

Extra-hepatic Medical Risk Stratification of the Potential Live Liver Donor

Authors: Jawad Ahmad, MD and Whitney E. Jackson, MD

Editor: AnnMarie Liapakis, MD

ISSUE

What is the medical evaluation of the potential live liver donor?

DATA

All potential live liver donors need to undergo extensive evaluation by an independent live donor advocacy team to ensure they are suitable as a donor with medical, surgical and psycho-social assessment. The psycho-social assessment is a critical part of the evaluation of the potential live donor and is described in detail in a separate Living Liver Donor Toolkit chapter. In those patients where the hepatic and vascular anatomy are acceptable and there are no psycho-social concerns, the most important part of the evaluation is optimizing donor safety by appropriate medical risk stratification. There are consensus guidelines from various societies and countries on the appropriate testing that is required.(1-3) The United Network for Organ Sharing (UNOS) in the U.S. has the OPTN Policy 14.4 (4), but most institutions have developed their own protocols. Several anesthesia and national healthcare agencies do not recommend any routine preoperative testing in an otherwise healthy adult undergoing surgery.(5) However, the live donor operation is unique in that it is an elective major surgery with no physical benefits. It is accepted that the risks to the donor are justified if that risk can be minimized in a setting of an acceptable outcome of the recipient (Vancouver forum) (1). Donor safety is of paramount importance so pre-operative testing is required to exclude medical conditions that may increase the risk of surgery and post-operative complications. These can be classified into: 1) history and physical examination; 2) laboratory testing; 3) cardio-respiratory risk stratification; 4) confirmation of age appropriate cancer screening; and 5) other testing based on findings during the routine assessment.

History and Physical

During the routine history and physical examination, the potential live donor should be evaluated for underlying conditions that may increase the risk of surgery. Although

programs vary, the typical age range for donors is 21-55 years, with some programs expanding the lower limit to 18 years and the upper limit to 60 years. Donors over age 60 years who are medically suitable may be considered on a case-by-case basis. Studies suggest live liver donors over age 50 years can be safely used (6) although there is an increased risk of graft loss in recipients with hepatitis C (in the pre-direct acting antiviral drug era).(7) During the history it is important to ask about any issues with bleeding or clotting tendency; smoking, alcohol, recreational drug use, high risk sexual behavior; and drug allergies or prior reactions to anesthesia.(8) Donors who smoke, drink or use recreational drugs would typically be expected to stop for a period of time before donation (typically at least a month). Donors with evidence of overuse or abuse of alcohol or recreational drugs should be screened for addiction. Depending on the recipient, a history of autoimmune disease should be noted. Diabetes is usually a contra-indication to donation. Evidence of decreased exercise tolerance or obstructive sleep apnea should be noted. Body mass index is a component of assessing metabolic risks and hepatic steatosis. Upper limit cutoffs are program dependent.(9, 10)

Laboratory testing

The potential donor should undergo routine laboratory studies including complete blood count, chemistry panel and serological testing for viral hepatitis, HIV, autoimmune and metabolic liver diseases. Significant abnormalities that would typically exclude donation include elevated liver function tests or evidence of renal dysfunction. Compatible ABO blood type is critical but in exceptional cases ABO incompatible blood type liver donation may be considered such as in children under age 1 year without the presence of isoagglutinins and in acute liver failure where deceased donor allograft is not available.(1) Iron deficiency anemia is not an absolute contra-indication if there is an obvious explanation such as menorrhagia and can be corrected with oral iron replacement. Laboratory testing for other infections that can influence the immunosuppressed recipient typically include CMV, EBV, and HSV. UNOS requires a written protocol for testing for endemic infections depending on donor exposures, ethnicity and region of the country such as Tuberculosis, Histoplasmosis and Strongyloides.(4) Urine toxicology screen is required to look for evidence of recreational drug use. Programs vary on permitting marijuana use but evidence of cocaine, heroin or other opioid drugs are a contra-indication. Coagulation profile should include PT/PTT and INR with other screening tests for a clotting/bleeding risk varying depending on program. Abnormalities detected on these tests may prompt further evaluation with hematology and ongoing risk stratification assessment.

Cardio-respiratory testing

Cardio-respiratory risk stratification is an essential component of the pre-operative medical evaluation. The donor surgery is classified as an elective major surgery with no direct physical benefit (based on AHA/ACC classification) and hence it is generally accepted that risk tolerance is low. All patients undergo electrocardiogram to screen for cardiac abnormalities. Based on age, risk stratification, and program preference, potential donors may undergo trans-thoracic echocardiogram and ischemic cardiac evaluation.(11) Evidence of cardiac ischemia, rhythm abnormalities or pulmonary hypertension are contra-indications for donation. Valvular abnormalities need to be

reviewed in relation to the risk of peri-operative or post-operative complications such as atrial fibrillation, clot formation or endocarditis. Similarly, a chest radiograph is performed and significant lung findings need additional review and discussion in terms of peri-operative or post-operative complications. Patients with obstructive sleep apnea (OSA) are at increased risk of peri-operative complications and any donors with suspected OSA should prompt additional discussion of risk stratification with a pulmonologist or anesthesiologist. Patients with any evidence of problems with gas exchange should be excluded from donation.(12)

Age Appropriate Cancer Screening

Age appropriate cancer screening in potential donors that complies with protocols developed by the American Cancer Society or the US Preventive Services Task Force is required by UNOS (OPTN Policy 14).(4) This includes cervical cancer screening with a PAP smear in women over 21 years within the last 3 years, a mammogram in women

Other testing

The need for further testing of the potential live liver donor will depend on the findings during the routine assessment and should be discussed in a multi-disciplinary setting with hepatologists, surgeons and radiologists. Reviewing data from the A2ALL study in the US of more than 1000 potential live liver donors, of the 60% of potential donors who were not accepted, almost a third were due to medical contra-indications.(14) In general, minor laboratory abnormalities found during routine evaluation should be rechecked and incidental findings on abdominal imaging such as pancreatic cysts, renal lesions, and vascular anomalies need to be reviewed by the appropriate specialist. Positive infectious disease serology should be discussed with a transplant infectious disease specialist and does not necessarily preclude donation if easily treated.

RECOMMENDATIONS

1. The potential live liver donor should undergo a thorough pre-operative evaluation including history, physical, laboratory testing, cardio-respiratory evaluation and age appropriate cancer screening.
2. The results of the evaluation should be reviewed in a multi-disciplinary setting.
3. Centers should develop their own individual protocol in conjunction with UNOS guidelines (OPTN Policy 14.4) (4), with the goal to identify medical conditions that would increase donor risk.

REFERENCES

1. M.L. Barr, J. Belghiti, F.G. Villamil, et al. A report of the Vancouver Forum on the care of the live organ donor: lung, liver, pancreas, and intestine data and medical guidelines. *Transplantation* 2006;81:1373-85.
2. C.M. Miller, F. Durand, J.K. Heimbach, et al. The International Liver Transplant Society Guideline on Living Liver Donation. *Transplantation* 2016;100:1238-43.
3. D. Manas, L. Burnapp, P.A. Andrews. Summary of the British Transplantation Society UK Guidelines for Living Donor Liver Transplantation. *Transplantation* 2016;100:1184-90.
4. https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf.
5. <https://www.uptodate.com/contents/preoperative-medical-evaluation-of-the-healthy-adult-patient>. Accessed October 18, 2019.
6. Goldaracena N, Sapisochin G, Spetzler V, et al. Live Donor Liver Transplantation With Older (≥ 50 Years) Versus Younger (< 50 Years) Donors: Does Age Matter? *Ann Surg* 2016;263:979-85.
7. Goldaracena N, Barbas AS, Galante A, et al. Live donor liver transplantation with older donors: Increased long-term graft loss due to HCV recurrence. *Clin Transplant* 2018;32:e13304. doi: 10.1111/ctr.13304. Epub 2018 Jul 16.
8. Brown RS. Live donors in liver transplantation. *Gastroenterology* 2008;134:1802-13.
9. J. Moss, D. Lapointe-Rudow, J.F. Renz, et al. Select utilization of obese donors in living donor liver transplantation: implications for the donor pool. *Am J Transplant* 2005;5:2974-2981.
10. Knaak M, Goldaracena N, Doyle A, et al. Donor BMI > 30 Is Not a Contraindication for Live Liver Donation. *Am J Transplant* 2017;17:754-760.
11. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol* 2014;64(22):e77.
12. American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. Practice guidelines for the perioperative management of patients with obstructive sleep apnea: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Management of patients with obstructive sleep apnea. *Anesthesiology* 2014;120:268-86.
13. <https://www.uspreventiveservicestaskforce.org/Page/Name/uspstf-a-and-b-recommendations/>. Accessed October 18, 2019.
14. Trotter JF, Wisniewski KA, Terrault NA, et al. Outcomes of donor evaluation in adult-to-adult living donor liver transplantation. *Hepatology* 2007;46:1476-84.