CORE CURRICULUM IN NEPHROLOGY

Evaluation of Adult Kidney Transplant Candidates

Suphamai Bunnapradist, MD, and Gabriel M. Danovitch, MD

Kidney transplantation is the treatment of choice for suitable patients with end-stage kidney disease and must be discussed with patients with advanced chronic kidney disease (CKD) preparing for renal replacement therapy. Referral to a transplant program should be performed early to assess candidacy for a preemptive transplantation.

One of the main goals of the visit to the transplant center is to educate patients about living and deceased donor transplant options. Potential transplant candidates and their family members should be encouraged to attend formal educational sessions and obtain further information through available literature, including center-specific outcomes. Potential transplant recipients also should be familiar with deceased donor organ allocation policy (Table 1).

Evaluation of kidney transplant candidates includes an initial assessment for transplantation suitability. This includes medical, surgical, immunologic, and psychosocial evaluations. The patient's individual risks and benefits of transplantation are discussed so that he or she can make an informed decision about whether to proceed with transplantation. After candidates are placed on the deceased donor list, a periodic reevaluation is necessary to address new issues that may impact on transplant suitability.

In this article, we provide guidelines for the evaluation of adult kidney transplant candidates. The workup should be tailored according to patient-specific conditions. Center expertise should be taken into account when determining which diagnostic studies should be performed.

From the Division of Nephrology, UCLA Medical Center, Los Angeles, CA.

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Address correspondence to Suphamai Bunnapradist, MD, Director of Clinical Research, Kidney and Pancreas Transplant Program, David Geffen School of Medicine at UCLA, 924 Weswood Blvd, Ste 860, Los Angeles, CA 90095. E-mail: bunnapradist@mednet.ucla.edu

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WHEN TO REFER

I. Kidney transplantation should be discussed with all patients with irreversible advanced CKD
II. Patients with CKD without known contraindications for transplantation should be referred to a transplant program when they approach CKD stage 4 or a glomerular filtration rate (GFR) less than 30 mL/min/1.73 m^2 (<0.5 mL/s/1.73 m^2)
III. Early referral will improve the chances of a patient receiving a preemptive transplant, especially those with a potential living donor; referral to a kidney transplant program does not imply immediate transplantation

TRANSPLANTATION WORKUP

The purpose of the evaluation is to identify contraindications for kidney transplantation and address and correct medical and psychological conditions that may affect transplant outcomes.

I. Comprehensive history and physical examination with emphasis on the following:
   A. Document the cause of renal disease and assess the risk of recurrence in the transplanted kidney; this includes review of the native kidney biopsy report, if available
   B. Family history, especially kidney disease, hypertension, and diabetes
   C. Evidence of coronary heart disease, cerebrovascular disease, and peripheral vascular disease
   D. Evidence of defects in coagulation
   E. Evidence of abnormalities of the urinary tract and bladder
   F. Financial evaluation to assess ability to afford transplant medications
   G. Psychosocial evaluation in conjunction with a transplant social worker to assess support network, determine suitability, and develop a plan to avoid adverse posttransplantation psychosocial outcomes

H. Evaluate sensitization risks, including a history of blood or platelet transfusions, pregnancies, abortions, and previous transplants
I. In retransplantation candidates, a detailed history of the prior transplantation courses and cause of graft loss, medication compliance, and previous transplant complications should be obtained

II. Contraindications for single-organ kidney transplant are listed in Table 2

III. Required laboratory tests
A. Blood type (need confirmatory test by 2 laboratories)
B. Complete blood count and comprehensive metabolic panel
C. Prothrombin time (PT), partial thromboplastin time (PTT)
D. Hepatitis serological tests
E. Venereal disease research laboratory (VDRL) serological test
F. Cytomegalovirus serological test
G. Tissue typing for HLA and panel-reactive antibody (PRA)
H. Identification of specific HLA antibody should be performed in patients with positive PRA
I. Electrocardiogram (ECG)
J. Chest X-ray
K. Renal ultrasound for those on dialysis therapy for more than 5 years in patients without recent imaging

IV. Optional laboratory tests as indicated

Table 1. United Network for Organ Sharing Point System for Allocation of Deceased Donor Kidney

Factor	Points	Condition
Time waiting	1	Each year of waiting time
Quality of HLA match	2	0-DR mismatch
	1	1-DR mismatch
Panel-reactive antibody	4	>80% panel-reactive antibody and negative cross-match

Note: The 0-HLA mismatched kidneys are mandated to be shared nationally. Potential recipients younger than 18 years are given priority to donors younger than 30 years and also receive extra points. Allocation policy is in the process of revision. Current allocation policy is available at the United Network for Organ Sharing website www.unos.org. Nationally approved local variance in organ allocation policy may take precedence over the national point system.

Table 2. Contraindications for Kidney Transplantation

Severe uncorrectable systemic conditions with short expected life expectancy
Reversible renal failure
Recent or untreatable malignancy
Uncontrolled psychiatric disorders and active substance abuse
Ongoing noncompliance
Chronic or ongoing active infection
Primary oxalosis (evaluate for combined liver-kidney transplantation)
Limited irreversible rehabilitative potential

Transplant programs and referring physicians should consider which of the following tests should be performed by the transplant programs and which by referring nephrologists

A. Purified protein derivative (PPD) test in those with a history of exposure to tuberculosis, prior residence in an endemic area, or chest X-ray suspicious of tuberculosis
B. Colonoscopy in patients older than 50 years
C. Gynecological evaluation, including Papanicolaou smear in women of childbearing age
D. Mammogram in women older than 40 years
E. Prostate-specific antigen (PSA) in men older than 45 years
F. Serum immunoelectrophoresis in patients older than 60 years and those with unexplained renal failure and anemia
G. Stress test, echocardiogram, and cardiac angiogram (see cardiac section)
H. Vascular study (see vascular section)
I. Detailed coagulation study in those with history of deep venous thrombosis, spontaneous abortion, recurrent clotting of a dialysis fistula or graft, or bleeding tendency
J. Toxoplasmosis, coccidioidomycosis, and histoplasmosis titers in residents of endemic areas

CARDIAC EVALUATION*

I. Assessment for cardiovascular disease (CVD) should be performed in all trans-

* *Conclusive data specific to the kidney transplant population are lacking. Our recommendation is based on our center's experience and published consensus reports.*

plant candidates; patients with CKD have a high prevalence of CVD, left ventricular hypertrophy, and congestive heart failure and therefore are at high risk of cardiovascular events perioperatively and posttransplantation

II. History and physical examination to assess cardiovascular symptoms and signs, risk factors, and physical status

III. ECG for all patients; abnormal results warrant additional cardiac evaluation

IV. Noninvasive screening to rule out occult CVD should be performed in patients with symptoms or clinical signs; given the high prevalence of occult CVD, those with significant CVD risk factors, including diabetes, age older than 50 years, severe peripheral vascular disease, cigarette smoking history, or long-term CKD should undergo a stress test

V. Patients with diabetes may benefit from a stress test with imaging due to the low sensitivity of exercise ECG stress test; type of imaging test should take into account the transplant center's experience

VI. Modifiable risk factors should be addressed and treatment should be delivered under the care of the primary nephrologist

VII. Although data are lacking, there is a general consensus to support repeated screening for cardiac disease; those with a normal coronary angiogram may not need reevaluation for 3 years; new cardiac symptoms warrant immediate evaluation

VIII. Echocardiogram should be obtained in those with suspected valvular disease or congestive heart failure

IX. Those with inducible ischemia should be referred for cardiology consultation and coronary angiography should be considered; if CVD is detected and amenable to revascularization, the procedure should be performed before transplantation

X. Smoking cessation is recommended in all patients, especially those with significant CVD; referral to smoking cessation program is recommended

CEREBROVASCULAR EVALUATION

I. Patients with symptoms and signs of cerebrovascular disease should be evaluated, and modifiable risk factors should be addressed

II. In patients with seizure disorders, certain anticonvulsants may interfere with the metabolism of calcineurin inhibitors; a neurology referral is recommended to assess whether medications can be safely discontinued or regimens with fewer drug interactions can be substituted

PERIPHERAL VASCULAR EVALUATION

I. Vascular disease is common in patients with end-stage renal disease (ESRD), and kidney transplantation involves major vascular surgery

II. Physical examination should focus on femoral and peripheral vascular arteries; Doppler studies of iliac and lower-extremity vessels or other imaging study may be performed in patients with symptoms and signs suggestive of peripheral vascular disease to evaluate the feasibility of allograft placement

III. Angiography and computed tomography (CT) with intravenous contrast should be avoided in patients with residual renal function; magnetic resonance imaging (MRI) with gadolinium should be ordered with caution given the emerged association with nephrogenic systemic fibrosis

PULMONARY EVALUATION

I. Evaluation should include assessment of general anesthetic risk

II. A pulmonary function test is indicated in patients with a significant smoking history and those with symptoms and signs of chronic lung disease, unexplained shortness of breath, or exercise limitation

III. Isoniazid (INH) prophylaxis should be considered in patients with a positive tuberculin skin test result or chest X-ray suggestive of tuberculosis

IV. Smoking cessation is recommended in all patients before transplantation

UROLOGICAL EVALUATION

I. Indications for a voiding cystourethrogram may include recurrent urinary tract infec-

tions, pyelonephritis, history of vesicoureteral reflux, history of urinary retention, or other abnormal voiding patterns

II. Renal ultrasound or other imaging studies should have been performed in all patients undergoing evaluation for renal transplantation and should be available for review; specific pathological conditions for which renal ultrasound is indicated include acquired cystic kidney disease, suspected kidney stones, unexplained hematuria, suspected renal mass, evaluation of hydronephrosis in children presenting with CKD, and those with a significant history of urinary tract infection

III. Urodynamic studies should be considered in patients with a suspected neurogenic bladder and may be indicated in young patients with unexplained CKD

IV. Patients with abnormal prostate examination findings and those with high PSA levels should be referred for a possible prostate biopsy

V. Patients with a history of obstructive voiding symptoms and benign prostatic hyperplasia should have an assessment for postvoid residual volume; those with high residual volume may need urological referral and further workup

VI. Indications for pretransplantation native nephrectomy
    A. Chronic pyelonephritis, infected stone, heavy proteinuria, intractable hypertension, polycystic kidney disease with severely enlarged kidneys, recurrent bleeding or infection, or renal mass suspicious for renal cell carcinoma

ASSESSMENT FOR IMMUNOLOGIC RISK

Screening tests to detect preformed HLA antibodies include an enzyme-linked immunosorbent assay (ELISA), flow cytometry, and cytotoxicity test to assess PRA; positive PRA results should be followed by specific HLA antibody tests

I. An ELISA is inexpensive and is used to detect antibody against purified class I and class II antigens

II. Flow cytometry is more sensitive and allows sera to be tested against whole lymphocytes, purified HLA antigens, or single antigen beads; without desensitizing treatment, antibodies to a specific antigen identify those antigens as unacceptable for transplant

III. Highly sensitized patients
    A. Sensitization is defined as the presence of preformed antibodies against HLA in the blood and is a major barrier to successful transplantation
    B. Available options include kidney paired donation, kidney list donation, and desensitization treatment
        1. Kidney paired donation involves 2 or more pairs of incompatible living donors and recipients; the mutual exchange results in 2 or more compatible transplants
        2. Kidney list donation involves a pair of an incompatible potential living donor and recipient and a waiting list recipient; a waiting list recipient receives the organ from the living donor; the donor's intended recipient is given priority to receive a deceased donor organ
        3. Patients with a cross-match–positive living donor or those on the top of the waiting list should be referred to a transplant center with expertise in desensitization protocols and/or a donor exchange program

EVALUATION OF COMORBID CONDITIONS

I. Diabetes
    A. In patients with type 1 diabetes with ESRD, early transplantation with a living donor followed by pancreas-after-kidney transplantation usually is regarded as the best option
    B. Due to the superior outcomes of simultaneous kidney-pancreas transplantation compared with deceased donor kidney transplantation, this option should be discussed with patients with type 1 diabetes, especially those without potential living donors; the additional risk and benefits should be discussed thoroughly with patients
    C. Due to the high prevalence of vascular disease, patients should be screened

vigorously for peripheral and coronary artery disease

II. Obesity
  A. Because morbid obesity is associated with increased risk of graft loss, delayed graft function, wound complications, prolonged hospitalization, and new-onset diabetes after transplantation, weight loss often is recommended before transplantation, although the benefit of this intervention is unclear; there is no specific guideline on body mass index (BMI) cutoff value, although most centers will decline candidates when BMI is greater than 40 kg/m^2

III. Patients with history of cancer
  A. Most, but not all, patients will benefit from waiting 2 to 5 years before transplantation; the exception may include cancer in situ, localized nonmelanoma skin cancer, and limited incidental renal cell cancer; general guidelines are listed in Table 3
  B. The optimal waiting time varies depending on type, stage, and localization of tumor, as well as response to therapy; data for exact risk of cancer recurrence are lacking; additional information can be obtained from the Israel Penn International Tumor Registry; oncology consultation may be beneficial

IV. Hypercoagulable state
  A. Patients with a history of spontaneous abortion or thrombosis, including recurrent clotting of a dialysis fistula and graft, should be screened
  B. Hypercoagulable states exist in up to 15% to 20% of patients with ESRD; common causes include activated protein C resistance, factor V Leiden gene mutation, prothrombin gene mutation, and antiphospholipid antibody
  C. A hypercoagulable state is rarely a contraindication for transplantation; patients need to be managed with anticoagulation therapy during and after transplantation; anticoagulation is associated with an increased risk of bleeding

V. Hepatitis C infection
  A. Liver biopsy should be performed to evaluate the extent of liver damage because clinical findings and biochemical markers may underestimate the degree of advanced liver disease in patients with ESRD
  B. Cirrhosis is a contraindication for kidney transplantation due to increased mortality in this group; instead, liver-kidney transplantation should be considered
  C. Consideration should be given to treatment of patients with hepatitis C before transplantation, especially those with a treatment-sensitive genotype (non–type 1)
  D. The option of hepatitis C–positive donor transplantation should be discussed with patients with active hepatitis C given the shorter waiting time for hepatitis C deceased donor kidney and acceptable outcome
  E. Patients who are hepatitis B naïve should be vaccinated against hepatitis B

VI. Hepatitis B infection
  A. With the introduction of effective antiviral therapy, hepatitis B infection is no longer considered an absolute contraindication for transplantation

Table 3. Recommendations for Minimum Tumor-Free Waiting Periods for Common Pretransplantation Malignancies

Tumor Type	Minimal Wait Time
Renal	
Wilm	2 y
Renal cell carcinoma	
Incidental tumors	None
Other	At least 2 years
Bladder	
In situ	None
Invasive	2 y
Prostate	2 y
Uterus	
Cervix (in situ)	None
Cervical invasive	2-5 y
Uterine body	2 y
Breast	2-5 y
Colorectal	2-5 y
Lymphoma	2-5 y
Skin (local)	
Basal cell	None
Squamous cell	Surveillance
Melanoma	5 y

Note: The broad recommendations must be individualized based on specific clinical and oncological information.

B. Patients with past natural infection with detectable antibody to hepatitis B surface antigen (HBsAb) and negative hepatitis B surface antigen (HBsAg) are at low risk of hepatitis B resurgence; antiviral prophylaxis may be beneficial
C. Liver biopsy should be performed in patients with active hepatitis B; if advanced liver disease is detected, patients should be referred for combined liver-kidney transplantation
D. Antiviral treatment should be initiated in patients with active viral replication (positive hepatitis B e antigen [HBeAg] or hepatitis B virus DNA)

VII. Human immunodeficiency virus (HIV)-infected patients
A. HIV infection is no longer considered an absolute contraindication for transplantation
B. Potential candidates should have no active acquired immunodeficiency syndrome (AIDS)-defining illness and have sustained CD4 counts greater than 200 cells/mL with undetectable serum HIV RNA on stable antiretroviral therapy
C. Coinfection with hepatitis virus is common, and each infection should be addressed before transplantation

VIII. Fabry disease
A. More than 200 patients with Fabry disease have undergone transplantation in the United States; early data showed good graft and patient survival; the role of enzyme replacement therapy before and after kidney transplantation is unclear

IX. Systemic lupus erythematosus and vasculitis
A. Transplantation should be delayed until patients have no clinically active disease and are on minimal immunosuppression; the duration of dialysis therapy before transplantation and serological status in the absence of clinically active disease do not predict recurrence
B. Previous treatment with steroids increases the risk of bone disease
C. Exposure to cytotoxic agents increases the risk of bone marrow toxicity and posttransplantation malignancy

X. Polycystic kidney disease
A. Pretransplantation nephrectomy may be indicated in patients with recurrent urinary tract infections, bleeding, or large kidneys extending into the pelvis to make room for placement of an allograft
B. Extrarenal manifestations, such as aneurysm, valvular heart disease, and diverticulosis, may complicate the transplantation course, and screening should be performed in suspected cases

XI. Primary oxalosis
A. Primary oxalosis is a contraindication for single-organ kidney transplantation, and patients should be referred for combined liver-kidney transplantation

XII. Blood dyscrasias
A. In the presence of paraproteinemia, a workup for myeloma is warranted; benign monoclonal gammopathy is a diagnosis of exclusion and serial monitoring for 12 months to rule out myeloma is recommended before transplantation; patients should be counseled about the long-term risk of developing frank myeloma
B. Patients with treated myeloma may be cautiously considered for transplantation; these patients remain at high risk of posttransplantation infections
C. Amyloidosis is associated with poorer prognosis after transplantation; however, patients with amyloidosis with limited extrarenal manifestations can be considered for kidney transplantation

XIII. Advanced age
A. Patients older than 60 years are at a greater risk of posttransplantation infection and are more susceptible to medication side effects
B. Appropriately evaluated and educated patients in their 70s may benefit in terms of life expectancy from transplantation and may be considered as transplant candidates
C. There are limited data on outcomes for patients in their late 70s and early 80s;

Table 4. Criteria for Expanded Criteria Donor

Donor Condition	Donor Age Categories (y)				
	<10	10-39	40-49	50-59	≥60
CVA + HTN + creatinine > 1.5 mg/dL				X	X
CVA + HTN				X	X
CVA + creatinine > 1.5 mg/dL				X	X
HTN + creatinine > 1.5 mg/dL				X	X
CVA					X
HTN					X
Creatinine > 1.5 mg/dL					X
None of the above					X

Note: Creatinine level greater than 1.5 mg/dL (>133 μmol/L).

Abbreviations: X, expanded criteria donor; CVA, cardiovascular accident as the cause of death; HTN, history of hypertension at any time.

most of these patients are better served by remaining on dialysis therapy

D. Counseling should emphasize the benefit of timely transplantation given the high mortality rate of elderly patients on the waiting list; living donor transplantation should be encouraged, and the option of expanded criteria donor (ECD) listing should be discussed; definition of ECD is listed in Table 4

E. ECD is particularly advisable for older patients without a living donor in whom a prolonged wait for standard criteria donor (SCD) is anticipated

F. Age-appropriate screening for malignancy should be maintained

XIV. Primary glomerular disease

A. Most, but not all, glomerular disease may recur after transplantation; recurrence of disease may result in graft loss; the rate of recurrence and risk of graft loss vary according to primary disease

B. Primary focal sclerosis may recur in 20% to 50% after kidney transplantation and lead to graft failure in up to 20% of patients after transplantation; risk factors include younger age and rapid progression in native kidneys; detailed counseling should be performed

C. Risk of graft loss is similar in living versus deceased donor transplantation and a living donor should be considered in the first transplantation; however, if the first graft is lost rapidly due to recurrent disease, the chance of recurrence in subsequent transplants is more than 80% and a living donor transplant should generally be avoided

XV. Patients with a previously failed graft

A. Referral should be made as patients approach stage 4 CKD

B. Patients with a failed graft are at risk of developing donor-specific antibodies, especially those with early graft loss due to severe rejection; screening followed by confirmation of donor-specific antibodies should be performed

C. Allograft nephrectomy generally is not indicated except in those with ongoing uncontrolled rejection, severe hematuria, and/or malignancy; allograft nephrectomy may be associated with a resurgence of donor-specific antibodies

D. Patients with early failed grafts due to recurrent glomerulonephritis are at very high risk of subsequent recurrence; patients with recurrent focal segmental glomerulosclerosis (FSGS) should be considered for pretransplantation plasmapheresis

E. Patients with graft failure due to BK nephropathy can successfully undergo retransplantation; allograft nephrectomy may not be necessary, especially in those who showed clearance of viremia; vigorous monitoring of BK viremia and adjust-

ment of immunosuppression posttransplantation are important

F. A hypercoagulable workup should be performed in patients with graft failure due to unexplained graft thrombosis

G. In patients approaching CKD stage 5 with a potential living donor, consideration should be given to maintain adequate immunosuppression, promptly followed by retransplantation to avoid immune activation

REEVALUATION OF PATIENTS AWAITING DECEASED DONOR KIDNEY TRANSPLANTS

I. Primary nephrologists and/or transplant candidates on the waiting list are expected to inform the transplant program of intercurrent illnesses that may affect their transplant candidacy

II. Due to the prolonged wait time for a deceased donor transplant and the high incidence of morbidity in dialysis patients, transplant candidacy needs to be reassessed periodically

III. The timing, frequency, and type of testing depend on comorbid conditions. The local allocation algorithm may predict the timing of transplantation and impact on the schedule of wait-list follow-up; centers that rely primarily on dialysis time may see patients when accrued time approaches expected wait time

IV. Proper vaccination, cancer screening, and other health maintenance should be continued

V. During the follow-up visit, reassessment of cardiovascular status is of utmost importance; routine cardiac rescreening is recommended in moderate- to high-risk patients; new symptoms and signs suggestive of coronary disease should be thoroughly evaluated

VI. Patients with correctable conditions should be made temporarily unavailable until the condition is successfully corrected; those with uncorrectable contraindication should be removed from the waiting list

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