Summary of the British Transplantation Society UK Guidelines for Living Donor Liver Transplantation

Derek Manas, MD, FCS (SA), FRCS,[1] Lisa Burnapp, MA,[2] and Peter Antony Andrews, MD, FRCP[3]

Abstract: The British Transplantation Society Guidelines for Living Donor Liver Transplantation was published in July 2015 and is the first national guideline in the field of living donor liver transplantation. The guideline aims to review the evidence relating to the evaluation process of both recipient and donor candidates; address the moral and ethical issues surrounding the procedure; outline the technical aspects of the procedure, including the middle hepatic vein controversy and the "small for size syndrome"; review donor and recipient outcomes and complications including donor mortality; and examine evidence relating to the advantages and disadvantages of living donor liver transplantation. In line with previous guidelines published by the BTS, the guideline has used the Grading of Recommendations Assessment, Development and Evaluation system to rate the strength of evidence and recommendations. This article summarizes the Statements of Recommendation contained in the guideline, which provide a framework for the delivery of living liver donation in the United Kingdom and may be of wide international interest. It is recommended that the full guideline document is consulted for details of the relevant references and evidence base. This may be accessed at http://www.bts.org.uk/BTS/Guidelines_Standards/Current/BTS/Guidelines_Standards/Current_Guidelines.aspx?hkey=e285ca32-5920-4613-ac08-fa9fd90915b5.

(*Transplantation* 2016;100: 1184–1190)

In most western countries, deceased donor liver transplantation (DDLT) remains the standard of care for patients with end stage liver disease. Split liver transplantation and subsequently living donor liver transplantation (LDLT) was first pioneered in children in the late 1980s due to a lack of appropriately sized donors and the high mortality rate among children awaiting liver transplantation. Because experience with liver resection techniques grew and success with pediatric living donor transplantation became apparent, LDLT was introduced for adults in the early 1990s, with the first successful adult LDLT being performed in Japan.

Living donor liver transplantation has now become an important part of many liver transplantation programs around the world. Although adult-to-adult LDLT remains the transplant procedure of choice in most Asian countries due to the lack of deceased donors in these areas, LDLT is less commonly undertaken in Western countries because of the greater availability of deceased donors.[1] This is especially true for the UK after a recent increase in the deceased donor pool (especially deceased circulatory death grafts). Living donor liver transplantation currently accounts for 7% of liver transplants performed per year in the United Kingdom.[2]

Obvious advantages of LDLT over DDLT include the ability to provide transplantation before the recipient becomes too ill, knowledge of donor history, the avoidance of the physiologic derangement induced by brain death in the donor, and reduced cold ischemic time. These advantages are balanced by the risk to the donor, the additional technical complexity of receiving a partial graft, and the need for careful medical and surgical judgment in choosing the appropriate donor and recipient. Although the risk-benefit ratio may favor LDLT in some parts of the world, the most appropriate role for LDLT in the United Kingdom is still to be defined.

This report summarizes the first national guideline in this rapidly evolving field. The guideline aims to review the current evidence relating to the evaluation process of both recipient and donor candidates, address the moral and ethical issues surrounding this procedure, outline the technical aspects of the procedure, including the middle hepatic vein controversy and the "small for size syndrome," review donor and recipient outcomes and complications including donor mortality, and examine evidence relating to the advantages and disadvantages of LDLT.

Process of Writing and Methodology

Posted online in July 2015,[3] the British Transplantation Society Guidelines for Living Donor Liver Transplantation were written under the auspices of the British Transplantation Society (BTS) Standards Committee. They were produced in line with the BTS Clinical Practice Guideline and the recommendations of National Health Service (NHS)

Received 28 August 2015. Revision received 21 December 2015.

Accepted 2 January 2016.

[1] University of Newcastle Upon Tyne and Newcastle NHS Trust, United Kingdom.

[2] NHS Blood and Transplant, Bristol, United Kingdom.

[3] SW Thames Renal & Transplantation Unit, St. Helier Hospital, Surrey, United Kingdom.

The authors declare no funding or conflicts of interest.

All authors contributed to the BTS guideline document and to this summary of the guideline. All have reviewed and approved the final article.

Correspondence: Peter A. Andrews, SW Thames Renal & Transplantation Unit, St Helier Hospital, Surrey SM5 1AA, United Kingdom. (peter.andrews@esth.nhs.uk).

ISSN: 0041-1337/16/10006-1184

DOI: 10.1097/TP.0000000000001128

Evidence.[4] The guidelines were produced with wide representation from UK clinicians and professional bodies involved in liver transplantation, including the British Association for the Study of the Liver.

The method used for producing these guidelines is detailed in the guideline and the BTS Guideline Development Policy available at http://www.bts.org.uk/.[4] In brief, a systematic review of the relevant literature and synthesis of the available evidence was commissioned from selected clinical experts working to the standards of the above document. Draft chapters were produced by groups of 2 to 4 expert authors, reviewed for content, and modified to house style by the editorial committee. This was followed by peer group appraisal and expert review. Draft proposals were collated by the editors, and the draft guidelines were presented to the UK transplant community for wider discussion at a BTS consensus meeting in London in November 2013. This was attended by transplant surgeons and physicians, intensivists, Clinical Leads in Organ Donation, Specialist Nurses in Organ Donation, and representatives of NHS Blood and Transplant (NHSBT). After revision of the text, appropriate levels of evidence were added to the recommendations by editorial and author consensus. The draft of the document was placed on the BTS website in April 2015 for a period of open consultation, to which patient and transplant groups and an international reviewer were actively encouraged to contribute. After a further round of editorial review, the final document was posted in July 2015.

The last date of formal literature review was June 2014, although additional references were included during the review process.

The guideline has used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to rate the strength of evidence and the strength of recommendations (Table 1).[5] This approach is consistent with that adopted by the Kidney Disease: Improving Global Outcomes foundation, and also with guidelines from the European Best Practice Committee[5,6] and previous BTS guidelines. It is recognized that the evidence base in this area of clinical practice is weak, and the grading of the recommendations reflects this. The guidelines are designed to indicate areas of agreement where they exist and to suggest good practice where they do not. As such, it is hoped that they will stimulate debate audit, research, and changes in practice, as well as a providing a reference point to current clinical practice.

The guideline comprises 153 pages and is freely available at http://www.bts.org.uk/BTS/Guidelines_Standards/Current/BTS/Guidelines_Standards/Current_Guidelines.aspx?hkey=e285ca32-5920-4613-ac08-fa9fd90915b5. Given the lack of a consistent evidence base and the range of practice encountered, the guideline does not attempt to be proscriptive or to define a standard of care. However, to be of value, it must indicate areas where the evidence or consensus of opinion is strong. Therefore, each section of the guideline is prefaced by 1 or several "statements of recommendation," which are explained and referenced in the subsequent text.

This article summarizes the statements of recommendation in the guideline together with selected references and in so doing represents an executive summary of the full guideline. For further details and references, the reader is directed to the main guideline document.

TABLE 1.

Summary of GRADE system

For each recommendation the *quality of evidence* has been graded as one of:
- A (high)
- B (moderate)
- C (low)
- D (very low)

For each recommendation, the *strength of recommendation* has been indicated as one of:
- Level 1 (we recommend)
- Level 2 (we suggest)
- Not graded (where there is not enough evidence to allow formal grading)

Statements of Recommendation

Legal Framework

- All transplants performed from living donors must comply with the requirements of the primary legislation (Human Tissue Act 2004 and Human Tissue (Scotland) Act 2006)[7,8] which regulate transplantation and organ donation across the United Kingdom (not graded).
- Consent for the removal of organs from living donors, for the purposes of transplantation, must comply with the requirements of the Human Tissue Act 2004,[7] the common law for those under 16 years of age, and the Mental Capacity Act 2005 in England and Wales.[9] Consent in Scotland must comply with the Human Tissue (Scotland) Act 2006[10] and the Adults with Incapacity (Scotland) Act 2000[11] (not graded).

Ethics

- All health professionals involved in LDLT must acknowledge the wide range of complex moral issues in this field and ensure that good ethical practice consistently underpins clinical practice.[12,13]
- The BTS has an ethics committee to provide additional support and advice if required (not graded).
- Regardless of potential recipient benefit, the safety and welfare of the potential living donor must always take precedence over the needs of the potential transplant recipient (not graded).
- Independence is recommended between the clinicians responsible for the assessment and preparation of the donor and the recipient. In living liver donation, the donor advocacy team provides an essential safeguard for the potential donor, in addition to the Independent Assessor for the Human Tissue Authority (not graded).

Indications for Living Donor Transplantation in Adults and Children

- Living donor liver transplantation must only be performed in specialist centers working with a multidisciplinary transplant team (1A).
- Decision making must be multidisciplinary and meet the national standards for transplant services in the United Kingdom[14] (1A).
- The UK standard for transplant benefit, an overall graft and patient survival of more than 50% at 5 years, is the recommended standard for both DDLT and LDLT. As liver transplant units are currently achieving more than 75% survival at 5 years for all pediatric transplants, an overall 5-year

patient survival of 70% is expected for pediatric LDLT recipients[15] (1B).
- Even though all elective transplant listed patients are entitled to a routine discussion about the option of LDLT, the increasing number of DDLT means that the requirement for LDLT will remain low. The number of transplant centers offering LDLT should be limited to allow them to gain the experience required to ensure donor safety and good recipient outcomes. A center starting a new program should be mindful of this and recipients should be carefully selected for the first 20 cases[16] (B2).
- The same recipient factors that influence survival in DDLT must be considered for LDLT in both adults and children. The presentation of a potential living donor must not influence the decision[15,17] (not graded).
- Adult and pediatric recipients with acute liver failure can be considered for LDLT provided the transplanting center has the expertise and experience required[16] (B2).
- Consideration of recipients for LDLT, who do not meet indications as agreed through the NHSBT Liver Advisory Group, is subject to the national appeals process until such time as Liver Advisory Group have been able to consider such indications[15] (1A).
- The same selection contraindications apply for LDLT as for DDLT. Living donor liver transplantation recipient selection in patients with alcohol or substance misuse must follow UK NHSBT guidance[17] (1A).
- Recipients must be advised and supported to stop smoking preoperatively and consideration given to not proceeding in the presence of ongoing smoking[18] (2B).
- Complete portal mesenteric vein thrombosis is an anatomical contraindication to LDLT (1B).
- Patients with hepatitis C virus cirrhosis who meet current UK minimal listing criteria can be considered for LDLT[15] (1A).
- Potential recipients with hepatocellular carcinoma who fall outside current UK guidelines (by tumour size and/or number) but who are within University of California San Francisco criteria and who also meet UK α-fetoprotein guidance less than 1000 ng/mL, can be considered for LDLT[19] (1B).
- In a potential recipient with hepatocellular carcinoma, a 3-month interval scan must confirm good tumour biology before LDLT proceeds. Bridging therapies must be used during this interval (2B).
- There is a lack of evidence about the long-term outcomes for recipients of liver transplants in some diseases, for example, alcoholism, cholangiocarcinoma, solitary colorectal tumours. In these cases, experienced centers may wish to consider adult recipients for LDLT, with appropriate protocols, patient information, and phased introduction (not graded).
- In diseases where long-term outcomes are unclear due to lack of evidence or reproducibility of results, LDLT may offer an opportunity for ethically approved research studies within the UK, but LDLT should only be performed under that condition (not graded).
- ABO incompatible LDLT can be considered for pediatric recipients younger than 3 years and for suitable adult recipients with appropriate protocols in experienced centers[20] (1B).

Informing the Donor and Donor Advocacy

- The living donor must be offered the best possible environment for making a voluntary and informed choice about donation (not graded).
- Relevant information about the recipient should be shared with the donor, provided that the recipient has given consent. The recipient must be informed that lack of permission for disclosure may jeopardize the transplant proceeding. To achieve the best outcome for donor, recipient, and transplant, the boundaries of confidentiality must be discussed and specified at the outset (not graded).
- Potential donors should be provided with center-specific complications rates (not graded).
- Independent assessment of the donor and recipient is a statutory requirement of the primary legislation (Human Tissue Act 2004)[7] (A1).
- Separate clinical teams for donor and recipient are considered best practice and a donor advocacy team should be assigned to every potential living liver donor. Healthcare professionals must work together to ensure effective communication and coordination of the transplant process without compromising the independence of either donor or recipient (not graded).
- The donor must be informed that he/she may not be suitable to donate and/or can withdraw from the process at any time. In either case, appropriate support must be provided by the transplant team (not graded).
- Support for the prospective donor, recipient and family is an integral part of the donation/transplantation process. Psychological needs must be identified at an early stage to ensure that appropriate support and/or intervention is provided. Access to specialist psychiatric/psychological services must be available for donors/recipients requiring referral (B2).

Psychological Aspects

- All potential donors must undergo assessment by a mental health professional, preferably a member of the Donor Advocate Team (B1).
- Mental health assessments can be undertaken by any suitably qualified mental health clinician. Centers with access to more than one type of clinician should direct referrals accordingly. Assessment by more than 1 professional may be appropriate in some cases (D2).
- The purpose of mental health assessment is to:

  (a) Identify potential donors who should be excluded from donation due to mental disorder or inappropriate motivation (B1).
  (b) Identify those who are more vulnerable to psychiatric risk and may need additional support after donation (B1).
  (c) Confirm capacity to consent (B1).
  (d) Explore motivation, particularly for altruistic donors (B1).

- Mental health professionals undertaking these assessments should be familiar with the general issues that might arise in living donor transplantation, as well as organ-specific concerns (not graded).
- Clear referral routes to specialist mental health services must be identified for donors who later develop mental health problems (C2).
- As part of the mental health assessment, it may be necessary to interview the donor's next of kin (other than the recipient) (B1).
- Particular consideration must be given to the mental health assessment and support for donors who donate to recipients in urgent need of a transplant (not graded).

Donor Evaluation

- Before starting donor evaluation:

  (a) Establish recipient suitability (A1).

(b) Provide information about alternative treatment options and potential outcomes (A1).
(c) Ensure donor confidentiality is assured (not graded).

- Identify unsuitable donors at the earliest possible stage of assessment. Initial donor triage can be performed using a standardized questionnaire by telephone interview or online (not graded).
- Plan assessment around the donors' commitments and constraints wherever possible. The organizational details for evaluating a prospective donor will vary between centers, reflecting available resources and personnel. Evaluation must be undertaken according to an agreed protocol (not graded).
- Relay the outcome of investigations accurately, appropriately, and efficiently to the potential donor. A designated senior coordinator facilitates optimal communication (not graded).
- Establish a policy for managing donors who are found to be unsuitable and provide appropriate follow-up and support (not graded).
- Timing of transplantation is optimized if donor evaluation is initiated early, allowing time for consideration of more than one donor where necessary. The pace of donor assessment must be tailored according to the rate of decline of recipient liver function, taking into account specific clinical and donor circumstances (C1).
- Donor safety and the provision of an adequate time for informed consent must drive the pace of the donor workup, even when the recipient is very sick (A1).

Donor Age

▪ There is no specific age beyond which donation is contraindicated, but the medical work-up of older donors must be especially rigorous (not graded).
▪ Both donor and recipient must be made aware that the older donor may be at greater risk of perioperative complications (not graded).

Donor Obesity

▪ Any donor with body mass index (BMI) greater than 30 kg/m^2 needs a liver biopsy because of the increased risk of donor hepatic steatosis and the possibility of steatohepatitis[21] (A1).
▪ Moderately obese donors (BMI, 30-35 kg/m^2) should be counselled about the increased risk of perioperative complications and long-term health risks. They should be advised to lose weight before donation and to maintain their ideal weight after donation[22] (B1).
▪ Donor BMI greater than 35 kg/m^2 may be considered by some centers as a contraindication to donation because of the high risk of postoperative complications (B2).

Donor Hypertension

▪ Donors with well-controlled hypertension and no major end organ damage can be considered for living liver donation[23] (B1).

Donor Diabetes Mellitus

▪ In the absence of evidence of target organ damage and having ensured that other cardiovascular risk factors, such as obesity, hypertension, or hyperlipidemia, are optimally managed, potential donors with both type 1 and type 2 diabetes can be considered for living liver donation (not graded).

Donor Cardiovascular Evaluation

▪ All potential donors should be screened for cardiovascular disease, and there should be a low threshold for their exclusion if significant risk factors are found (B1).
▪ Potential donors with reduced exercise capacity or greater than 5% estimated risk of significant coronary atherosclerosis should undergo formal cardiovascular assessment (A2).
▪ Cardiopulmonary exercise testing should be available at all centers (not graded).

Donor Hematological Disease

▪ Patients with a personal or family history of bleeding or thrombosis should be screened for hematological abnormalities using evidence-based protocols (A1).

Liver Integrity

- The donor must undergo comprehensive laboratory assessment (A1).
- Imaging must assess fatty infiltration in addition to the biliary and vascular anatomy[22] (A1).
- Liver biopsy is indicated in the presence of biochemical, serological, or imaging evidence of liver disease (A1).
- The possibility of genetic liver disease in the donor requires specialist evaluation[24] (A1).
- When the cause of liver failure in the recipient is due to an inherited condition, reasonable steps must be taken to exclude genetic disease in the potential donor if he/she is a blood relative (B1).
- Inherited liver disorders are rare, so a specialist pediatric hepatologist or clinical genetic service must assess likely risks to family members (B2).
- The discovery of a potential familial or genetic risk must be conveyed to the donor, with advice on sharing this information with appropriate family members[24] (B2).

Donor-Recipient Transmissible Disease: Infection

- Infection screening is important to identify potential risk for the donor from previous or current infection and to assess potential risk of transmission to the recipient (A1).
- Active hepatitis B virus and hepatitis C virus (HCV) infection are contraindications to donation. Hepatitis B virus core antibody-positive patients and HCV antibody-positive/HCV RNA-negative patients can be considered as liver donors in exceptional circumstances[25] (A1).
- Cytomegalovirus or Epstein-Barr virus positivity is not a contraindication to donation but counselling must be provided re the risk of primary infection and lymphoproliferative disorder (B1).
- Human immune deficiency virus or human T lymphotrophic virus infection is an absolute contraindication to donation[26] (A1).

Donor-Recipient Transmissible Disease: Malignancy

- Careful history taking, clinical examination and investigation of potential donors are essential to exclude occult malignancy, particularly in older (age, >45 years) donors[27] (A1).

- Active malignant disease is a contraindication to living donation, but donors with certain types of successfully treated low-grade tumours may be considered after careful evaluation and discussion[28] (A1).
- Axial imaging of the abdomen by computed tomography (CT) or magnetic resonance examination is mandatory, with specific liver review for secondary malignant disease (A1).

Donor Surgery

- Computed tomography or magnetic resonance imaging of the donor liver with intravascular contrast must be performed. (A1)
- Three-dimensional reconstructions, using either in house or propriety software, are recommended to create detailed 3-dimensional models of liver anatomy for volumetric analysis and determination of vascular/biliary anatomy (B1).
- Conventional arteriography and hepatic venography must only be used in exceptional circumstances when conventional enhanced CT fails to give adequate imaging information (B1).
- Magnetic resonance cholangiopancreatography is the gold standard for biliary anatomy. Endoscopic retrograde cholangiopancreatography must not be used to assess biliary anatomy. Computed tomography cholangiography and intraoperative cholangiography are suitable alternatives (B1).
- Steatosis assessment:
  - Ultrasound can be used as a screening tool. Magnetic resonance imaging provides a better assessment in grading steatosis than CT and is the preferred option[29] (A1).
  - With CT, the liver-to-spleen attenuation ratio (difference between hepatic and splenic attenuation) and blood-free hepatic parenchymal attenuation must be used. The maximum amount of steatosis is not well defined but acceptable limits range from 10% to 30%[30] (B1).
- For volume calculation, the percentage of steatosis must be subtracted from the estimated liver mass for the graft[31] (C2).
- Liver biopsy is reserved for the potential donor with unexplained abnormalities in liver function tests, BMI approaching 30 kg/m^2, or aspartate aminotransferase > alanine transaminase (B2).
- For donors who are initially rejected due to steatosis, a low-calorie "defatting diet" and reassessment with new volumetry can be considered[32] (B1).
- For calculation of donor graft volume, software-assisted image post processing is recommended because it provides the most accurate method of assessment[33] (A1).
- In calculating the standard liver volume of the recipient, published formulae with error rates less than 10% must be used[34] (1B).
- In adults, the choice of donor graft is aimed at reducing donor risks by achieving a large remnant volume, that is, a small resection. A left graft should usually be considered first (B1).
- In most centers, a graft weight (GW)/standard liver volume of 40% is the acceptable lower limit. If less than 40%, outflow and inflow modulation techniques should be considered[35] (C1).
- Using small for size grafts (GW to recipient weight (RW) ratio <0.8) can result in good outcomes but caution is advised in decompensated patients[36] (B1).
- It is widely accepted that the absolute minimum donor remnant volume is 30%[37] (A1).
- To avoid congestion in segment 5/8 for a right lobe graft, a "with middle hepatic vein graft" or venous reconstruction of the anterior segment with an interposition vein graft should be considered if the volume of the graft is borderline for the recipient and the portal pressures are elevated[38] (B2).
- The left graft is procured with the left and the middle hepatic veins (A2).
- Although good outcomes have been reported from small series using laparoscopic or laparoscopy-assisted donor hepatectomy for the left lateral and left lobe, open donor hepatectomy is recommended in the interests of donor safety (B1).
- If the operating surgeon encounters an unexpected finding that, in his/her opinion, jeopardizes the safety of the donor, donation must not proceed (B1).
- If a graft is explanted and cannot be used, a policy to use the organ must be in place. The donor must be informed in advance about this possibility and preoperative consent should be obtained to use the graft for another recipient (B1).
- For the purposes of consent, information about all aspects of morbidity and mortality associated with living liver donation must be provided. For new programs, international statistics on morbidity and mortality must be used and the center must make it known to the donor that it is an "emerging" program. For established programs (>20 cases per year), center-specific activity and morbidity and mortality data must be provided during the donor consent process (B1).
- A 2-stage consent process is best practice to ensure that the donor can give valid consent based upon the information provided[39] (B1).
- The donor may choose to withdraw consent at any time before donation and the reasons must remain confidential (B1).

Recipient Surgery: Technical Aspects, Risk and Perioperative Care for Adults and Children

- Standardization of surgical techniques is limited (not graded).
- Techniques for left lateral segment pediatric LDLT are the same as for DDLT (2A).
- Specific attention in recipient assessment is given to the anatomy of the vasculature and biliary tree to enable planning of surgery. Issues to be addressed include the proximity of cancer to vascular structures, portal vein thrombosis, and a detailed vascular anatomy of inflow and outflow structures in recipients considered for re-transplantation (1B).
- Predicting graft size must rely on preoperative volumetry with the understanding that predicted values often overestimate the size of the graft by a margin of 10% to 20%[40] (1B).
- University of Wisconsin and histidine-tryptophan-ketoglutarate solutions are equally effective for perfusion of the graft[41] (1A).
- In recipient surgery, hilar dissection differs significantly from DDLT. Every attempt should be made to preserve as long a length of the hilar structures as possible and to avoid devascularizing the extrahepatic common duct[42,43] (1B).
- In grafts that are considered small for size (GW/RW ratio <0.8), the portal pressure should be modulated to less than 20 and preferably 15 mmHg, especially in patients with high Model for End Stage Liver Disease[44,45] (1B).
- The hepatic arterial, portal venous, and venous outflow must be assessed with Doppler ultrasound prior to abdominal closure (2A).
- When managing early venous outflow problems, especially with venous reconstructions from segment 5 and 8 veins, interventional radiological techniques should be considered[46] (B2).

Outcomes

- As for DDLT, only recipients with greater than 50% 5-year survival should be considered for living donor living transplantation (2A).

- Adult-to-adult LDLT is associated with a significant learning curve within the first 20 cases.[1] All emerging centers must have access to mentoring over this period (1B).
- 21% is an acceptable overall complication rate for donors after left hepatic lobectomy[47] (1B).
- There is a 40% risk of complications in the first year after right living donor lobectomy[48-50] (1B).
- The incidence of donor death is not well defined, but in the United States and Europe is approximately 0.2%[51] (2B).
- Reporting of donor death and morbidity is mandatory via the NHSBT incident reporting process (2A).
- In the event of donor death:

  (a) Root cause analysis must be performed to identify possible causes and the center LDLT programme suspended pending the outcome of the investigation (2B).
  (b) A documented national disaster and media communication plan agreed by all centers performing LDLT must be followed (2B).

- Recipient outcome and graft survival at 12 months after LDLT must be at least equivalent to that from DDLT. Graft survival critically depends upon case mix, but averages around 80% at 1 year posttransplantation[51,52] (1B).
- It is accepted that the frequency of biliary complications in LDLT recipients is 25% to 35%, which is higher than in DDLT[53] (1B).

Expanding the Donor Pool

- Left lobe liver grafts can be used if the graft size is at least 40% of the recipient's standard liver volume and achieves a GW/RW ratio greater than 0.8[54] (2C).
- If the GW/RW ratio is less than 0.8 or the graft size is less than 35%, a right lobe graft must be considered. If this is not possible, graft inflow modulation should be considered[55] (2B).
- Dual living donor living transplants have only been performed in highly specialized, high volume centers (not graded).
- Dual transplants are indicated when the donor's left lobe is too small to meet the metabolic demands in the larger recipient, for example, GW/RW ratio less than 0.8, or the graft volume to standard liver volume is less than 40%[56,57] (C2).
- Dual transplants can also be used when a potential right lobe graft makes up greater than 70% of the donor's total liver volume meaning the remnant left lobe volume (<30%) would put the donor at risk of small for size syndrome after donation[56] (C2).
- Altruistic living donation of part of a liver can be considered where such donation is considered to be at low risk[58] (C2).
- If a potential liver donor has previously donated another organ, the transplant center should ask the patient for permission to contact the original transplant team to ensure that there are no concerns regarding mental or physical suitability for donation (not graded).
- The donor assessment must comply with Human Tissue Authority requirements and include a review by an independent assessor[59] (A1).
- Mental health assessment by a mental health expert is compulsory and best performed at an early stage in the donor assessment (C1).
- ABO blood group incompatible (ABOi) living donor liver transplants must only be performed in centers with considerable experience of both LDLT and ABOi kidney transplantation and using an established protocol (B1).
- The ABOi LDLTs should only be considered when all other options have been excluded, for example, DDLT or living donor ABO compatible liver transplantation (B1).
- There is insufficient evidence and limited experience to make precise recommendations for ABOi treatment protocols (not graded).

Donor Follow-Up

- Lifelong follow-up is recommended after donor hepatectomy.[60] For donors who are residents in the United Kingdom, this can be offered locally or at the transplant center according to the wishes of the donor, but such arrangements must facilitate the collection of data for submission to the UK Living Donor Registry. Donors from overseas who travel to the UK to donate (privately or to a NHS entitled recipient) are not entitled to NHS follow-up but must be given advice about appropriate follow-up before returning to their country of origin (C1).
- Potential donors who are unable to proceed to donation must be appropriately followed up and referred for further investigation and management as required (B1).

Logistical Considerations

- Wherever possible, the aim must be to ensure that the financial impact on the living donor is cost neutral by the reimbursement of legitimate expenses incurred as a direct result of the preparation for and/or act of donation. There is a clear UK policy for claiming such expenses, which must be followed so that claims may be settled in full and in a timely manner[61] (B1).
- Donors from overseas present unique logistical challenges. To ensure the process is clinically effective and to comply with visa and immigration requirements, there is an agreed visa application process and duration of stay in the United Kingdom (6 months) for the donor which must be honored except in exceptional or unforeseen circumstances[62] (B1).

ACKNOWLEDGMENTS

The authors wish to thank those who contributed to or commented upon this guideline, and the Council of the BTS for permission to produce this summary. Authors of the guideline were as follows (asterisk denotes member of the editorial committee): V Aluvihare (London), P Andrews* (Surrey), L Burnapp* (NHS Blood & Transplant), J Devlin (London), N Heaton (London), M Heneghan (London), J Hennessy (London), J Issac (Birmingham), J Jeffery (Leeds), R Jones (Leeds), M Malagó, (London), D Manas* (Newcastle), P McKiernan (Birmingham), S Potts (Edinburgh), R Prasad (Leeds), P Tachtatzis (Leeds), S White (Newcastle). External review was provided by D Grant (Toronto).

REFERENCES

1. Porret PM, Olthoff KM. *Clin Liver Dis*. 2013;2:160–164.
2. NHS Blood and Transplant, Annual Activity Report, 2012/13. www.odt.nhs.uk.
3. BTS. British Transplant Society. http://www.bts.org.uk/transplantation/standards-and-guidelines/. Updated 2016. Accessed May 5th, 2016.
4. Andrews PA. British Transplantation Society Guideline Development Policy. http://www.bts.org.uk/BTS/Guidelines_Standards/Current/BTS/Guidelines_Standards/Current_Guidelines.aspx?hkey=e285ca32-5920-4613-ac08-fa9fd90915b5. Updated 2016. Accessed May 5th, 2016.
5. Uhlig K, Macleod A, Craig J, et al. Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int*. 2006;70:2058–2065.
6. Berthoux F, Abramowicz D, Bradlet B, et al. European best practice guidelines for renal transplantation (Part 1). *Nephrol Dial Transplant*. 2000;15(Suppl 7).

7. Human Tissue Act 2004. www.opsi.gov.uk/acts/acts2004/ukpga_20040030_en_1. Published 2004. Accessed May 5th, 2016.
8. The Human Tissue (Scotland) Act 2006. www.opsi.gov.uk/legislation/scotland/acts2006/asp_20060004_en_1. Published 2006. Accessed May 5th, 2016.
9. Mental Capacity Act 2005. www.opsi.gov.uk/acts/acts2005/ukpga_20050009_en_1. Published 2005. Accessed May 5th, 2016.
10. The Human Tissue (Scotland) Act 2006, sections 6–10. www.opsi.gov.uk/legislation/scotland/acts2006/asp_20060004_en_2#pt1-pb2-l1g6. Published 2006. Accessed May 5th, 2016.
11. Adults with Incapacity (Scotland) Act 2000. www.opsi.gov.uk/legislation/scotland/acts2000/asp_20000004_en_1. Published 2000. Accessed May 5th, 2016.
12. Kahn J, Matas AJ. What's special about the ethics of living donors? *Transplantation*. 2002;74:421–422.
13. Truog RD. The ethics of organ donation by living donors. *N Engl J Med*. 2005;353:444–446.
14. National Institute for Health and Clinical Excellence. Living donor liver transplantation. Interventional procedure guidance 194.2011. http://www.nice.org.uk/guidance/IPG194/Guidance/pdf.
15. Liver transplantation: selection criteria and recipient registration policy Pol 195/4. http://www.odt.nhs.uk/pdf/liver_selection_policy_2015/pdf.
16. Olthoff KM, Merion RM, Ghobrial RM, et al. Outcomes of 385 adult-to-adult living donor liver transplant recipients: a report from the A2ALL consortium. *Ann Surg*. 2005;242:314–325.
17. Murray KF, Carithers RL Jr. AASLD Practice Guidelines: evaluation of the patient for liver transplantation. *Hepatology*. 2005;41:1407–1432.
18. Pungpanong S, Manzarbeita C, Ortiz J, et al. Cigarette smoking is associated with an increased risk of vascular complications after liver transplantation. *Liver Transpl*. 2002;8:582–587.
19. Mazzaferro V, Llovet JM, Miceli R, et al. Predicting survival after liver transplantation in patients with hepatocellular carcinoma beyond the Milan criteria: a retrospective exploratory analysis. *Lancet Oncol*. 2009;10:35–43.
20. Wu J, Ye S, Xu X, et al. Recipient outcomes after ABO-incompatible liver transplantation: a systematic review and meta-analysis. *PLoS One*. 2011;6:e16521.
21. Brandhagen D, Fidler J, Rosen C. Evaluation of the donor liver for living donor liver transplantation. *Liver Transpl*. 2003;9:S16–S28.
22. Chu MJ, Dare AJ, Phillips AR, et al. Donor hepatic steatosis and outcome after liver transplantation: a systematic review. *J Gastrointest Surg*. 2015.
23. Chen YS, Cheng YF, De Villa VH, et al. Evaluation of living liver donors. *Transplantation*. 2003;75:S16–S19.
24. Schielke A, Conti F, Gourmard C, et al. Liver transplantation using grafts with rare metabolic disorders. *Dig Liver Dis*. 2015;47:261–270.
25. 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.
26. Advisory Committee on the Safety of Blood Tissues and Organs (SaBTO). Guidance on the microbiological safety of human organs, tissues and cells used in transplantation. https://www.gov.uk/government/publications/guidance-on-the-microbiological-safety-of-human-organs-tissues-and-cells-used-in-transplantation.
27. Trotter JF, Wisniewski KA, Terrault NA, et al. Outcomes of donor evaluation in adult-to-adult living donor liver transplantation. *Hepatology*. 2007;46:1476–1484.
28. Israel Penn International Transplant Tumor Registry. https://ipittr.uc.edu/.
29. van Werven JR, Marsman HA, Nederveen AJ. Assessment of hepatic steatosis in patients undergoing liver resection: comparison of US, CT, T1-weighted dual-echo MR imaging, and point-resolved 1H MR spectroscopy. *Radiology*. 2010;256:159–168.
30. 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.
31. Kim KM, Choi WB, Park SH, et al. Diagnosis of hepatic steatosis and fibrosis by transient elastography in asymptomatic healthy individuals: a prospective study of living related potential liver donors. *J Gastroenterol*. 2007;42:382–388.
32. Oshita A, Tashiro H, Amano H, et al. Safety and feasibility of diet-treated donors with steatotic livers at the initial consultation for living-donor liver transplantation. *Transplantation*. 2012;93:1024–1030.
33. Tongyoo A, Pomfret EA, Pomposelli JJ. Accurate estimation of living donor right hemi-liver volume from portal vein diameter measurement and standard liver volume calculation. *Am J Transplant*. 2012;12:1229–1239.
34. Pomposelli JJ, Tongyoo A, Wald C, et al. Variability of standard liver volume estimation versus software-assisted total liver volume measurement. *Liver Transpl*. 2012;18:1083–1092.
35. Ishizaki Y, Kawasaki S, Sugo H, et al. Left lobe adult-to-adult living donor liver transplantation: should portal inflow modulation be added? *Liver Transpl*. 2012;18:305–314.
36. Kiuchi T, Tanaka K, Ito T, et al. Small-for-size graft in living donor liver transplantation: how far should we go? *Liver Transpl*. 2003;9:S29–S35.
37. Facciuto MI, Contreras-Saldivar A, Singh MK, et al. Right hepatectomy for living donation: role of remnant liver volume in predicting hepatic dysfunction and complications. *Surgery*. 2013;153:619–626.
38. Radtke A, Sgourakis G, Sotiropoulos GC, et al. Donor/recipient algorithm for management of the middle hepatic vein in right graft live donor liver transplantation. *Am J Surg*. 2010;199:708–715.
39. Broelsch CE, Whitington CF, Emond JC, et al. Liver transplantation in children from living related donors. Surgical techniques and results. *Ann Surg*. 1991;214:428–437; discussion 437–439.
40. Hill MJ, Hughes M, Jie T, et al. Graft weight/recipient weight ratio: how well does it predict outcome after partial liver transplants? *Liver Transpl*. 2009;15:1056–1062.
41. Song GW, Lee SG. Living donor liver transplantation. *Curr Opin Organ Transplant*. 2014;19:217–222.
42. Ikegami T, Shirabe K, Morita K, et al. Minimal hilar dissection prevents biliary anastomotic stricture after living donor liver transplantation. *Transplantation*. 2011;92:1147–1151.
43. Kim SH, Kim YK. Improving outcomes of living-donor right hepatectomy. *Br J Surg*. 2013;100:528–534.
44. Troisi R, de Hemptinne B. Clinical relevance of adapting portal vein flow in living donor liver transplantation in adult patients. *Liver Transpl*. 2003;9:S36–S41.
45. Sánchez-Cabús S, Fondevila C, Calatayud D, et al. Importance of the temporary portocaval shunt during adult living donor liver transplantation. *Liver Transpl*. 2013;19:174–183.
46. Umehara M, Narumi S, Sugai M, et al. Hepatic venous outflow obstruction in living donor liver transplantation: balloon angioplasty or stent placement? *Transplant Proc*. 2012;44:769–771.
47. Freise CE, Gillespie BW, Koffron AJ, et al. Recipient morbidity after living and deceased donor liver transplantation: findings from the A2ALL retrospective cohort study. *Am J Transplant*. 2008;8:2569–2579.
48. 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.
49. Iida T, Ogura Y, Oike F, et al. Surgery-related morbidity in living donors for liver transplantation. *Transplantation*. 2010;89:1276–1282.
50. Abecassis MM, Fisher RA, Olthoff KM, et al. Complications of living donor hepatic lobectomy: a comprehensive report. *Am J Transplant*. 2012;12:1208–1217.
51. Middleton PF, Duffield M, Lynch SV, et al. Living donor liver transplantation—adult donor outcomes: a systematic review. *Liver Transpl*. 2006;12:24–30.
52. Thuluvath PJ, Yoo HY. Graft and patient survival after adult live donor liver transplantation compared to a matched cohort who received a deceased donor transplantation. *Liver Transpl*. 2004;10:1263–1268.
53. Melcher ML, Pomposelli JJ, Verbesey JE, et al. Comparison of biliary complications in adult living-donor liver transplants performed at two busy transplant centers. *Clin Transplant*. 2010;24.
54. Soejima Y, Shirabe K, Taketomi A, et al. Left lobe living donor liver transplantation in adults. *Am J Transplant*. 2012;12:1877–1885.
55. Harada N, Shimada M, Yoshizumi T, et al. A simple and accurate formula to estimate left hepatic graft volume in living-donor adult liver transplantation. *Transplantation*. 2004;77:1571–1575.
56. Lee S, Hwang S, Park K, et al. An adult-to-adult living donor liver transplant using dual left lobe grafts. *Surgery*. 2001;129:647–650.
57. Chen Z, Yan L, Li B, et al. Prevent small-for-size syndrome using dual grafts in living donor liver transplantation. *J Surg Res*. 2009;155:261–267.
58. Wright L, Ross K, Abbey S, et al. Living anonymous liver donation: case report and ethical justification. *Am J Transplant*. 2007;7:1032–1035.
59. Human Tissue Authority. Guidance to Transplant teams and Independent Assessors March 2015. https://www.hta.gov.uk/policies/guidance-transplant-teams-and-independent-assessors.
60. Directive 2010 /45/EU of the European Parliament and of the Council of 7 July 2010. http://www.hta.gov.uk/_db/_documents/EUODD_Directive_August_2011.pdf. Published 2010. Accessed May 5th, 2016.
61. Commissioning policy statement: reimbursement of expenses for living organ donors. NHS Commissioning Board. https://www.england.nhs.uk/wp-content/uploads/2013/04/a07-ps-a.pdf. Published 2013. Accessed May 5th, 2016.
62. Visas and immigration, routes for living organ donors. Government of UK. https://www.gov.uk/search?q=living+organ+donors. Published 2014. Accessed May 5th, 2016.