

Medical Evaluation, Informed Consent, and Follow-up of the Living Liver Donor – a Consensus Document from the AST/ASTS/NATCO/UNOS Joint Societies Work Group

In August 2012, the Joint Society Steering Committee formed a Joint Societies Work Group (JSWG) to provide recommendations for Living Donor Liver policy development. The individuals appointed to represent the societies and the OPTN Living Donor Committee were:

1. AST: Susan L. Orloff MD, Dilip K. Moonka, MD, James R. Rodrigue, PhD
2. ASTS: Talia B. Baker, MD, Chris E. Freise, MD, Elizabeth A. Pomfret, MD, PhD
3. NATCO: Dianne LaPointe Rudow, ANP-BC, DNP, CCTC Patricia M. McDonough, RN, CCTC, CPTC
4. OPTN/UNOS: Christie Thomas MB, FRCP, FASN, FAHA, Carlos Marroquin, MD, Donald Olenick, Esq.

The charge to the JSWG was to provide recommendations to OPTN/UNOS regarding:

- Appropriate requirements for the medical evaluation (including psycho-social evaluation) ;
- Informed consent of potential living liver donors; and
- Post-donation follow-up and data submission.

The JSWG carried out a series of bimonthly and weekly teleconferences over the late summer and fall of 2012. During its initial call, the working group elected Elizabeth Pomfret, MD, PhD, as its chair. The working group also determined that additional expertise was needed in the areas of hepatology, clinical coordinator/nursing, and psychosocial aspects of living liver donation. The following individuals were added to the working group to provide this additional expertise:

- Hepatology : James Trotter, MD and Richard Stravitz, MD
- Clinical Coordinator/Nursing: Lori Clark, RN
- Psychosocial: Mary Amanda Dew, PhD and Cheryl Jacobs, ACSW

HRSA representatives were also invited to participate on each conference call.

In order to accomplish the charge of the JWSG, three subcommittees were formed, each with representation of ASTS, AST, NATCO, UNOS, and with at least one person from each discipline (surgery/medicine/clinical/psychosocial) on each. The three subcommittees developed recommendations for (1) medical evaluation; (2) informed consent and (3) follow-up. Drafts of each set of recommendations were shared with the full working group during bi-weekly calls.

The JSWG believes that living liver donor transplantation is an essential part of liver transplant practice, and that this activity can go forward only if potential donors have full faith and confidence that their transplant professionals and transplant centers are looking out for their best interests and well being. To provide this degree of confidence the JSWG believes these guidelines represent the best available information for transplant centers to help potential donors make the decision to donate in an informed fashion, and to maximize donor safety.

Informed Consent of Living Liver Donors

Introduction:

Education is important to enable the potential donor to understand all aspects of the donation process, especially the risks and benefits.

The goal of informed consent is to ensure that a potential donor understands:

- 1) That he or she will undertake risk and will receive no medical benefit from the donor hepatectomy.
- 2) That there are both general risks of the operation as well as center-specific risks.

This consensus document contains recommendations from the Joint Societies Working Group for Live Donor Liver Policies for informed consent of living liver donors. The Working Group recommends that these be incorporated into OPTN policy; these requirements would be monitored and enforced by UNOS. Guidance for discussing potential complications with a donor candidate is contained in Appendix A and is not expected to be part of OPTN policy.

Living Liver Donor Consent

The recovery hospital must obtain informed consent from any potential living liver donor which must include, but is not limited to, documentation in the donor chart of the following:

- a. Written assurance by the potential donor that he or she is willing to donate, free from inducement and coercion, and has been informed that he or she may decline to donate at any time. Potential donors must be offered an opportunity to discontinue the donor consent or evaluation process and to do so in a way that is protected and confidential. The independent donor advocate (IDA) must be available to assist the potential donor during this process. (Policy 12.4)
- b. Instruction about all phases of the living donation process, which include consent, medical and psychosocial evaluations, pre and post operative care, and required post operative follow-up. (Policy 7.3.2) Teaching or instructional material can include any media (e.g., written, video, audio) or one-on-one or small group interaction. Teaching or instruction must be provided in a language in which the donor is able to engage in a meaningful dialogue with the transplant program staff.
- c. Disclosure that the recovery hospital will take all reasonable precautions to provide confidentiality for the donor and recipient.
- d. Disclosure that it is a federal crime for any person to knowingly acquire, obtain or otherwise transfer any human organ for valuable consideration (i.e., for anything of value such as cash, property, vacations).
- e. Disclosure that the recovery hospitals must provide an Independent Donor Advocate (IDA).

f. Data about the center’s overall transplant volume and living donor transplant volumes and outcomes:

If the recovery hospital and the recipient hospital...	Then...	Including <i>all</i> the following information....
Are the same	<p>The recovery hospital must provide the potential donor with:</p> <ul style="list-style-type: none"> • The total volume of living donor liver transplants performed by that hospital; and • both the national and that hospital’s program-specific transplant recipient outcomes from the most recent SRTR center-specific reports. 	<ol style="list-style-type: none"> 1. National 1-year patient and graft survival 2. The hospital’s 1-year patient and graft survival 3. Notification about all CMS outcome requirements not being met by the transplant hospital
Will not be the same	<p>The recovery hospital must provide the potential donor with:</p> <ul style="list-style-type: none"> • The total volume of living donor liver transplants performed by the recipient hospital; and • both the national and the recipient hospital’s program-specific transplant recipient outcomes from the most recent SRTR center-specific reports. 	<ol style="list-style-type: none"> 1. National 1-year patient and graft survival 2. The recipient hospital’s 1-year patient and graft survival 3. Notification about all CMS outcome requirements not being met by the recipient hospital

g. Education about expected post-donation liver function and how this might potentially impact the donor in the future to include:

- 1) Donor risks must be interpreted in light of the known epidemiology of chronic liver disease. The medical evaluation of a young potential donor cannot predict lifetime risk of liver disease.
- 2) Removal of a portion of the liver may cause symptoms of a small liver until the remaining liver grows back, which can take several weeks. These symptoms can include jaundice (yellow skin and eyes with dark urine), fatigue, easy bruisability and/or bleeding, poor appetite, and swelling in the abdomen and legs.

- 3) Should a liver donor develop liver failure as a result of partial liver donation, or any type of ESLD in the future, he or she would receive priority for a transplanted liver solely as a function of the severity of the donor's liver dysfunction and failure, as is the current allocation practice (Policy 3.6). There is no priority given on the liver transplant list because of prior living liver donation, however, if the donor later requires a kidney transplant, the current practice is to prioritize prior living liver donors who become kidney transplant candidates. (Policy 12.9.3)
- h. Disclosure of alternate procedures or courses of treatment for the recipient including deceased donor transplantation.
 1. The donor must be informed that a deceased donor liver might become available for the recipient before the donor evaluation is completed or the living donor transplant occurs.
 2. Potential donors should be provided a realistic estimate of the likelihood of successful transplantation for the recipient. If there are factors that increase the risk of morbidity or mortality in the recipient these must be discussed openly with the donor, but only if the potential recipient has agreed to share this information.
 - i. The disclosure that the donor will receive a thorough medical and psychosocial evaluation.
 - j. Inform the donor that health information obtained during their evaluation will be subject to the same regulations as all records and could reveal conditions that the transplant center must report to local, state or federal public health authorities.
 - k. Inform the donor of the potential for other medical complications, including long- term complications currently unforeseen. Potential donors must be informed of the need for lifetime yearly primary care follow up for health maintenance and risk reduction.
 - l. Disclosure that recovery hospitals are required to report living donor follow-up information at the time intervals specified in Policy 12.8.3, and have the potential donor commit to post-operative follow-up testing coordinated by the living donor recovery hospital.

Living Liver Donor Evaluation Consent

The recovery center must maintain documentation in the donor chart that it informed the potential donor of the following:

- a. That the potential donor must undergo a medical and psychosocial evaluation as required in Policy 12.3.
- b. That the transplant hospital may refuse the potential donor. In such cases, potential donors must be informed that they could be evaluated by another transplant program that may have different selection criteria.
- c. That the following are inherent risks associated with evaluation for living donation:
 1. allergic reactions to contrast,
 2. discovery of reportable infections,
 3. discovery of serious medical conditions,

4. discovery of adverse genetic findings unknown to the donor, and
 5. discovery of certain abnormalities that will require more testing at the donor's expense or create the need for unexpected decisions on the part of the transplant team.
- d. That the following surgical, medical, psychosocial, and financial risks are associated with living liver donation. This disclosure must state that these risks may be transient or permanent and include, but are not limited to the following:
1. Potential Medical or Surgical Risks (Appendix A):
 - a. The risk of death in the acute setting after donation is between 1-5 in 1,000 transplants and is likely relative to the amount of liver tissue removed.
 - i. An interrupted donor procedure may occur if after opening the donor's abdomen, the surgical team believes that it is too risky to proceed with the donor surgery. This happens infrequently but may be related to one of the following situations:
 1. Unexpected findings may be encountered after opening the donor's abdomen which could cause undue risk to the donor
 2. The recipient may become unable to receive a transplant and therefore the donor hepatectomy may be aborted. This may occur at any point during the surgical procedure and may occur after the donor's bile duct has been divided or even after the graft has been removed ("orphan graft")
 3. In the event of a divided bile duct the donor may require reconstructive hepatobiliary surgery
 4. The donor should be informed preoperatively that, in the event of graft removal ("orphan graft"), the graft could potentially be offered to another unspecified recipient if the donor consents.
 - b. Hernia, wound infection, scars, blood clots, pneumonia, nerve injury, pain, fatigue, and other consequences typical of any surgical procedure.
 - c. Transient liver dysfunction with recovery. The potential for transient liver dysfunction depends upon the amount of the total liver removed for donation.
 - d. Acute liver failure with need for liver transplant.
 - e. Biliary complications including leak or stricture that may require additional intervention.
 - f. Risk of red cell transfusions or other blood products.
 - g. Abdominal or bowel symptoms such as bloating, nausea, and development of bowel obstruction.
 - h. Impact of obesity, hypertension, or other donor-specific medical condition on morbidity and mortality of the potential donor.
 - i. Inform the donor of the potential for other medical complications, including long-term complications currently unforeseen. Potential donors must be informed of the need for lifetime yearly primary care follow up for health maintenance and risk reduction.
 - j. Inform the donor that the required post-donation laboratory tests may result in abnormal or false positive results that may trigger additional tests that have associated risks as well. These potential risks must be balanced against the benefits of follow-up testing.

2. Potential Psychosocial Risks:
 - a. Problems with body image.
 - b. Post-surgery depression and, anxiety (including but not limited to symptoms of post-traumatic stress disorder, anxiety related to dependence on others, and feelings of guilt).
 - c. Feelings of emotional distress or bereavement if the transplant recipient experiences any recurrent disease or in the event of the transplant recipient's death.
 - d. Impact of donation on the donor's lifestyle.

3. Potential Financial Impacts:
 - a. Personal expenses of travel, housing, child care costs, and lost wages related to donation might not be reimbursed; however, resources might be available to defray some donation-related costs.
 - b. Need for life-long primary care follow-up at the donor's expense.
 - c. Loss of employment or income.
 - d. Negative impact on the ability to obtain future employment.
 - e. Negative impact on the ability to obtain, maintain, or afford health, disability, and life insurance.
 - f. Future health problems experienced by living donors following donation may not be covered by the recipient's insurance.

Pre-Donation Evaluation of Living Liver Donors

While it must be recognized that each potential donor is unique, and no single evaluation protocol is applicable to all living donors, the potential living donor should be informed about all phases of the transplant center's evaluation protocol. The donor evaluation includes psychosocial and medical components. These evaluations should help determine if an individual is a suitable donor. The psychosocial evaluation should determine the presence of psychosocial risks and/or contraindications to donation. The medical evaluation may uncover conditions that could significantly increase the risk of donation to the potential donor. However a normal medical evaluation cannot accurately predict future risk of developing liver disease, especially in a very young donor. The evaluation should also screen for diseases that the donor could transmit to the potential recipient, particularly in the presence of immunosuppression. Lastly, this evaluation should define the anatomy of the potential organ so the surgical team can assess potential risk to the donor, determine the anatomical suitability of the organ and properly plan both the donor and recipient surgery.

This document contains recommendations from the Joint Societies Working Group for Live Donor Liver Policies for the evaluation of living liver donors. It includes items that the Working Group strongly feels should be incorporated into OPTN policy; these requirements would be monitored and enforced by UNOS. There are also recommendations that the Working Group agrees are best practices that every center should strive to adopt, but that should not be enforced as policy. These recommendations should be part of a guidance document or white paper and made available to all living donor liver programs. The items recommended for inclusion in policy are provided in Table 1.

Psychosocial Evaluation

The psychosocial evaluation must be performed by a psychiatrist, psychologist, and/or clinical social worker. Documentation of the psychosocial evaluation must be maintained in the donor record. The psychosocial evaluation must include the following components:

- a. Assess for any psychosocial (including mental health) issues that might complicate the living donor's recovery and identify potential risks for poor psychosocial outcome;
- b. Assess for the presence of high-risk behaviors as defined by the US Public Health Service (PHS) that have the potential to increase the risk of disease transmission to the recipient;
- c. Assess history of smoking, alcohol, and drug use/abuse and dependency;
- d. Identify factors that warrant educational or therapeutic intervention prior to final donation decision;
- e. Determine that the potential donor understands the short and long-term medical and psychosocial risks associated with living donation, for both donor and recipient; determine the donor's ability to access, and receive future follow-up as it pertains to the recommendations made by the donor team.

- f. Assess whether the decision to donate is free of inducement, coercion, and other undue pressure; by exploring the reason(s) for volunteering to donate and the nature of the relationship (if any) to the transplant candidate;
- g. Assess the potential donor's ability to make an informed decision and the ability to cope with the major surgery and related stress. This includes the potential donor having a realistic plan for donation and recovery, with social, emotional and financial support available as recommended; and
- h. Review the occupation, employment status, health insurance status, living arrangements, and family/social support of the potential donor and determine if she/he understands the potential financial implications of living donation.

The Independent Donor Advocate

The living donor recovery hospital must provide an independent donor advocate (IDA) who is not involved with the potential recipient evaluation and is independent of the decision to transplant the potential recipient.

The IDA must assist the potential donor with the evaluation process and focus on their needs and questions. The IDA must be knowledgeable about risks and benefits associated with all phases of the donation process. IDA responsibilities include, but are not limited to the following:

- Promote the best interests of the potential living donor
- Advocate for the rights of the potential donor
- Assist the potential donor in obtaining and understanding information regarding the:
 - 1) Consent process;
 - 2) Evaluation process;
 - 3) Surgical procedure;
 - 4) Medical and psychosocial risks;
 - 5) Benefit and need for follow-up.

Medical Evaluation of the Living Liver Donor

The medical evaluation must be performed by the recovery hospital and by a physician or surgeon experienced in liver living donation. The goal of the medical evaluation is to:

1. Assess the general health and surgical risk of the donor;
2. Determine if there are diseases present that may be transmitted from donor to recipient; and,
3. Assess the anatomy and function of the liver. Anatomical assessment must include assessment of adequate liver remnant volume, and must include venous and arterial anatomy. Preoperative assessment of the biliary anatomy is recommended but not required.

Documentation of the Medical Evaluation must be maintained in the donor record. The Medical Evaluation must include the following components:

A) General History:

1. Evaluate for a personal history of significant medical conditions which include but are not limited to hypertension, diabetes, renal diseases, lung disease, heart disease, gastrointestinal disease, autoimmune disease, neurologic disease, genitourinary disease, hematologic disorders, bleeding or clotting disorders, history of cancer, history of infections and obesity.
2. Evaluate for Liver-Specific Personal History:
 - a. Risk factors for and/or actual history of viral hepatitis
 - b. History of abnormal liver function tests
 - c. Diabetes
 - d. Fatty Liver Disease
 - e. Jaundice
 - f. Bleeding
 - g. Pruritis
3. Evaluate for hypercoagulable state: history of DVT, pulmonary emboli
4. Active and past medications with special consideration for known hepatotoxic medications or chronic use of pain medications
5. Allergies

B) Family history of coronary artery disease, cancer, bleeding and/or clotting disorders

C) Liver-Specific Family History:

1. Liver disease
2. Autoimmune Disease
3. Diabetes
4. Viral Hepatitis

D) Social History:

The medical evaluation must determine:

1. Occupation, employment status, health insurance status, living arrangements, and social support
2. Smoking, alcohol and drug use and/or abuse
3. High risk behavior as defined by the US PHS
4. Psychiatric illness, depression, suicide attempts

E) Physical Exam:

1. Height, weight, BMI, vital signs
2. Examination of all major organ systems
3. Stigmata of liver disease

F) General Laboratory Tests:

1. Complete blood count (CBC)
2. Blood type and screen
3. Partial thromboplastin time (PTT)
4. International Normalized Ratio (INR) or Prothrombin time (PT)
5. Metabolic testing (to include electrolytes, BUN, creatinine, albumin, calcium, phosphorus)
6. Pregnancy test for premenopausal women without surgical sterilization
7. Chest X-Ray
8. Electrocardiogram (ECG)
9. Urinalysis
10. Programs must develop and follow a policy for hypercoagulable state evaluation (see Appendix B)
11. Programs should develop and follow a policy for the evaluation for coronary artery disease consistent with that of the American College of Physicians
12. Programs should develop and follow a policy for pulmonary function tests for smokers consistent with that of the American College of Anesthesiology and American Lung Association

G) Other Metabolic Testing:

1. Fasting blood glucose
2. Fasting lipid profile (cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol)
3. Glycosylated hemoglobin in first degree relatives of diabetics and in high risk individuals such as those with metabolic syndrome

H) Liver-Specific Tests:

1. Hepatic function panel
2. Ceruloplasmin in a donor with family history of Wilson's Disease
3. Iron, iron binding capacity, ferritin
4. Alpha-1-antitrypsin level: those with low alpha-1-antitrypsin levels should have a phenotype.
5. Programs must develop and follow a policy for screening for autoimmune disease (Appendix C)

I) Anatomic Assessment:

A radiological assessment must be performed to determine if the liver is anatomically suitable for transplantation, and to assess safety of resection for the donor. Evaluation must include assessment of projected graft volume, donor's remnant volume, vascular anatomy and presence of steatosis. Pre-operative imaging of the potential donor's biliary anatomy is recommended.

Based on these findings, the surgeon can determine the suitability of the liver, and any additional risks associated with anatomical variants. The radiologic imaging may reveal unexpected findings that will need to be investigated. These findings may be related or unrelated to the organ of interest.

The test of choice will depend upon the local radiological expertise and surgical preference, but may include CT angiogram, MR angiogram or angiogram, used singly or in combination.

A liver biopsy may be warranted if the imaging or other studies suggests significant fatty liver in the potential donor (Appendix D).

J) Liver Biopsy:

If and when to perform a liver biopsy is controversial and practice varies. Transplant centers must develop and then follow a policy for pre-donation liver biopsy (Appendix E). If the liver biopsy reveals histological abnormalities they must be reviewed by a hepatologist. If clinically significant pathological findings exist a donor may be ruled out.

K) Screening for transmissible diseases:

Infectious disease testing must include:

1. CMV (cytomegalovirus) Antibody
2. EBV (Epstein Barr virus) Antibody
3. HIV 1,2 (human immunodeficiency virus) antibody testing
4. HepBsAg (hepatitis B surface antigen)
5. HepBcAb (hepatitis B core antibody) *
6. HepBsAb (hepatitis B surface antibody)
7. HCV (hepatitis C virus) antibody testing
8. RPR (Rapid Plasma Reagin test for syphilis)

*** HBV DNA must be tested if HBcAB is positive**

For tuberculosis (TB), living donor recovery centers must determine if the potential donor is at increased risk for this infection, and if so testing must include:

- Screening for latent TB using either intradermal PPD or interferon gamma release assay (IGRA)

The work group recommends that the DTAC develop evidence-based guidelines for screening for rare infectious diseases only prevalent in certain endemic areas. Until guidelines have been developed for the following infectious diseases, transplant centers should determine if the potential donor is from an endemic area, and if so testing should include:

- Strongyloides
- Trypanosoma cruzi
- West Nile

L) Cancer Screening:

Centers must develop protocols consistent with the American Cancer Society (ACS), and once developed follow their own protocols for screening for:

1. Cervical Cancer
2. Breast Cancer
3. Prostate Cancer
4. Colon Cancer
5. Skin Cancer
6. Lung cancer

M) EXCLUSION CRITERIA

Transplant programs that perform living liver donor recoveries may exclude a donor with any condition that, in the Transplant Program's medical judgment, causes the donor to be unsuitable for organ donation. Transplant programs that perform living liver donor recoveries must exclude all donors who meet any of the following exclusion criteria:

1. Both age less than 18 years and mentally incapable of making an informed decision
2. HIV positive
3. HCV RNA positive
4. HBsAg positive
5. Donors with ZZ, Z-null, null-null and S-null alpha-1-antitrypsin phenotypes and untype-able phenotypes
6. Active malignancy, or incompletely treated malignancy
7. High suspicion of donor coercion
8. High suspicion of illegal financial exchange between donor and recipient
9. Evidence of acute symptomatic infection (until resolved)
10. Uncontrolled diagnosable psychiatric conditions requiring treatment before donation, including any evidence of current suicidality
11. Untreated and active substance abuse
12. Donor remnant volume less than 30% of native liver volume

N) Relative Contraindications

The impact of the co-morbidities below on the donor's future health is dependent upon age of onset, gender, access to healthcare, ethnicity, and family history as well as other criteria. An aggregate of relative contraindications in a given individual may also preclude donation.

1. Diabetes or impaired fasting glucose with other features of the metabolic syndrome (low HDL and high triglycerides)
2. Unexplained liver function test (LFT) abnormalities
3. Vascular or biliary anatomy in the donor liver that makes the likelihood of successful transplantation low or increases the risk in the potential donor
4. Multiple or complex upper abdominal surgeries
5. Significant hepatic steatosis
6. Chronic kidney disease
7. Significant history of thrombosis or embolism
8. Bleeding disorders
9. BMI > 35 Kg/m²
10. Age > 60 years
11. Clinically significant cardiovascular disease
12. Clinically significant pulmonary disease
13. History of cancer.
14. Prior history of substance abuse
15. Lack of or insufficient family, caregiver, social, and/or economic support
16. Strained donor/recipient relationship
17. Absence of health insurance
18. Active smoker
19. Active oral contraception

Table 1. Live Liver Donor Policy Recommendations

Psychosocial Evaluation of the Living Liver Donor
The psychosocial evaluation must be performed by a psychiatrist, psychologist, and/or clinical social worker.
Documentation of the psychosocial evaluation must be maintained in the donor record
The psychosocial evaluation must include the following components: <ol style="list-style-type: none">1. Assess for any psychosocial issues that might complicate the living donor’s recovery and identify potential risks for poor psychosocial outcome;2. Assess for the presence of high-risk behaviors as defined by the US Public Health Service (PHS) that have the potential to increase the risk of disease transmission to the recipient;3. Assess history of smoking, alcohol, and drug use/abuse and dependency;4. Identify factors that warrant educational or therapeutic intervention prior to final donation decision;5. Determine that the potential donor understands the short and long-term medical and psychosocial risks associated with living donation, for both donor and recipient; determine the donor’s ability to access, and receive future follow-up as it pertains to the recommendations made by the donor team.6. Assess whether the decision to donate is free of inducement, coercion, and other undue pressure; by exploring the reason(s) for volunteering to donate and the nature of the relationship (if any) to the transplant candidate;7. Assess the potential donor’s ability to make an informed decision and the ability to cope with the major surgery and related stress. This includes the potential donor having a realistic plan for donation and recovery, with social, emotional and financial support available as recommended;8. Review the occupation, employment status, health insurance status, living arrangements, and family/social support of the potential donor and determine if she/he understands the potential financial implications of living donation.
Independent Donor Advocate
The living donor recovery hospital must provide an independent donor advocate (IDA) who is not involved with the potential recipient evaluation and is independent of the decision to transplant the potential recipient.
The IDA must be knowledgeable about risks and benefits associated with all phases of the donation process.
IDA responsibilities include: <ol style="list-style-type: none">1. Promote the best interests of the potential living donor2. Advocate for the rights of the potential donor3. Assist the potential donor in obtaining and understanding information regarding the:<ul style="list-style-type: none">▪ Consent process;▪ Evaluation process;▪ Surgical procedure;▪ Medical and psychosocial risks;▪ Benefit and need for follow-up.

Medical Evaluation of the Living Liver Donor

The medical evaluation must be performed by the recovery hospital and by a physician or surgeon experienced in liver living donation.

The goal of the medical evaluation is to:

1. Assess the general health and surgical risk of the donor.
2. Determine if there are diseases present that may be transmitted from donor to recipient; and
3. Assess the anatomy and function of the liver. Anatomical assessment should include assessment of adequate liver remnant volume, venous and arterial anatomy.

Social History: The medical evaluation must determine:

1. Occupation, employment status, health insurance status, living arrangements, and social support
2. Smoking, alcohol and drug use/abuse
3. High risk behavior as defined by the US PHS
4. Psychiatric illness, depression, suicide attempts

Physical Exam:

1. Height, weight, BMI, vital signs
2. Examination of all major organ systems

General Laboratory Tests:

1. Complete Blood Count (CBC) with platelet count
2. Blood Type and Screen
3. Partial Thromboplastin Time (PTT)
4. International Normalized Ratio (INR) or Prothrombin Time (PT)
5. Metabolic testing (to include electrolytes, BUN, creatinine, albumin, calcium, phosphorus,)
6. Pregnancy test for premenopausal women without surgical sterilization
7. Chest X-Ray
8. Electrocardiogram (ECG)

Programs must develop and follow a policy for hypercoagulable state evaluation

Liver-Specific Tests:

1. Hepatic function panel
2. Ceruloplasmin in a donor with family history of Wilsons Disease
3. Iron, Iron Binding Capacity, Ferritin
4. Alpha 1 antitrypsin level
 - low alpha 1 antitrypsin levels should have a phenotype.

Each center must develop and follow a policy for screening for autoimmune disease

Anatomic Assessment:

A radiological assessment must be performed to determine if the liver is anatomically suitable for transplantation, and to assess safety of resection for the donor.

Evaluation must include:

1. assessment of projected graft volume,
2. donor's remnant volume,
3. vascular anatomy
4. presence of steatosis

Liver Biopsy:

1. Transplant Centers must develop and then follow a policy for liver biopsy.
2. If the liver biopsy reveals histological abnormalities they must be reviewed by a hepatologist

Screening for transmissible diseases:

Infectious disease testing must include:

1. CMV (Cytomegalovirus) Antibody
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3. HIV 1,2 (Human Immunodeficiency Virus) antibody testing
4. HepBsAg (Hepatitis B surface antigen)
5. HepBcAB (Hepatitis B core antibody) *
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7. HCV (Hepatitis C Virus) antibody testing
8. RPR (Rapid Plasma Reagin Test for Syphilis)

** HBV DNA must be tested if HBcAB is positive*

For tuberculosis (TB), living donor recovery centers must determine if the potential donor is at increased risk for this infection, and if so testing must include:

- Screening for latent TB using either intradermal PPD or Interferon Gamma Release Assay (IGRA)

Cancer Screening:

Centers must develop protocols consistent with the American Cancer Society (ACS), and once developed follow their own protocols for screening:

1. Cervical Cancer
2. Breast Cancer
3. Prostate Cancer
4. Colon Cancer
5. Skin Cancer
6. Lung cancer

Exclusion Criteria

Transplant programs that perform living liver donor recoveries must exclude all donors who meet any of the following exclusion criteria:

1. Both age less than 18 years and mentally incapable of making an informed decision
2. HIV
3. HCV RNA positive
4. HBsAg positive
5. Donors with ZZ, Z-null, null-null and S-null alpha-1-antitrypsin phenotypes and untype-able phenotypes
6. Active malignancy, or incompletely treated malignancy
7. High suspicion of donor coercion
8. High suspicion of illegal financial exchange between donor and recipient
9. Evidence of acute symptomatic infection (until resolved)
10. Uncontrolled diagnosable psychiatric conditions requiring treatment before donation, including any evidence of current suicidality
11. Donor remnant volume less than 30% of native liver volume

LIVING LIVER DONOR FOLLOW-UP

An individual's decision to pursue living liver donation for the continued survival of another person reflects a high level of altruism, courage, and selflessness. Implicit in this decision is the individual's high level of trust that the transplant community will make every effort to protect their safety and to minimize risks to their future health. The working group reaffirms that comprehensive follow-up care of the living liver donor is a core responsibility and obligation of the transplant community, is consistent with the implicit contract that exists between the donor and transplant providers, and preserves public trust in living donation.

There are several reasons why follow-up monitoring of the living liver donor should be required of all transplant programs. First, potential living donors must be provided with accurate outcome data to effectively consider the relative risks and benefits of donation and to make an informed donation decision that is consistent with their values and preferences. The provision of such information during the donor evaluation period is possible only if the transplant community systematically collects and disseminates such data. Second, routine monitoring ensures that adverse events or complications for an individual donor are identified and appropriate care is provided in a timely manner, with the goal of restoring optimal health and well-being to the donor as quickly as possible. Third, close monitoring of living liver donors will generate more reliable data on surgical, medical, and functional outcomes that have strong potential to guide the development of future living donation clinical practices and policies.

The working group considers mandatory monitoring of the living liver donor follow-up at 6 months, 1 year and 2 years following surgery as reflective of the transplant community's minimum fulfillment of its responsibility and obligation to optimize donor safety and well-being. These time points are not intended to obviate the usual post-operative and post-discharge care that is commonly provided to living liver donors. Ideally, transplant centers would extend their follow-up monitoring of living liver donors to include annual health assessments, in perpetuity. Several transplant centers have effectively integrated such long-term follow-up practices into their donor care clinical pathways. The introduction of and rationale for donor follow-up during the donor evaluation process, reducing financial disincentives for getting laboratory tests, and building a strong relationship with donors have been identified as "best practices" for successful follow-up monitoring of living donors.¹ In addition, at a minimum, donors must be advised to receive lifetime annual primary care examinations for health maintenance.

The working group recognizes the relative utility of multiple status, clinical, and laboratory parameters in the monitoring of living liver donors. Complications, if any, following living liver donation are most likely to occur and be identified in the early phases of recovery. Therefore, obtaining clinical information and laboratory data through the 1 year follow-up time point is considered essential for optimal donor care.

While programs should continue to gather and report donor status and clinical information through the 2 year time point, it was the consensus of the working group that laboratory data beyond the 1 year time point are unlikely to be of clinical benefit to the donor. Importantly, the working group recognizes that obtaining laboratory data presents more practical challenges for transplant centers than the acquisition of donor status and clinical information. Abnormalities in liver function tests can be expected in up to 4% and 8% of asymptomatic non-donors² and liver donors³, respectively, which are of uncertain significance. This may trigger additional diagnostic procedures with their attendant risks to the living liver donor. On the basis of the foregoing considerations, the working group

recommends the following elements and minimum reporting standards be established for the 6 month, 1 year, and 2 year follow-up time points:

Follow-up time point	Required data elements	Programs must obtain and report data for at least...
6 months	<ul style="list-style-type: none"> • Donor Status and Clinical Information <ul style="list-style-type: none"> ○ Patient status ○ Cause of death, if applicable and known ○ Working for income, and if not working, reason for not working ○ Loss of medical, health and/or life insurance due to donation ○ Hospital readmission since last LDF was submitted ○ Liver complications <ul style="list-style-type: none"> ▪ Bile leak ▪ Hepatic resection ▪ Abscess ▪ Liver failure ▪ Added to UNOS TX candidate waiting list ▪ Incisional hernia due to donation surgery 	80% of their living liver donors
	<ul style="list-style-type: none"> • Liver Laboratory Data <ul style="list-style-type: none"> ○ Total bilirubin ○ ALT ○ Alkaline phosphatase ○ Platelet count 	75% of their living liver donors
1 year	<ul style="list-style-type: none"> • Donor Status and Clinical Information <ul style="list-style-type: none"> ○ Patient status ○ Cause of death, if applicable and known ○ Working for income, and if not working, reason for not working ○ Loss of medical, health and/or life insurance due to donation ○ Hospital readmission since last LDF was submitted ○ Liver complications <ul style="list-style-type: none"> ▪ Bile leak ▪ Hepatic resection ▪ Abscess ▪ Liver failure ▪ Added to UNOS TX candidate waiting list ▪ Incisional hernia due to donation surgery 	80% of their living liver donors

	<ul style="list-style-type: none"> ● Liver Laboratory Data <ul style="list-style-type: none"> ○ Total bilirubin ○ ALT ○ Alkaline phosphatase ○ Platelet count 	70% of their living liver donors
2 year	<ul style="list-style-type: none"> ● Donor Status and Clinical Information <ul style="list-style-type: none"> ○ Patient status ○ Cause of death, if applicable and known ○ Working for income, and if not working, reason for not working ○ Loss of medical, health and/or life insurance due to donation ○ Hospital readmission since last LDF was submitted ○ Liver complications <ul style="list-style-type: none"> ▪ Bile leak ▪ Hepatic resection ▪ Abscess ▪ Liver failure ▪ Added to UNOS TX candidate waiting list ▪ Incisional hernia due to donation surgery 	80% of their living liver donors

These particular clinical and laboratory parameters are based on the best available published data to date and they, as well as the thresholds for complete follow-up listed in the table, are believed by the working group to be minimally necessary to monitor donor safety.³⁻⁸ Programs are expected to develop clinical pathways designed to maximize data collection and reporting at all follow-up time points for 100% of their living donors. Although requests for data on more elements or increased length of follow-up are desirable, the listings above should be an expected minimum on all donors following surgery at 6 months, 1 year, and 2 years. Transplant centers must meet the minimum standards of obtaining and reporting these data as an obligation to operate as a living liver donor transplant center. The working group acknowledges that these recommendations involve a very dynamic area and are likely to evolve over time as new information becomes available.

¹ OPTN/UNOS Living Donor Committee. Guidance for Developing and Implementing Procedures to Collect Post-Donation Follow-up Data from Living Donors.

http://optn.transplant.hrsa.gov/ContentDocuments/Guidance_Post_Donation_Donor_FollowUp.pdf

² Krier M, Ahmed A. The asymptomatic outpatient with abnormal liver function tests. Clin Liver Dis. 2009; 13:167-77

³ Trotter JF, Gillespie BW, Terrault NA, Abecassis MM, Merion RM, Brown RS Jr, Olthoff KM, Hayashi PH, Berg CL, Fisher RA, Everhart JE; Adult-to-Adult Living Donor Liver Transplantation Cohort Study Group. Laboratory test results after living liver donation in the adult-to-adult living donor liver transplantation cohort study. Liver Transpl. 2011; 17:409-17.

- ⁴ Ghobrial RM, Freise CE, Trotter JF, Tong L, Ojo AO, Fair JH, Fisher RA, Emond JC, Koffron AJ, Pruett TL, Olthoff KM; A2ALL Study Group. Donor morbidity after living donation for liver transplantation. *Gastroenterology*. 2008; 135:468-76.
- ⁵ Yuan D, Wei YG, Li B, Yan LN, Wen TF, Zhao JC, Zeng Y, Chen KF. Evaluation outcomes of donors in living donor liver transplantation: a single-center analysis of 132 donors. *Hepatobiliary Pancreat Dis Int*. 2011; 10:480-8.
- ⁶ Iida T, Ogura Y, Oike F, Hatano E, Kaido T, Egawa H, Takada Y, Uemoto S. Surgery-related morbidity in living donors for liver transplantation. *Transplantation*. 2010; 89:1276-82.
- ⁷ Jinjing Z, Jianyong L, Wentao W, Lunan Y. Systematic Review of the Safety of Living Liver Donors. *Hepatogastroenterology*. 2012; 60 [epub ahead of print].
- ⁸ Giannini EG, Testa R, Savarino V. Liver enzyme alteration: a guide for clinicians. *CMAJ*. 2005; 172:367-79.

Appendix A

Guidance for centers discussing donor complications with potential donor candidates:

Donor complications should be discussed with the donors in very clear and specific terms using national statistics as well as center specific data. Complication rates for right lobe donors should be distinguished from left lobe donors and the following literature can be used as guidance:

Right lobe donors:

M. M. Abecassis, R. A. Fisher, K. M. Olthoff, C. E. Freise, D. R. Rodrigo, B. Samstein, I. Kam, R. M. Merion and the A2ALL. Complications of Living Donor Hepatic Lobectomy—A Comprehensive Report. *American Journal of Transplantation* 2012; 12: 1208–1217

Muzaale AD, Dagher NN, Montgomery RA, Taranto SE, McBride MA, Segev DL. Estimates of early death, acute liver failure, and long-term mortality among live liver donors. *Gastroenterology*. 2012 Feb;142(2):273-80. Epub 2011 Nov 19.

Left Lobe Donors:

Soejima, Y., Shirabe, K., Taketomi, A., Yoshizumi, T., Uchiyama, H., Ikegami, T., Ninomiya, M., Harada, N., Ijichi, H. and Maehara, Y. (2012), Left Lobe Living Donor Liver Transplantation in Adults. *American Journal of Transplantation*, 12: 1877–1885. doi: 10.1111/j.1600-6143.2012.04022.x

The following tables may be helpful in outlining the classification schemes as well as the specific donor complications (in these examples of right lobe donors):

Table 1. Clavien system for classification of negative outcomes in general surgery and solid organ transplantation (2–4)

Grade 1	Any alteration from ideal postoperative course with complete recovery or which can be easily controlled and which fulfills the general characteristics:
	a) Not life-threatening.
	b) Not requiring use of drugs other than immunosuppressive agents, analgesics, antipyretic, anti-inflammatory and antiemetic, drugs required for urinary retention or lower urinary tract infection, arterial hypertension, hyperlipidemia or transient hyperglycemia.
	c) Requiring only therapeutic procedures that can be performed at the bedside.
	d) Postoperative bleeding requiring ≤ 3 units of blood.
	e) Never associated with a prolongation of ICU stay or total hospital stay to more than twice the median stay for the procedure in the population of the study.
Grade 2	Any complication that is <i>potentially life-threatening</i> or results in ICU stay ≥ 5 days, hospital stay ≥ 4 weeks for the recipient or ≥ 2 weeks for the donor, <i>but which does not result in residual disability or persistent diseases</i> .
Grade 3	Any complication with <i>residual or lasting functional disability</i> or development of malignant disease.
Grade 4	Complications that lead to transplantation (grade 4a) or death (grade 4b)

Table 2: Most common complications that happen soon after right lobe liver donation

13 out of 100 patients who donate a liver	Get an infection
11 out of 100 patients who donate a liver	Get fluid inside their chest making it hard to breathe (pleural effusion)
8 out of 100 patients who donate a liver	Get bile (a liquid made by the liver)that leaks and causes pain and sometimes infection {bile leak}
3 out of 100 patients who donate a liver	Get pinched nerve causing pain or numbness in their hands and arms { neuropraxia}
3 out of 100 patients who donate a liver	Have difficulty in digesting their food which can cause pain, bloating, and constipation {ileus}
2 out of 100 patients who donate a liver	Have fluid in their lungs that makes it hard to breathe {pulmonary edema}

Table 3: Most common complications more likely to occur 1 year after right lobe liver donation

7 out of 100 patients who donate a liver	Get an incisional hernia which is a bump under the skin near the scar from surgery {hernia}
6 out of 100 patients who donate a liver	Have psychological problems such as suicidal ideation or depression
3 out of 100 patients who donate a liver	Need to have more surgery to fix a problem with the hernia such as pain or bleeding
2 out of 100 patients who donate a liver	Need surgical intervention to clear a blockage in the intestines

Appendix B: Hypercoagulable Evaluation:

- Venous thromboembolism is an important complication in patients undergoing major abdominal surgery, and therefore is a theoretical concern in living liver donation. However, there are no specific data supporting the value of an evaluation for hypercoagulable states to reduce the incidence of perioperative thromboembolism in living liver donors.
- Tests routinely done to evaluate for a hypercoagulable state include the following:
 - Lupus anticoagulant
 - Factor V Leiden
 - Prothrombin gene mutation
- Centers must have a policy for evaluating liver donor candidates for hypercoagulable states.
- Centers should consider counseling and excluding donor candidate with a positive screening test for a hypercoagulable state.
- A history of venous thromboembolism in a liver donor candidate should be considered a relative contraindication to donation.

Appendix C: Autoimmune Evaluation:

- Evaluation of autoimmune markers is recommended in all living liver donor candidates. These include anti-nuclear, anti-mitochondrial, and anti-smooth muscle (anti-actin) antibodies.
- The interpretation of a positive autoimmune marker, and further action to determine its clinical significance, must be with the knowledge that many normal patients test positive for one or more autoimmune markers (for example, approximately 8 % of the US population is ANA-positive). In addition, the risk of developing clinically significant autoimmune liver disease in an asymptomatic patient with a positive autoimmune marker is unknown.
- Living liver donor candidates with certain positive autoimmune markers need to be carefully evaluated, especially if a family member) suffers from chronic liver disease due to an autoimmune disorder.
- The evaluation of living liver donor candidates who are positive for one or more autoimmune markers should consider the following to determine their suitability for donation:
 - A family history of autoimmune disease: A donor candidate with a family member with clinically significant autoimmune liver disease might warrant further investigation.
 - The liver biopsy: Histologic evidence of autoimmune liver disease is a contraindication for donation.
 - A personal history of extra-hepatic autoimmune disease in the donor candidate.

Appendix D: Assessment for Steatosis

- All living liver donor candidates should undergo an assessment for steatosis.
- Living liver donor programs must establish a non-invasive evaluation protocol for hepatic steatosis, including biochemical testing and imaging of the liver.
- Data suggests that patients with a BMI > 28 have a higher incidence of steatosis in the liver; however, donors with normal BMI can have steatosis as well.
- Steatosis present on imaging would require the consideration of liver biopsy.

Appendix E: Indications for a biopsy

Indications for liver biopsy may include:

- Abnormal liver function tests;
- Steatosis on imaging;
- BMI $>30\text{Kg/m}^2$;
- Genetic relation to a person with autoimmune or genetic liver disease;
- HBV core positive serology;
- Prior history of alcohol abuse