

Guidance for the Development of Program-Specific Living Kidney Donor Medical Evaluation Protocols

Summary and Goals

On June 16, 2006, HRSA published a notice in the Federal Register in which the Secretary of HHS directed the OPTN to develop policies regarding living organ donors and organ donor recipients. The notice stipulated that noncompliance with such policies will subject OPTN members to the same consequences as noncompliance with OPTN policies regarding deceased donor transplantation. In response, the Board of Directors adopted changes to the Bylaws requiring transplant programs that perform living donor transplants to develop and follow written protocols that address all phases of the living donation process, including the evaluation, pre-operative, operative, and post-operative care, as well as the submission of data.¹

To assist members, the Living Donor Committee developed a non-exhaustive set of elements to serve as a resource that could be used by transplant programs in developing their own program specific living kidney donor medical evaluation protocols, as required by the Bylaws. Since this resource is not considered OPTN or UNOS policy, it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, and it is not intended to be clinically prescriptive or to define a standard of care. This resource will not be used to determine member compliance with policies or Bylaws; rather it is a resource being provided to the members for examples and amplification of the elements mentioned in the Bylaws. It is intended for members' voluntary use.

Both new and existing living donor transplant programs can use this guidance when developing medical evaluation protocols for their potential living donors. A parallel document will be developed for use by potential donors and the public.

I. Pre-evaluation Guidance

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 problems that might complicate donation (e.g., lack of social support to aid in their post operative recovery). The medical evaluation

may uncover conditions that could significantly increase the risk of donation to the potential 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 the anatomical suitability of the organ and properly plan the surgery.

To the extent possible, the potential donor and the intended recipient should be made aware of the alternatives to living donor transplantation prior to beginning the donor evaluation. Both the potential donor and intended recipient should be informed of the donor and recipient outcomes of living donor transplantation nationally and at the particular institution.

It is important to inform the potential donor that he/she can stop the evaluation or donation process at any time. If a potential donor chooses to not proceed with the evaluation or donation process, the center may state that the donor did not meet the program's criteria for donation to help avoid difficult social situations.

Donor Risk

Living kidney donation involves risk.

Most of the risks and complications associated with the donor nephrectomy procedure occur in the peri-operative period, are relatively well known, and can include:

- Risks associated with anesthesia;
- Surgical complications such as pain, infection, blood loss, blood clots; and
- Death - the risk of dying from living donor surgery is 0.04%.

Further study comparing the risk of ESRD in the general public to that in living kidney donors is needed. Since there has been no national systematic long-term data collection on the risks associated with living organ donation, the risk of renal dysfunction for the living kidney donor is not well known. However, recent OPTN data do reveal:

- The risk of end stage kidney disease, and the need for dialysis or to receive a kidney transplant is between 0.10 to 0.52%;
- This risk may be higher if the prospective donor is African American;
- Between January, 1996 and February, 2008, there were 172 kidney waiting list candidates identified to be previous living kidney donors. The median time from donation to listing was 19 years.

The concern about the long-term risk of donation has to be balanced against the benefit of transplantation for the recipient.

It is clear that those patients who remain on dialysis have an increased risk of death as compared to patients who are transplanted. Furthermore, there is strong evidence that the longer a transplant candidate remains on dialysis, the greater the risk of graft loss and mortality after transplantation.

The potential donor and the medical team should discuss these risks and whether the risk of nephrectomy to the living donor is warranted in comparison to the benefit the recipient receives from transplantation.

Risks of Donor Evaluation

Risk's associated with medical screening may include:

- Contrast materials used in abdominal imaging may cause mild to severe allergic reaction;
- Both risks and benefits may result from medical testing. The evaluation may lead to the early discovery of infections or malignancies unknown to the potential donor;
- Positive test results for some infections must be reported by law to health agencies;
- HLA testing could reveal the true identity of family relationships, and create issues that the donor or other family members may not wish exposed; and
- Testing may bring unexpected decisions for the donor and medical team as well as the need for additional testing and treatments that may be the financial responsibility of the donor or donor's insurance.

Physician knowledge and experience are important components in this process. The involved professionals' medical judgment will always need to direct the course of the evaluation. The health care team should be judicious in the choice of screening tests and circumspect in the interpretation of the positive findings.

Decision Regarding Donation

The final decision regarding whether the donor can donate an organ is based upon:

- the medical test results;
- the donor's psychosocial evaluation;
- the relationship of the donor to the prospective recipient and;

- assessment of risk based upon current medical knowledge.

The donor should make the decision to donate in concurrence with the independent donor advocate and the medical team.

If a decision to donate is made, the recipient should be consulted to determine if transplantation should proceed. Under these circumstances, both the donor and recipient should be informed of the risks of both procedures given the specifics of the donor and recipient circumstances (e.g. severity of recipient illness, donor anatomy, etc).

Prospective living donors may be willing to undergo varying degrees of personal risk to provide an organ needed by a transplant candidate, and this difference needs to be taken into consideration.

Transplant candidates may be willing to undergo varying degrees of communicable disease and organ quality risk from acceptance of the prospective living donor's gift of his or her organ.

II. Evaluation Guidance

This document presents a list of tests and procedures that may be necessary to assess the medical and psychosocial suitability of the donor.

To date, there have been no randomized controlled trials to determine the testing required for the evaluation of a living kidney donors. The process described here is representative of general medical practice for the assessment of living donors at existing practices at US transplant programs.

This list should be viewed as suggestive and opinions will vary. The list will require modification over time as improved screening tests become available. At all times, the transplant program should assess the risk of the screening procedures versus the benefit of the information derived.

Psychosocial Evaluation

As required by the Bylaws, this evaluation be performed by a psychiatrist, psychologist or social worker with experience in transplantation. The psychosocial evaluation should:

- Review psychosocial issues that might complicate the living donor's recovery and identify potential risks for poor psychosocial outcome;
- Attempt to identify factors that warrant educational or therapeutic intervention prior to donation and provide the necessary referrals for further psychological or psychiatric evaluation if current or prior psychiatric disorders are suspected;

- Determine if the potential donor understands the short- and long-term medical risks associated with living donation as currently understood with the information available;
- Allow the transplant program to explore the reason(s) for volunteering to donate to determine that the decision is free of coercion;
- Determine if the potential donor is able to make an informed decision and has the ability to cope with the major surgery and related stress. This includes a realistic plan for donation and recovery, with social, emotional and financial support available as needed;
- Review the financial circumstances of the potential donor (employment, insurance coverage, etc) and determine if the potential donor understands the possible financial implications of living donation and the availability of financial resources where applicable;
- Inform the donor that he/she may experience problems in obtaining future disability and health insurance following donation; and
- Inform the donor that health information obtained during their evaluation will be subject to the same regulations as regular medical records and may not be additionally protected.

To protect the potential donor, the most sensitive questions should be asked at the end of the psychosocial evaluation, which prevents recording responses to very sensitive questions in the medical record of inappropriate candidates.

DONOR MEDICAL EVALUATION

The OPTN/UNOS Bylaws state that a thorough medical evaluation be performed by a physician or surgeon experienced in living donation. The goal of the medical evaluation is to:

- Assess the immunologic compatibility of the donor to the recipient;
- Assess the general health and surgical risk of the donor including screening for conditions that may predict complications from having one kidney in the future;
- Determine if there are diseases present that may be transmitted from donor to recipient; and
- Assess the anatomy of the kidneys.

The OPT/UNOS Living Donor Committee, in consultation with experts, will at the appropriate time, review and update the guidance in this document.

Components of the Medical Evaluation

1. General History:

- Evaluate for significant medical conditions such as hypertension, diabetes, lung disease, heart disease, gastrointestinal disease, autoimmune disease, neurologic disease, genitourinary disease, history of cancer, history of infections, hematologic disorders, and bleeding/clotting disorders
- Smoking, alcohol and drug use/abuse, including intravenous drug use/abuse and other high risk behavior
- Active and past medications (nephrotoxic, chronic use of pain medications and NSAIDS, other)
- Allergies
- Family history (coronary artery disease, cancer, other)
 - Kidney Specific Personal History:
 - Kidney disease, proteinuria
 - Kidney injury
 - Diabetes
 - Chronic infection
 - Nephrolithiasis
 - Recurrent urinary tract infections
 - Gout or other arthritis
 - Gestational diabetes
 - Kidney Specific Family History:
 - Kidney disease
 - Diabetes
 - Hypertension
 - Reflux

2. Social History:

Although a full psychosocial evaluation will be carried out, an evaluation should be part of the medical evaluation to include special emphasis on:

- Employment, health insurance status, living arrangements, social stability
- Psychiatric illness, depression, suicide attempts

3. Physical Exam:

- Height, weight, BMI
- Examination of all major organ systems

4. Kidney-specific:

- Blood pressure (Measure after sitting for 5 minutes, take twice at the same visit, and obtain 2 different assessments of blood pressure on different days). It may however be preferable to perform a 24-hour blood pressure monitor as cohort studies show improved accuracy for determining the correct blood pressure category with 24-hour monitoring
- Vascular evaluation (abdominal, femoral, carotid bruits, etc)
- Microscopic evaluation

5. General Laboratory Tests:

- CBC with platelet count
- Prothrombin Time/Partial Thromboelastin Time
- Comprehensive panel (electrolytes, transaminase levels, albumin, calcium, phosphorus, alkaline phosphatase, bilirubin)
- HCG quantitative pregnancy test for women < 55 years old
- Age and gender appropriate cancer screening tests. The transplant program may choose to follow the screening recommendations from the American Cancer Society.
- Chest X-Ray
- Electrocardiogram (ECG)
- Evaluation for coronary artery disease, as suggested by the American College of Physicians
- Pulmonary function tests for smokers, as suggested by the American College of Anesthesiology and American Lung Association

6. Kidney-specific Tests:

- Urinalysis; microscopy as indicated
- Urine culture if clinically indicated
- Measurement of protein excretion
- Measurement of glomerular filtration rate by 24 hour urine collection or equivalent testing
- Screening for Polycystic Kidney Disease as indicated by family history. If the prospective donor is over age 30, this is usually accomplished with an ultrasound. In those under age 30, genetic testing remains the gold standard.
- Uric acid
- GTT in relatives of diabetics as indicated

7. Immunological testing:

- ABO blood group typing
- Human Leukocyte Antigen (HLA) typing
- Cross match

8. Metabolic Focused Testing:

- Fasting blood glucose
- Fasting cholesterol levels (Cholesterol, Triglycerides, HDL Cholesterol, and LDL Cholesterol) with Fasting Lipid Profile if cholesterol/triglycerides are elevated.
- Uric acid (High uric acid levels are associated with the metabolic syndrome and independently with reduced kidney function)
- If the risk of diabetes is higher than the general population by presence of a first degree relative with diabetes or the presence of metabolic syndrome characteristics, but the prospective donor does not meet the definition of diabetes, they should be counseled that he or she are at an increased risk to develop diabetes and perhaps kidney disease

The goal of these tests is to determine the number of elements of the metabolic syndrome present: Donor may be at increased risk of kidney disease if ≥ 3 risk actors (central obesity, high blood pressure BP $>130/85$, fasting blood glucose $\geq 100\text{mg/dl}$, triglyceride levels $> 150\text{mg/dl}$, HDL < 40 for a man and $<50\text{mg/dl}$ for a woman).

9. Anatomic Assessment:

This assessment is used to determine which kidney is most anatomically suitable for transplantation (typically dependent upon the number of arteries going to the kidneys) and whether the kidneys are of equal size or have masses, cysts, or stones. The donor should preferably keep the kidney with the fewest issues. Based on these findings, the surgeon will determine 1) the suitability of the organ, and 2) any additional risks associated with anatomical variants. The radiologic imaging may reveal serendipitous findings that will need to be investigated. These finding 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.

10. Screening for transmissible diseases:

This screening is used to identify the risk of passing an infection or disease to a recipient. This screening may also identify a condition that may require donor treatment or may increase the risk of donation. Infectious disease testing typically includes testing for the following:

- CMV (Cytomegalovirus)
- EBV (Epstein Barr Virus) – VCA or EBNA antibody test may be performed if the recipient is EBV seronegative
- HIV 1,2 (Human Immunodeficiency Virus)
- HTLV I (Human T-cell Lymphotropic Virus) antibody testing
- HBsAg (Hepatitis B surface antigen)
- HBcAB (Hepatitis B core antibody)

- HBSAB (Hepatitis B surface antibody)
 - HCV (Hepatitis C Virus)
 - RPR (Rapid Plasma Reagin Test for syphilis)
 - Tuberculosis
- Other diseases may be tested for depending on program preference and donor risk profile:
- Strongyloides for donors from endemic areas
 - Trypanosoma cruzi for donors from endemic areas
 - West Nile for endemic areas
 - Toxoplasmosis: Transmission is low if recipients are treated with trimethoprim-sulfamethoxazole

11. Cancer screening:

The screening tests follow the practices advised by the American Cancer Society. Screenings to be performed depending upon gender, age, or family history include:

- Cervical Cancer
- Breast Cancer
- Prostate Cancer
- Colon Cancer
- Skin Cancer

Lung cancer screening is not currently recommended by the American Cancer Society, but could be considered in the older patient with a strong smoking history.

POSSIBLE EXCLUSION CRITERIA

A variety of criteria may make an individual unsuitable for living donation. Some of these may include:

- Age < 18 years, or mentally incapable to make an informed decision,
- Uncontrollable hypertension, history of hypertension with evidence of end stage organ damage, history of hypertension in a Caucasian younger than age 50 or greater than age 50 on more than one anti-hypertensive medication, or hypertension in a non-Caucasian. High blood pressure is associated with a more significant effect on progression of kidney disease in the non-Caucasian population, or in patients taking more than one anti-hypertensive medication.
- Diabetes
- Significant history of thrombosis or embolism
- Bleeding disorders
- Uncontrollable psychiatric illness
- Morbid obesity
- Clinically significant Coronary and/or Peripheral Vascular Artery Disease

- Symptomatic Valvular Disease
- Chronic lung disease with impairment of oxygenation or ventilation
- Recent malignancy, or cancers with long times to recurrence (e.g., breast cancer)
- History of melanoma
- History of metastatic cancer
- Bilateral or recurrent nephrolithiasis
- Significant urologic abnormalities of donor kidney
- Creatinine clearance $< 80 \text{ ml/min/1.73m}^2$, or projected GFR with removal of one kidney at 80 years old of $< 40 \text{ cc/min/1.73m}^2$ (based upon Thiel in Living Donor Kidney Transplantation, editors Gaston and Wadstrom, 2005)
- Proteinuria (protein in the urine) $> 300 \text{ mg/24 hours}$, excluding postural proteinuria
- Human Immunodeficiency Virus infection
- Hepatitis C Virus infection
- Active Hepatitis B Virus infection

OPTN/UNOS LIVING DONOR FOLLOW-UP

The organ recipient's transplant center is required to submit to OPTN/UNOS information on the status of each living donor for a minimum of two years. Any information received is used to determine if living donors experience short term health complications and how living donation may impact quality of life. Follow up information submitted by transplant centers is the only method currently available to obtain information on living donors.

MEDICAL EVALUATION AFTER LIVING DONATION

Following kidney donation, donors should remain informed about their health and have the basic evaluations performed as listed below:

- Blood pressure
- Height, weight and waist circumference
- An age appropriate physical exam

Laboratory studies may include:

- Urinalysis
- Urine albumin:creatinine ratio
- Serum creatinine
- Fasting blood glucose
- Lipid profile

All living kidney donors are encouraged to maintain lifestyle choices that will protect their overall health and in particular kidney health. Like all adults, kidney donors should be advised to establish a health evaluation schedule as recommended by the American

College of Physicians. These evaluations may be the financial responsibility of the donor.

¹ Bylaws, Appendix B, Attachment I, Section XIII, D (2) and (4), Designated Transplant Program Criteria

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