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Journal of Hepatology 43 (2005) 13–37

Journal of Hepatology

www.elsevier.com/locate/jhep

Forum on Liver Transplantation

Special Section Editor and Associate Editor: Pierre-Alain Clavien

Adult living donor liver transplantation: Who is the ideal donor and recipient?

Henkie P. Tan, Kusum Patel-Tom, Amadeo Marcos*

Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, Montefiore University Hospital, Pittsburgh, PA 15213 , USA

Efforts to increase the number of deceased donors (DD) for liver transplantation have been unsuccessful to meet the demands for end stage liver disease (ESLD). Living donors represent a large pool of organs and seem to be the only immediately available alternative. However, there is a significant cost to drawing from this pool, and it is not measured monetarily but rather in lives and morbidities. Living donor surgery is the only major surgery performed on an individual for whom it is not medically indicated. The risk for the donor is balanced by the great benefit to the recipient, as well as the donor's psychological benefit. However, every effort must be taken to minimize morbidities, making this procedure the most challenging in the field of surgery.

Selection of the ideal donor for adult living donor liver transplantation (LDLT) is guided by two key principals: (1) donor safety with unavoidable minimal but never acceptable morbidity and no mortality, and (2) identifying the optimal partial liver allograft with resultant graft and recipient survival at least equivalent to that of DD liver transplantation. Because of these reasons, frequently not more than one-third of potential donors are accepted as candidates for this procedure [1,2]. The evaluation of a potential donor is a complex and expensive process costing about $5500/donor [2]. The costs of evaluation of potential donors who are rejected during the selection process are not covered by the donors' or recipients' insurance.

1. Donor selection and evaluation

Several guidelines for donor selection and evaluation have been published: (1) authors for the live organ donor consensus group have published practice guidelines about the well-being of the live organ donor [3], (2) the American Society of Transplant Surgeons (ASTS) has published a position paper on LDLT [4], and (3) a summary of the conference at the National Institute of Health on LDLT is available [5]. The published donor evaluation protocols are all very similar. The protocol performed at the University of Pittsburgh Medical Center Thomas E. Starzl Transplantation Institute (UPMC STI) is listed in Table 1 (modification of [6]). In brief, most potential donors are excluded based on the initial studies to rule out underlying conditions that represent increased surgical risk, such as diabetes, severe or uncontrolled hypertension, and hepatic, cardiac, pulmonary, renal, and occult infectious disease. Immediate exclusion criteria include donors who are currently pregnant, less than 18-year-old or older than 55-years old with co-morbidities. Selection criteria are rigid to ensure donor safety with no exception to accommodate the needs of the recipients.

Donors with positive hepatitis B and C, and human immunodeficiency virus (HIV) serologies are absolute contraindications for living donations even to positive hepatitis and HIV recipients, with the exception of donor positive hepatitis B core antibody in the presence of a negative hepatitis B surface antigen for hepatitis B positive recipients. These donors, in addition, should have a non-detectable hepatitis B quantitative polymerase chain reaction, have normal liver enzymes and histology.

* Corresponding author. Tel.: +1 412 692 4553.
E-mail address: marcosa@upmc.edu (A. Marcos).

Abbreviations: DD, deceased donor; ESLD, end stage liver disease; LDLT, living donor liver transplantation; ASTS, American Society of Transplant Surgeons; UPMC STI, University of Pittsburgh Medical Center Thomas E. Starzl Transplantation Institute; HIV, human immunodeficiency virus; GRBW, graft to recipient body weight ratio; BMI, body mass index; UNOS, United Network for Organ Sharing; MELD, model for endstage liver disease; HCC, hepatocellular carcinoma; HCV, hepatitis C viral infection.

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doi:10.1016/j.jhep.2005.05.002

Table 1
Evaluation protocol for potential adult living liver donors (UPMC STI)

Step 1
Clinical evaluation: history and physical. First informed consent
Laboratory: ABO, hematology, chemistry (including liver function tests) and coagulation profiles, drug screen, hypercoagulable workup (Factor V Leiden, prothrombin mutation G20210A, antithrombin III and protein C&S deficiencies), factors V, VII, VIII, antiphospholipid or cardiolipin antibodies, ceruloplasmin, α-1-antitrypsin
Serology: hepatitis A, B, and C; HIV PCR
Imaging studies: chest X-ray, EKG
Step 2
Multidisciplinary team clinical evaluation: hepatology, psychology, etc, consults
Laboratory: HLA, cross-match, tumor markers (AFP, CEA), UA C&S, pregnancy test (female)
Serology: CMV, HSV, EBV, RPR
Imaging studies: helical CT-angiogram with portal phase and 3D reconstruction with liver volumetric
Special studies when indicated: echocardiogram, cardiac stress test, pulmonary function test, glucose tolerance test, colonoscopy, mammography
Histology: liver biopsy
Step 3
Clinical evaluations: update history and physical. Second informed consent
Anesthesiology consults
Laboratory: cross-match, and blood consent
Final approval at the multidisciplinary transplantation conference prior to surgery

Hypercoagulable states (Factor V Leiden [7], prothrombin mutation G20210A, antithrombin III and protein C&S deficiencies, Factor VIII elevation, antiphospholipid or cardiolipin antibodies) are relative contraindications for donation for fear of increase donor mortality from pulmonary emboli. Smokers are strongly encouraged to quit and oral contraceptive cessation is encouraged 4 weeks prior to surgery.

Donors should never be compelled to donate. The psychological or psychiatric evaluation focuses on the emotional stability of the potential donor and is used to verify and reaffirm the informed consent. Donors should be permitted to change their mind up until the induction of general anesthesia, and they should be given every opportunity to withdraw at any time if they have any reservations. Psychological counseling can be very helpful, and multiple consents encourage donors to reconsider their decision [8].

A spiral or helical CT-angiogram with portal phase and 3D reconstruction liver volumetric is used in our center to determine the donor's vascular anatomy and accurate measurement of the graft and liver volume. An ideal graft to recipient body weight ratio (GRBW) of 0.8 corrected for the degree of steatosis is a safe lower limit for adult recipients [9] with a maximal 60% resection of the donor liver volume to ensure consistent donor safety. The left hemiliver will almost always be adequate for the donor if the plane of transaction is to the right of the midhepatic vein, with the segments IV representing approximately 40% of graft mass [9,10]. Its devascularization could be catastrophic, and protection of significant portal and arterial tributaries is essential. For this reason the right hemiliver (segments V–VIII) is preferred. We do not routinely perform a magnetic resonance cholangiopancreatography to evaluate the biliary ducts pre-operatively but an intra-operative cholangiogram is performed routinely. Biliary complications in both donors and recipients are potentially highly morbid, and their prevention is a priority (see article by S Todo, H Furukawa and T Kaminiyama in this Forum). Optimal management requires knowledge of both primary and secondary biliary drainage. Recently, Schroeder et al. [11] have concluded in a preliminary study that the three-phase dual-enhancement multi-detector row CT, which includes CT cholangiography and CT angiography, has the potential to replace the combinations of various partially invasive diagnostic procedures.

We have always made mandatory the performance of a liver biopsy pre-operatively. We previously demonstrated in 100 consecutive hepatic biopsies in the workup of living donors for right lobe liver transplantation, body mass index (BMI) correlated only weakly with biopsy, with 73% of overweight (BMI >25) donors having little or no hepatic fat [12]. Imaging was only 12% sensitive to small amounts (5–10%) of fat. Moreover, three candidates were denied surgery because biopsy detected an occult liver disease. Screening liver biopsy has a low complication rate and may actually serve to increase donor safety. This issue is exemplified in the recent first living-related liver donor death in Japan [13]. The healthy donor had undiagnosed nonalcoholic steatohepatitis. A liver biopsy is also mandatory in the Essen group after the loss of a donor due to congenital lipodystrophy [2]. Eight to 22% of potential donors evaluated were rejected because of abnormal liver biopsy [2,14,15]. We consider $>20\%$ steatosis a relative contraindication for donation and highly recommend a diet to decrease this, and we proceed with repeat liver biopsy to confirm decrease steatosis.

Emergency LDLT for fulminant hepatic failure should be perform only on a case by case basis as the donor is placed in a very compromised medical and emotional/psychological position with ethical, medical, logistic and economic concerns [16].

Poor outcomes that cannot be blamed on underlying medical conditions can often be traced to intra-operative events, suggesting that most of the risk to healthy donors can be controlled and minimized. Even with refinement of surgical technique, risk will never be eliminated completely and an ethical dilemma will, therefore, always remain. This risk must be offset by beneficence to the recipient, and the continued use of these organs can only be justified if the outcome is consistently good for both the healthy donor and sick recipient.

Using continuous intra-operative cell-saver, maintenance of low central venous pressure, and meticulous parenchymal

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