver transplantation. Am J Transplant. 2010;10:612–618.
- 98. Yaprak O, Demirbas T, Duran C, et al. Living donor liver hilar variations: surgical approaches and implications. *Hepatobiliary Pancreat Dis Int.* 2011;10:474–479.
- Saidi RF, Jabbour N, Li Y, et al. Is left lobe adult-to-adult living donor liver transplantation ready for widespread use? The US experience (1998–2010). HPB (Oxford). 2012;14:455–460.
- Kokudo N, Sugawara Y, Imamura H, et al. Tailoring the type of donor hepatectomy for adult living donor liver transplantation. Am J Transplant. 2005;5:1694–1703.
- 101. Roll GR, Parekh JR, Parker WF, et al. Left hepatectomy versus right hepatectomy for living donor liver transplantation: shifting the risk from the donor to the recipient. *Liver Transpl*. 2013;19:472–481.
- Yoshizumi T, Ikegami T, Kimura K, et al. Selection of a right posterior sector graft for living donor liver transplantation. Liver Transpl. 2014;20:1089–1096.
- 103. Kokudo T, Hasegawa K, Arita J, et al. Use of a right lateral sector graft in living donor liver transplantation is feasible, but special caution is needed with respect to liver anatomy. Am J Transplant. 2016;16:1258–1265.
- Hwang S, Lee SG, Lee YJ, et al. Donor selection for procurement of right posterior segment graft in living donor liver transplantation. *Liver Transpl*. 2004;10:1150–1155.