Review Article

Patient and donor selection in living donor liver transplantation

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Abstract: The impetus for the development of living donor liver transplantation (LDLT) has been the gross mismatch in the number of recipients to available deceased donor organs. Its complex ethical issues notwithstanding, LDLT remains a technically demanding procedure. However, since the turn of the millennium the operation has dramatically improved, rendering results on par with those of deceased donor liver transplantation (DDLT). In these surgeries, donor safety is of paramount importance as are recipient outcomes with preservation of liver graft function. The ultimate goals of LDLT are to achieve very low morbidity and near-zero mortality to the live donor, while providing a survival benefit to those who need it most. LDLT is comparable to other demanding procedures, where the commitment and experience of a team is intimately entwined with the development and results of the operation. Apart from technical excellence, selecting the best possible 'transplant pair' remains the sine-qua-non for good outcomes in LDLT. An "ideal LT survivor" is one with a stable first allograft function, normal growth, and absence of immunosuppression related complications, a goal which every clinician works towards. An algorithmic protocol-based multidisciplinary approach to donor and recipient selection is the first step in achieving this not-so-utopian goal. This review provides an overview of the donor and recipient selection criteria in LDLT.

Keywords: Living donor liver transplantation (LDLT); donor; recipient; selection; outcomes

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Introduction

The impetus for the development of living donor liver transplantation (LDLT) has been the ever increasing disparity between number of patients requiring a liver transplant (LT) and the availability of deceased donor organs. Apart from its complex ethical issues, LDLT remains a technically demanding procedure. However, since the turn of the millennium the operation has dramatically improved, rendering results on par with those of deceased donor liver transplantation (DDLT). In these surgeries, donor safety is of paramount importance as are recipient outcomes with preservation of liver graft function. LDLT is comparable to other demanding procedures, where the commitment and experience of a team is intimately entwined with the development and results of the operation. Apart from technical excellence, strict protocolised selection criteria for donor and recipients remain the sine-qua-non for good outcomes. This review provides an overview of the donor and recipient selection criteria in LDLT.

Need for LDLT

Soon after LT became a standard treatment for end-stage liver disease (ESLD), it became apparent that there was a gross mismatch in the number of recipients to available organs. This discrepancy between supply and demand led to an ever growing burden on the waiting list. Technical

innovations which significantly expanded the scarce donor pool, like split liver transplantation, simultaneously helped in the development of LDLT (1). Apart from a simple expansion of the donor pool, there are certain other discernible merits of LDLT over DDLT. These include, the capability of performing an elective LT before the recipient becomes too unwell, excellent quality grafts devoid of the uncertainties associated with DDLT livers (donor comorbidities, brain death induced physiologic derangements, and cold ischemic time), and in certain other situations the possibility of LT for patients who would otherwise not fall within the standard inclusion criteria for DDLT.

There has been an asymmetrical growth of LDLT across the globe. It is well embraced by Asian countries due a multitude of factors which include a lack of an organised system for identification and distribution of deceased-donor organs, cultural and religious barriers to the widespread acceptance of brainstem death and deceased donation and the presence of individual surgical practices (2,3). With a greater availability of deceased donor organs, the demand and hence the number of LDLT in the west has traditionally been lower than in the east.

The finite risk of complications and/or death in an otherwise healthy live donor is the single biggest detriment to performing LDLTs. Others drawbacks include those of receiving a partial liver which may lead to inadequate graft volume and attendant early poor graft function. There also remains the additional technical complexity with smaller vessels and multiple bile ducts for anastomoses along with the need for careful and methodical selection of the appropriate "donor and recipient pair" for the best possible result.

Ethical considerations

The two basic tenets of LDLT include ensuring that donor morbidity and mortality are kept to a minimum and that recipient outcomes are not inferior to a full size DDLT. It is also sobering to appreciate that it may never be possible to justify a surgery which violates the core medical principle of 'above all, do no harm'. Despite taking every precaution, even in the most experienced of hands, donor deaths may be inevitable (4-6). While the true incidence of donor deaths may be under-reported, the purported risk of mortality to a live liver donor is 0.15% to 0.30%; this may be higher (0.5%) when a larger volume of liver is donated (5).

In 2005, an international forum which convened in Vancouver, Canada focused on practice principles with an aim to ensure the safety of living organ donors (7,8). This forum formulated a set of guidelines with regards to LDLT which included the following points: (I) An LDLT should only be performed if the risk to the donor can be balanced by an acceptable outcome in the recipient. (II) Apart from in an approved study protocol scenario, the indications for LDLT should be the same as those established for DDLT. Examples of such indications would include hepatocellular carcinoma (HCC) beyond Milan/UCSF criteria, and LT for selected cases of HCC with portal vein tumour thrombi post-neoadjuvant radiotherapy (2,9-12). (III) Obviating the waiting period for a deceased donor organ by performing an LDLT should provide a survival benefit to the recipient. Hence, the factors to be considered before offering a patient LDLT include the person's quality of life, the severity of the patient's liver failure, the expected waiting time for a deceased donor, and the recipient's risk-to-benefit ratio (13).

It is heartening to note that post-donation quality of life analyses on liver donors have reported increased self-esteem and satisfaction, with up to 92% of all donors willing to donate again (14-17). An important contributing factor in this regard is a detailed multi-stage counselling during the donor work-up with regards to the operation, complications and outcomes, which enabled these donors to have a realistic view of procedure. Despite this, ethicists will undoubtedly continue to debate the risks and benefits of living organ donation.

Donor evaluation

Donor evaluation is aimed at revealing conditions that could increase the risk perioperative complications in the healthy donor. This systematic evaluation should be able to exclude an unfit prospective donor at an early stage, while allowing for suitable candidates to proceed towards donation.

Every living donor transplant program is required to have its own well defined criteria and algorithmic process of selecting the transplant pair. This process needs to be transparent and patients should have access to the information before and during the work-up. The practice of selecting an appropriate donor is based on the following tenets: (I) the donation is truly altruistic and there is no pecuniary or other self-interested motive involved. (II) The donor is of a sound mind, understands the risks and has the capacity for an informed consent for donation. (III) The whole process is voluntary and there is no coercion. It is

Table 1 Acceptability criteria for live liver donors

Acceptable donors
Age 18–50 years
ABO compatible blood group
No comorbidities, or 1 comorbidity such as well controlled HT.
LAI ≥+6
BMI <25 kg/m^2
GRWR >0.8
Remnant volume >30% of TLV
Anatomically suitable for donation
To be discussed multi-disciplinary team (MDT) meeting—before accepting for donation
Age >50 years
Comorbidities such as systemic hypertension, bronchial asthma.
LAI between –5 to +5
BMI 25–30 kg/m^2
GRWR <0.8 and/or donor liver remnant volume 28–30%
Any unusual anatomic feature

LAI, liver attenuation index; TLV, total liver volume; BMI, body mass index; GRWR, graft to recipient body weight ratio.

also important for the donor to be aware that there is no compulsion to proceed with donation even after completion of assessment, and that the donor is at liberty to withdraw consent at any time. (IV) The donor meets all stipulated criteria for medical suitability.

The multi-step donor evaluation protocol includes exhaustive medical and psychological evaluations of the donor, as well as a precise anatomical study of the liver. LDLT donor evaluation protocols published by teams across the globe are very similar (18-21). Although there is an ongoing debate whether a correlation exists between the extent of hepatectomy and the risk to the donor, most transplant teams are likely to have more stringent criteria for right lobe donors, especially with regards to donor age and steatosis (21). While selecting a suitable donor, the recipient's status should always be taken into account. The donor evaluation should only begin after ascertaining that the recipient is an appropriate candidate for LT. It is this combination of both their favourable and unfavourable characteristics which determines whether the 'transplant pair' is suitable or not for LDLT. Below is the donor evaluation protocol as followed by our team (*Table 1*).

Donor selection criteria

Blood group

The blood group criteria for blood transfusion and organ donation are similar. Therefore, AB group individuals are universal recipients and those with O group blood group are universal donors. It is preferable to choose ABO identical or ABO compatible donors. Breaching the ABO blood group barrier is a way to increase donor access for an individual patient and ABO-incompatible LT (ABOi LT) may be the only potentially lifesaving option in the absence of a suitable ABO compatible deceased or live donors. In adults, desensitisation protocols using drugs, biologic agents, plasmapheresis, splenectomy and other immune-modifying therapy have successfully enabled physicians to cross the blood group incompatibility barrier (12,22,23). With a better understanding of transplant immunology and these optimised immunosuppressive protocols, outcomes of ABOi LT are now comparable to ABO identical LT (12,22-24). Currently, ABOi LT account for 5–20% of the total LDLTs performed. One of the largest meta-analysis comparing ABOi LT with ABO compatible (ABOc) LT of nine high-quality studies conducted between 2015 and 2018 included a total of 3,858 patients (ABOi =639 and ABOc =3,219) (25). Desensitisation process with rituximab was used in all the ABOi patients. Incidences of postoperative complications were comparable between both groups. However, ABOi LT had higher incidences of CMV infection, antibody mediated rejection (AMR), overall biliary complications, and biliary stricture than adult ABOc. Despite this and in contrast to earlier studies, there was no significant difference between the ABOi and ABOc LT groups in terms of 1-, 3-, and 5-year graft survival and overall survival (24-26).

The paediatric population have a privileged immune system which helps support ABOi LT better than adults. Infants do not produce isohemagglutinins, therefore, their anti-A and -B antibody titres remain at low levels even beyond 12 months of age. Additionally, activation of their complement system is also relatively suppressed. Taken together, infants have fewer mediators for an antibody-mediated rejection. Desensitisation protocols as used in adult ABOi LT are therefore usually not required in children under 2 years of age (27-29).

Relationship

Most state authorities across the world stipulate that the prospective donor and recipient be related. There are

however, certain countries like USA, Canada, the UK, Iran, Saudi Arabia, Israel, the Netherlands, Switzerland and Hong Kong which allow for anonymous altruistic donation (30-33). Any donor from outside the country is considered "unrelated" for this purpose, even if he/she happens to be a primarily "related" donor. If the donor and recipient are foreigners, a clearance has to be obtained from the relevant embassy regarding the genuine relationship between donor and recipient.

Age

The rate of hepatic regeneration has obvious implications for both the donor and recipient. As there is a correlation between advancing age and a marked decline in the rate of hepatic regeneration, age remains a crucial deciding factor in selecting a prospective donor (19,34). Donors should strictly be above the age of 18 years. The upper limit however varies, and is more dependent on their physiological age. Most LDLT units across the globe use an arbitrary cut-off number for age, this varies between centres from 50–65 years (35). Graft volumes must also be taken into consideration; it is preferable to avoid a low graft weight to recipient's body weight ratio (GRWR expressed as %) liver from an older donor. Despite reports of successful right lobe donations from septuagenarian live-donors, extreme caution must be exercised in the selecting elderly donors and cannot be recommended as a routine (36).

Weight and body mass index (BMI)

An ideal donor's BMI should be below 25 kg/m^2. Large cohort studies and meta-analyses have shown that compared with normal BMI, the risk of fatty liver increases approximately 4 to 14-fold in higher BMI individuals (37,38). Dose-response analyses also show that the risk increases in a nonlinear fashion (approximate J-shaped fashion), indicating higher BMI is an independent, dose-dependent risk factor for fatty liver (37,39). However, if the degree of steatosis as below 20% as estimated by liver attenuation index (LAI) and the functional remnant volume is over 35%, the BMI criterion may be relaxed to 30 kg/m^2. As shown by several regional studies, Asians as compared to the western population have a higher percentage of body fat for a specified BMI (40-42). Therefore, a more stringent BMI cut-off of 27.5 kg/m^2 is recommended for prospective donors of Asian ethnicity. A BMI of over 30 kg/m^2 is generally considered a relative contraindication for living donation. Albeit, in certain situations donors with a higher BMI may be considered. One such example is when the BMI is falsely elevated in a very muscular donor. Another example being where there are no other suitable donors, and the donor's BMI is between 30 and 35 kg/m^2. The prospective donor is offered a diet/exercise regime, and re-evaluated after 6 weeks to ascertain suitability for donation. The pre-donation BMI should ideally have fallen below 30 kg/m^2 and there should be a marked improvement in the degree of steatosis (should now be below 20%). A liver biopsy at the end of the weight reduction programme is however, mandatory. It must nevertheless be kept in mind that BMI is not an infallible marker of steatosis. This is true especially in the South-Asian population where individuals within normal-range BMI have unexpectedly shown fatty livers on imaging. This subset, which is becoming increasingly prevalent, is diagnosed to have 'lean non-alcoholic fatty liver disease (NAFLD)' or 'non-obese NAFLD' (43-45). These prospective donors are offered a diet/exercise regime, and re-evaluated with a follow-up imaging after 6 weeks to ascertain their suitability for donation.

Comorbidities

An ideal donor is without any comorbidities. Due to its negative influence on liver regeneration, Diabetes remains a contraindication. A single controlled comorbidity like Hypertension may be considered acceptable. Other more severe comorbidities like significant renal or cardiorespiratory disease are also considered contraindications to donation. It is however, advisable to discuss any prospective donor's comorbidity in a multi-disciplinary team meeting before making a formal decision.

Previous abdominal surgery is not a contraindication to donation; however, the indication might be more important than the operation itself. An interesting and ethically charged situation arises when a combined liver kidney transplant (CLKT) is indicated. While there may be a compounded morbidity due to the two donations, receiving two organs from the same donor provides the recipient with an obvious immunological advantage. Potentially three situations arise, the first is when the two organs are transplanted simultaneously, the second when the LT is performed first followed by a kidney transplant (KT) at a second operation. This sequential operation is done after the donor has recovered from his liver donation. The rarest scenario is when a LT is done sequentially after a KT (46-48).

The basic concept of minimising donor risk remains

essential to any living donor program. Sequential kidney donation after a liver donation, is well described. Given that the liver has regenerated during the lag-time between the two donations, no additional morbidity is added onto the now kidney donor (12,47,49). Simultaneous liver-kidney donations especially when a left lobe/left lateral segment of the liver is donated have also been described (46,47). Reports of right lobe liver donation along with kidney exist, however cannot be recommended due to higher risks involved in a major hepatectomy (48). There is also a report of a donor donating the right lobe of his liver 20 years after a kidney donation to the same recipient (50). This situation nevertheless is significantly different from the others, as the prospective liver donor now has a single kidney and hence its associated risks. While the safety of this liver-after-kidney donation has been demonstrated by two recent series, strict donor selection criteria is necessary to ensure donor safety. Extreme caution must be exercised in selecting these donors and may be performed in exceptional circumstances rather than as a routine (51,52).

Steatosis

Estimation of LAI (defined as the difference between the liver and spleen's attenuation values on non-contrast CT) is a quick and easy method of assessing the degree of steatosis. An ideal donor should have less than 20% liver steatosis which correlates with an LAI of ≥+6. Steatosis of >30% (LAI <–5) is a contraindication for live liver donation. For donors with LAI between these values (LAI –5 to +5), a liver biopsy may be indicated for a more objective estimation of steatosis.

Technical developments in recent years has transformed non-invasive qualitative imaging techniques into rigorous quantitative methods. MRI as a quantitative tool for intracellular liver fat measurement has shown good correlation with histological grading and holds promise to provide a cost-effective, accessible and accurate evaluation in the future (53,54).

Graft volumes

Volumetric evaluation of a donor's liver requires that both the graft and remnant liver volumes be taken into consideration. GRWR is commonly used to assess the adequacy of a liver graft with respect to the recipient. An ideal GRWR is above 0.8. In the presence of favourable donor (e.g., young age, no steatosis etc.) and recipient characteristics (e.g., low MELD), lower GRWR (0.7–0.8) may also be considered adequate. Grafts with GRWR <0.7 are usually considered unsuitable. However, these grafts may be used successfully in highly selected patients with low MELD and minimal portal hypertension. These recipients may need portal modulation to reduce the risk of small-for-size syndrome (55,56).

Children as a rule need larger GRWR grafts. Grafts with GRWR between 1.5 and 3 are considered ideal. Should the GRWR be over 4, or in the presence of a significant size mismatch, anatomical or non-anatomical reduction of left lateral section grafts may be needed in very small children (<6 months of age, <5 kg) (57).

While GRWR is commonly used in western centres, LDLT centres in Japan and Hong Kong use mathematical formulae-based calculations of the recipient's standard liver volume (SLV) to determine adequate graft volume. These formulae are usually based on body weight or body surface area. Most centres use 30-40% of the SLV as the minimum requirement for a liver graft (2,20,58).

Anatomical suitability

A triphasic CT scan along with an MRCP are the most commonly employed modalities for evaluating the anatomical suitability of a donor liver. Anatomical anomalies which may complicate the donor or recipient surgery should be carefully identified (*Figures 1-3*). Certain anatomical variations like a single portal venous supply to the entire liver is an absolute contraindication to donation (*Figure 2E*).

Due to the shared drainage of segments V, VIII & IV, one the biggest dilemmas in LDLT is that of the middle hepatic vein (MHV); and its anatomy holds the key to right lobe (RL) living donation. A detailed study of the hepatic venous anatomy is imperative in deciding whether the MHV is left behind with the donor liver or is partially or totally taken with the graft liver. While there is centre-to-centre variation in this protocol, traditionally, the MHV was taken with the RL graft. However, with donor safety as paramount, more recently there has been a decisive shift towards retaining the MHV with the donor.

Donor evaluation algorithm

Stage I of the evaluation process commences with a detailed interview with the prospective donor and their family. The donor should also be given the option to discuss the process privately with the physician. This face-to-face consult includes an overview of the evaluation process and

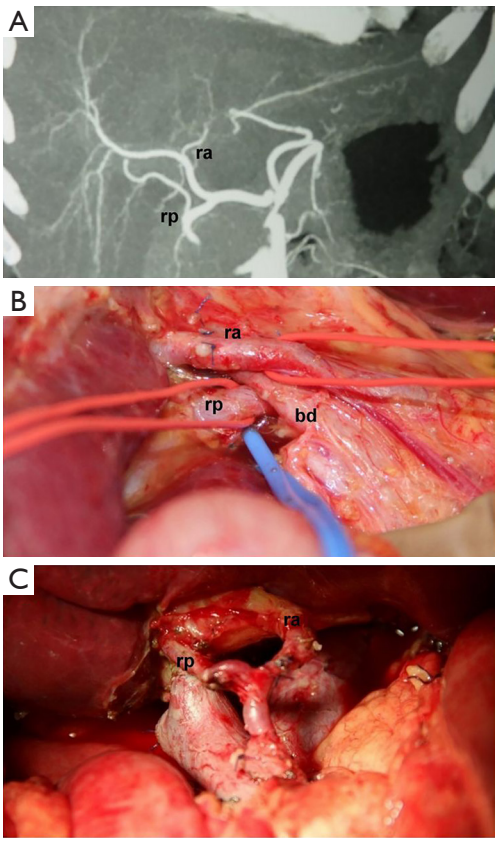

Figure 1 Variation in the Donor's Right Hepatic Artery which complicates both donor and recipient operation. (A) CT scan showing extrahepatic bifurcation of right hepatic artery into its anterior (ra) and posterior (rp) divisions; (B) intraoperative view showing the right anterior (ra) and posterior (rp) branches of the right hepatic artery coursing on either side (above and below) the common bile duct (bd). This variation leads to two arteries in a right lobe graft. (C) Arteries (ra & rp) reconstructed in the recipient.

the donor's perioperative course including the likelihood of complications. The interview also addresses the short and long term donor outcomes, with an aim to provide a realistic picture of the donation. This is followed by a clinical examination of prospective donor, and an initial series of blood tests which include complete blood count, renal function test, lipid profile, liver function tests, thyroid function tests, immune & viral markers. Stage I of assessment also includes a non-contrast CT for liver fat estimation. Donors initially found unsuitable due to reversible causes like high BMI are advised to lose weight, and are offered an exercise and diet plan. Donors need to abstain from smoking and discontinue contraceptive pills 6 weeks before the donation.

Stage II includes donor's liver volumetry and evaluation of the anatomy with a triphasic CT scan. Based on these, a decision on the type of graft is made. Factors which influence this decision include the donor's functional liver remnant volume, recipient's expected GRWR and the donor's vascular anatomy (*Figure 4*).

All donors undergo an initial cardiac evaluation with an ECG, and echocardiogram. Subsequent tests include a treadmill test or Dobutamine Stress echocardiogram. Protocols across the globe differ slightly in this regard. Transplant centres in the west assess an otherwise healthy prospective donor's cardiac status based on an ECG and echocardiogram (59-61). Given the above described high prevalence metabolic syndrome in the younger population in the Indian sub-continent, centres including ours routinely add a treadmill test to cardiac evaluation (38,41,43-45). Conventional coronary angiograms and more recently CT-coronary angiograms are selectively performed in those prospective donors who have an abnormal result in either of the above tests. Suitable donors go onto a multidisciplinary assessment by the Psychiatrist, the Physician, the Gynaecologist, and the Anaesthesiologist. Specific other investigations are performed on a case-to-case basis. This is based on any significant positive clinical or biochemical findings flagged up during the evaluation process. Specific tests to rule out inherited/familial liver diseases which may compromise both the recipient and donor's short- & long-term outcomes are also performed (Serum Copper, Ferritin, auto-immune markers etc.). Care should be taken to exclude diseases prevalent in certain ethnic populations (G6PD deficiency & sickle cell disease amongst middle eastern and African donors), as these could adversely affect the donor's intraoperative & postoperative course.

Rapid donor assessment in acute liver failure

Despite time being the essence, donor evaluations in LDLT for acute liver failure (ALF) should follow the same systematic approach as is followed for other LDLTs. Some concessions can however be made with regards to combining a few of the above mentioned steps. Briefly, following a detailed face-to-face interview, counselling and preliminary blood tests, all imaging is done simultaneously. Prospective donors are then fast-tracked through the multi-speciality assessments. There always remains a concern that the rapidity of the process may preclude the donor

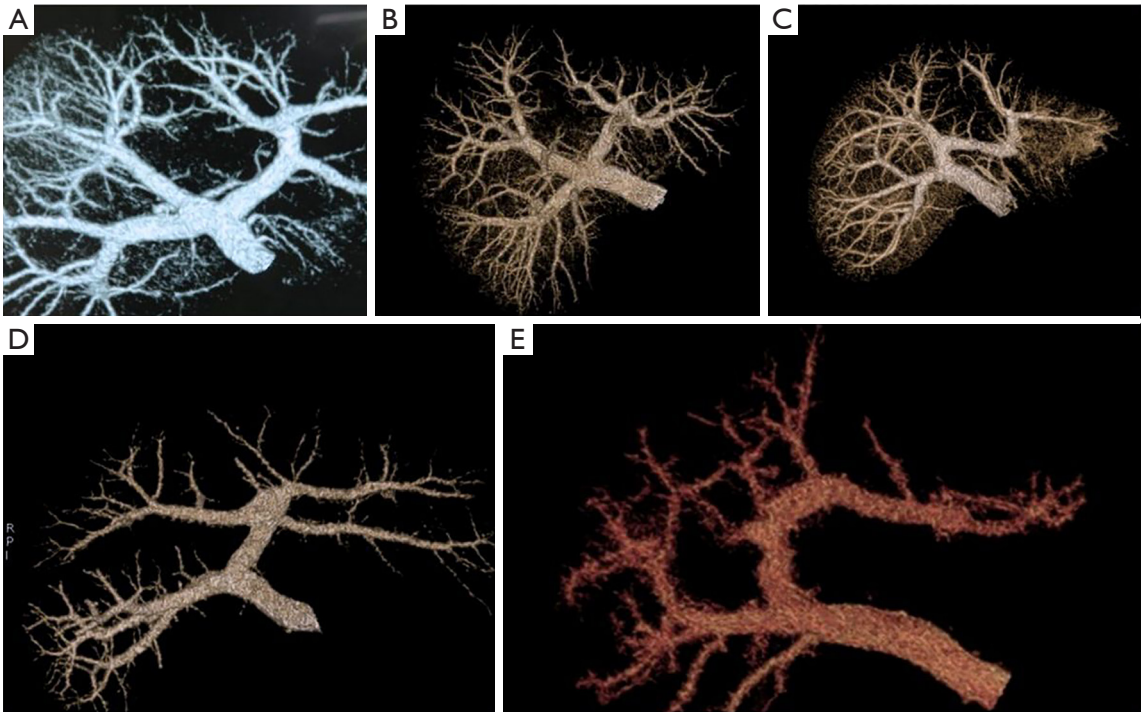

Figure 2 Variations in the Donor's portal venous anatomy which may complicate the donor and recipient operations. (A) Type A anatomy with a short stump of right portal vein. (B) Type B anatomy with trifurcation of the main portal vein. (C,D) Type C,D anatomies with right anterior portal vein arising from the left portal vein. Types B,C,D will lead to two portal veins in a right lobe liver graft which will need reconstruction in the recipient. Donor's portal vein stump closures must be done carefully to avoid narrowing the left portal vein. (E) Type E Single portal vein supplying the liver. This anatomical variation is an absolute contraindication to liver donation.

from making a careful, reasoned decision about donation. A donor advocate is always present with the donor to help him/her through the process and ensure that there is no coercion for donation. A detailed Psychiatric evaluation for psycho-social issues is imperative in these situations. The aim is to complete the donor evaluation and approval documentation within 48 hours.

Routine vs. selective liver biopsy

Routine liver biopsy before living donation remains controversial. LDLT centres in the past performed routine biopsies to ascertain the presence of steatosis, inflammation or fibrosis not picked up on routine imaging (13,19,41,62). However, liver biopsies come with their own set of complications, which in an otherwise normal prospective donor may not entirely be justified. With the advent of reliable non-invasive modalities to qualitatively assess the liver, more centres across the globe are moving away from routine liver biopsies as a part of donor evaluation (53). At our centre, liver biopsies are performed selectively in donors with BMI over 30 kg/m^2, dyslipidaemia, presence of metabolic risk factors or LAI <5 and when elevated liver enzymes are noted. Older donors or those with any of the previously described factors also undergo a liver biopsy.

Donor hospital stay & follow up

Antibiotic prophylaxis is with 5 doses of perioperative piperacillin and tazobactam. Following their extubation in the OR, donors are transferred to the high dependency unit where they are monitored with serial arterial blood gas and lactate measurements. They are retained in the HDU for 24–48 hours and discharged from hospital on the 5th post-operative day. They are discharged from clinic after a month. During this time, they visit the out-patient unit on a weekly basis. Long term follow of these donors is either by the transplant team or a local physician with standard blood investigations performed at 3 monthly intervals for the first 6 months and then annually.

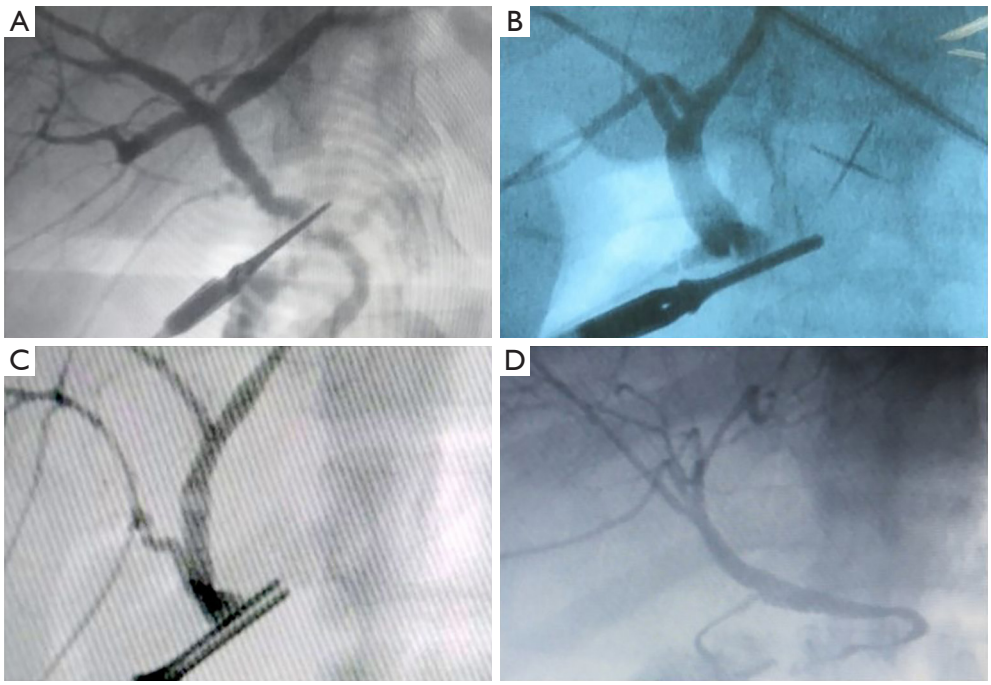

Figure 3 Variations in the Donor's bile duct anatomy which may make the bile duct reconstruction in the recipient more complex. (A) Standard anatomy however with a short stump of the right hepatic duct. May lead to two ducts in the graft; (B,C) Huang A3 & Huang A5 variations which will lead to two bile ducts in the liver graft; (D) complex biliary anatomy, leading to 3 or more ducts in a right lobe graft.

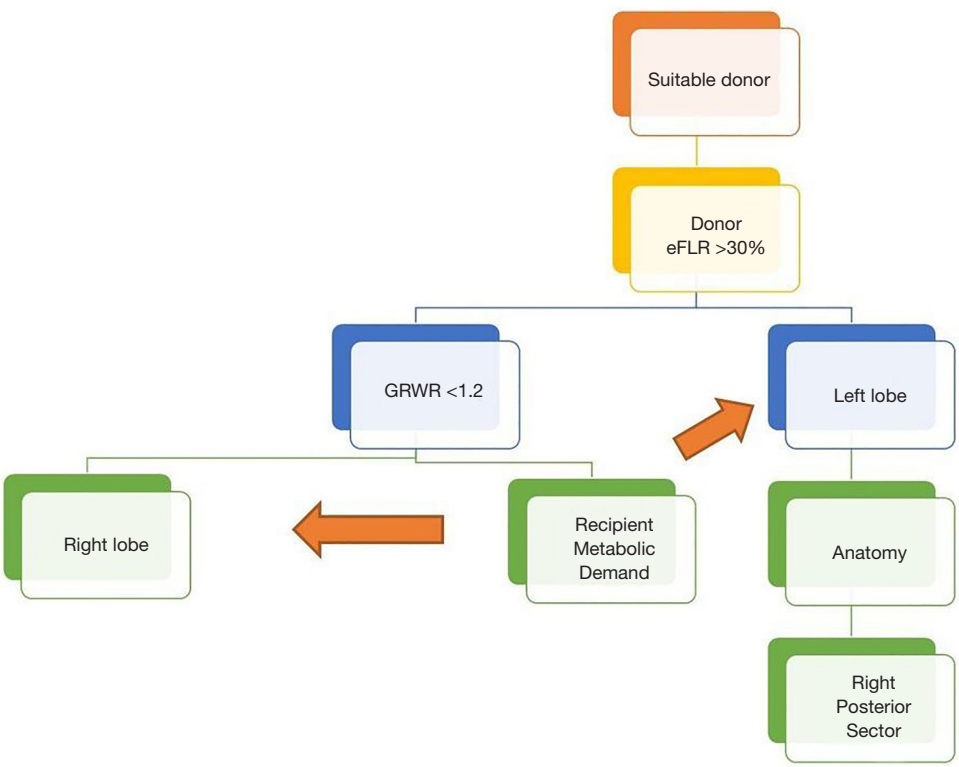

Figure 4 Donor selection protocol.

LDLT recipient evaluation

Unlike LDLT, in the case of DDLT, organs must be distributed in an equitable manner by an organized system, this system for allocation should be built on the principles of autonomy, benevolence, justice and non-malfeasance. LDLT on the other hand is a directed organ donation and a clear judgment is needed to balance the donor risk *vs.* the recipient benefit, satisfying the tenet of "double equipoise" (13,19,63). It is also essential to appreciate that with emerging data the indications for LDLT will also keep evolving.

Principles of defining indications

With advances in technology and a better understanding of the disease processes, the indications for LT are constantly being revisited and modified. However, the basic principles based on which these indications are defined have remained constant (13,19,64,65). Patients are offered LT when there exists no other equally effective alternate medical or surgical treatment to it and their life expectancy without a transplant is likely to be significantly be lower than that after a LT. As accepted by transplant physicians worldwide, a recipient's minimum 5-year post-transplant life expectancy should be over 70%. LT is also offered with an aim to improve patient's quality of life. Once listed for LT, it is imperative that patients are reviewed on a regular basis to ensure that these fragile patients continue to meet the listing criteria. Patients may not be offered a LT if they have improved or become too sick to benefit from a LT (64,66,67). Apart from a poor quality of life and a lowered life expectancy, children are offered LT when there is a likelihood of neurological impairment, irreversible end-organ damage or growth failure due to the liver disease (68,69).

Broad indications for LT

Indications for LT may be broadly classified into conditions which result in chronic liver disease and those which lead to acute liver failure. Indications for re-transplantation would include causes which lead to early or late graft failure like hepatic artery thrombosis, chronic rejection or recurrence of primary disease (*Table 2*). Indications for LDLT have conventionally been derived from DDLT dominant systems in the west. Most of these allocation systems use an objective score like model for end-stage liver disease (MELD) to ensure that the sickest get transplanted first. There may however be certain "exceptions" where a higher score is awarded to those who would otherwise not qualify for an earlier transplant, this is done to give additional weightage to their pathology (67,70-72).

Due to the intrinsic differences in the type of donation in LDLT, the ethical question of "double equipoise" should at all times be maintained before hastily expanding the indications for LDLT beyond the realm of DDLT. It is important to realise that many with cirrhosis, irrespective of the etiology may never develop hepatic decompensation. Despite the fact that these patients have a lower life expectancy as compared to the general population, the mere presence of cirrhosis does not inevitably qualify them for a LT. Complications of end stage liver disease (ESLD) include variceal bleed, spontaneous bacterial peritonitis (SBP), renal dysfunction, refractory ascites, hepatic encephalopathy, fluid overload, and hepatopulmonary syndrome (HPS) amongst others. It the presence of these complications which drastically reduce survival and justify need for a LT.

LT dramatically improves survival in ESLD patients with complications. Several series have shown a 26% 5-year survival in HPS patients who did not undergo a LT, as compared to 76% for those with an equivalent severity of hypoxemia who did (64,70,72,73). Renal dysfunction remains an important predictor of prognosis in cirrhotics and there is up to 7-fold increase in the risk of mortality in these subset of patients. Cirrhotics who develop SBP have a one-year survival of 40%, thereby making even a single episode of SBP an indication for transplantation (64,66,72-74). Apart from subjective symptoms like intractable pruritus, cholestatic pathologies (e.g., primary biliary cirrhosis) have objective scoring systems to help guide the need for a LT.

There are no separate LDLT listing criteria for ALF patients and those used for DDLT ALF-listing are usually extrapolated for this purpose. Validated criteria like the King's College Criteria, ALFED criteria and the Clichy criteria are commonly used (75,76). Apart from these, criteria specific to certain countries (USA-UNOS-status 1, UK-allocation policy etc.) exist in listing these fragile patients for a LT. ALF listing criteria for children is more varied, and are usually offered LT when under 2 years of ago with INR >4 or have grade 3–4 hepatic encephalopathy (69).

Contraindications

It is imperative that an objective and impartial decision

Table 2 Indications & contraindications for liver transplantation

Indications for liver transplantation
Acute liver failure
Chronic liver disease
Child Pugh C
MELD >15
Hepatorenal syndrome
Spontaneous bacterial peritonitis
Variceal bleed
Hepatopulmonary syndrome
Hepatic encephalopathy
Diuretic resistant ascites
Hepatocellular carcinoma
Early graft failure
Primary non-function
Hepatic artery thrombosis
Late graft failure
Chronic rejection
Biliary cirrhosis
Recurrent disease
Contraindications for liver transplantation
Absolute
Compensated cirrhosis, CTP <7
Severe Pulm-HT (MPAP >50 mmHg)
Recent myocardial infarction
FiO2 ≥50%—ventilator dependence
PEEP >10 mmHg—ARDS
Angiosarcoma
Active substance abuse
Uncontrolled extrahepatic infection
Brain death
Relative
Treated extrahepatic malignancy
Cholangiocarcinoma
Technical/operative challenge
Age >75 years
Mod Pulm-HT (MPAP 35–50 mmHg)
No psychosocial support
Psychiatric illness

MELD, model for end-stage liver disease; ARDS, acute respiratory distress syndrome; Pulm-HT, pulmonary hypertension; PEEP, peak end expiratory pressure.

is taken not to offer livers to those who are unlikely to benefit from a LT. The decision to not transplant is a very difficult one, which the transplant Physician must make. It affects not only the patient, but also their family in a life changing manner. Hence, criteria for delisting patients and contraindications for LT are as important as the indications. Depending on local expertise and level of comfort, they tend to be dynamic and may vary between centres.

Over the years, certain general principles which define the contraindications for LT have remained constant (19,65-67,70). These include patients who are physiologically poor and are unlikely to tolerate the operation (advanced pulmonary or cardiac disease), presence of active sepsis and likely poor quality of life after LT. LT should also not be offered to those who have a metastatic disease, whereby the survival after LT may not justify the risk of the surgery. Another absolute contraindication for LT is when the recipient exercises his autonomy to refuse the operation. The surgical team may sometimes deem the surgery technically unfeasible (e.g., extensive venous thromboses); these contraindications however, depend on the expertise of the team and may vary between centres.

Currently, the objective criteria which are considered absolute contraindications for LT include recent myocardial infarction, severe pulmonary hypertension [mean pulmonary artery pressure (MPAP) >50 mmHg], ventilator dependence and ARDS amongst others. With emerging data in this relatively nascent medical field, the dynamic list of contraindications is likely to shrink rapidly. The changing list of relative contraindications reflect this trend, a few of which include elderly age, HIV, previously treated extrahepatic malignancy, and moderate Pulmonary hypertension (19,65-67,70,77,78) (*Table 2*).

Conclusions

Survival after LT has progressively improved. This has led to an expansion in the indications for LT, reflecting advances in our understanding and ability to treat various disease processes. The ultimate goals of LDLT are to achieve very low morbidity and near-zero mortality to the live donor while providing a survival benefit to those who need it most. An "ideal LT survivor" is one with a stable first allograft function, normal growth, and absence of immunosuppression related complications, a goal which every clinician works towards. The first step in achieving this not-so-utopian goal is through an algorithmic protocol-based multidisciplinary approach to donor and recipient selection.

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Footnote

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