How to Prepare a Chronic Kidney Disease Patient for Transplantation

35

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Before You Start: Facts You Need to Know

- Preparing a patient with CKD for transplantation involves careful evaluation for contraindications of transplantation and potential medical and surgical complications.
- A potential renal transplant recipient (RTR) should be evaluated for underlying cause of ESRD, comorbidities such as obesity and diabetes mellitus, malignancies, infectious diseases, gastroenterological evaluation, urologic disorders, hematologic disorders, and cardiovascular status.
- Evaluation of a potential RTR should be initiated with a thorough medical, surgical, and psychosocial history and a detailed physical examination.
- Pretransplantation workup includes a number of serologic tests and radiologic and immunologic studies.
- HLA alloantibody profile of potential RTRs should be assessed to delineate the antigens regarded as unacceptable for transplantation.
- Immunologic evaluation should include the detection and characterization of clinically relevant antibodies.

35.1 Time for Referring to Transplant

Renal transplantation should be recommended to patients with irreversible advanced chronic kidney disease (CKD). The rate of progression in renal injury among patients with CKD is unpredictable because of underlying various kidney diseases and superimposed acute kidney injury attacks. Therefore, for patients not requiring dialysis, time referring to a transplant program remains unclear (Box 35.1). However, referral to a renal transplant program does not imply immediate transplantation. Patients with CKD stage 4 or a glomerular filtration rate (GFR) less than 30 mL/min/1.73 m^2 should be referred to a transplant program [1]. The 2005 Canadian Society of Transplantation consensus guidelines suggest that transplantation should not be performed unless the GFR is less than 20 mL/min and there is evidence of progressive irreversible deterioration over a period of 6–12 months [2]. Patients with a potential contraindication to transplantation

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Box 35.1. What the Guidelines Say You Should Do: Time for Referring to Transplant

- The timing of transplantation should maximize the use of the patient's own kidneys, but avoid the morbidity and expense of access placement and dialysis treatments [1].
- Potential transplant recipients should be referred for evaluation by a transplant program once renal replacement therapy is expected to be required within the next 12 months [2].
- Preemptive kidney transplantation should not proceed unless the measured or calculated glomerular filtration rate is less than 20 mL/min and there is evidence of progressive and irreversible deterioration in renal function over the previous 6–12 months [2].

should be individually discussed with a transplant center to determine candidacy. Several studies have reported improved patient and graft survival when patients receive their first transplant before the need for maintenance dialysis, although this is not the case for patients who are receiving a second transplant; among the latter, a period of dialysis prior to retransplantation is associated with better patient survival [3].

35.2 Evaluation of a Potential Renal Transplant Recipient

Evaluation of a potential renal transplant recipient (RTR) should be initiated with a thorough medical, surgical, and psychosocial history and a detailed physical examination. History of blood transfusion, pregnancies, and previous transplantation should be assessed for potential risks for sensitization. Previous cardiopulmonary diseases and abdominal operations should be carefully evaluated. In addition to history and physical examination, a number of routine laboratory tests are required. After this information is collected, possible contraindications for renal transplantation in each case should be reviewed.

35.2.1 Contraindications to Transplantation

The main contraindications are infections, malignancies, obesity, and cardiovascular diseases (Box 35.2). Serious cardiac dysfunction and untreatable cardiovascular diseases are absolute contraindications for transplantation. Some guidelines listed cardiovascular contraindications as follows: patients who had a myocardial infarct within the last 6 months, patients with a left ventricular ejection fraction less than 35 %, or patients with a stroke or transient ischemic attack within the past 6 months [4, 5]. Despite the lack of long-term data, the benefits of myocardial revascularization procedures before wait-listing are recommended [5]. Diabetes is not contraindicated unless associated with multiple organ failure or significant cardiovascular complications [6]. It is important to note that diabetics gain survival advantage with transplantation as compared to those remaining on dialysis even though long-term survival of diabetic transplant recipients was poor. Guidelines suggested simultaneous pancreas-kidney transplantation for patients with type 1 diabetes [4, 6, 7]. Obesity is associated with more transplant surgery-related complications; however, it is not an absolute contraindication. However, there are some data suggesting that no benefit from kidney transplantation was noted in patients with a BMI greater than 40. In those patients, diet, exercise, and lifestyle changes have to be recommended to achieve a target body mass index (BMI) of <30 kg/m^2 before transplantation [6, 7]. Active cancer is an absolute contraindication for transplantation. Immunosuppression could accelerate progression of the cancer or early recurrence of malignancy associated with high morbidity and mortality. Patients with previous cancer could be eligible for transplantation, but various cancer-free periods are recommended [4, 6, 7]. If possible, acute or chronic infections should be treated before transplantation. However, in some situations infections such as hepatitis B and C and HIV infections are not completely curable. Therefore in those patients, risks and benefits of transplantation must be carefully considered. Guidelines recommended that patients with active HBV, HCV, and HIV

infection must be individually assessed, and wait-listing is delayed until completing the treatment [2, 6, 7]. Patients with liver cirrhosis from HBV or HCV infection should be wait-listed for a combined liver and kidney transplantation [1, 2, 6, 7]. There are several comorbidities including some metabolic and severe airway and gastrointestinal diseases which may be contraindications for transplantation. Patients with severe primary oxalosis should be recommended for a liver-kidney transplant [1, 2, 7, 8]. Severe Fabry disease and systemic amyloidosis [2], severe chronic obstructive pulmonary disease or cor pulmonale [2], and acute pancreatitis or active inflammatory bowel disease [2, 7, 8] are contraindications for renal transplantation. Cholecystectomy for gallstones and partial colectomy for colonic diverticulitis are recommended before wait-listing [1, 8]. Surgical interventions and treatment with medication are recommended to patients with genitourinary disorders for appropriate urinary tract drainage before transplantation [1, 9, 10]. Smoking cessation is strongly recommended in some guidelines before wait-listing [6]. Evaluation of psychosocial factors is an important aspect of the transplantation workup. Despite the influence of mental illness on treatment adherence; it is not an absolute indication for elimination from the wait list. However, uncontrolled psychosis or psychiatric disorders and active substance abuse are absolute contraindications for transplantation [7, 8].

Box 35.2. Contraindications to Renal Transplantation [4–7]

Untreatable cardiovascular disease
Obesity (BMI >40 kg/m^2)
Active malignancy
Active infection
Life expectancy <2 years
Severe Fabry disease
Severe systemic amyloidosis
Severe chronic obstructive pulmonary disease and cor pulmonale
Uncontrolled psychosis or psychiatric disorders
Active substance abuse
Immunologic barriers (positive T-cell crossmatch)

35.2.2 Medical Evaluation of a Potential Renal Transplant Recipient

35.2.2.1 Age

Advanced age alone is not a contraindication for renal transplantation but age-related comorbidity is an important limiting factor [7]. Many elderly patients (over 65 years old) have been transplanted successfully and with an acceptable rate of long-term graft function. Additionally, global mortality in elderly patients on the wait list is higher than among elderly RTRs. However, those patients have a greater risk of developing concomitant illnesses or neoplasms and limited life expectancy which reduces the potential benefit of transplantation. Therefore, life expectancy is a more important factor rather than identifying a specific age cutoff. Estimated life expectancy of those patients should be longer than predictable waiting time and enough to reveal the benefits of renal transplantation. A recommended criterion is that the patient would be expected to survive for at least 5 years after transplantation [1, 4].

35.2.2.2 Obesity

Obesity is related with increased posttransplant complications, delayed graft function, surgical wound infection, higher mortality (associated cardiovascular complications), and poorer graft survival. Although upper limit of BMI is controversial, no benefit was noted in patients with BMI greater than or equal to 40 kg/m^2 [7]. Therefore, weight reduction to BMI of 30 kg/m^2 or less should be recommended before the transplantation [1, 4, 6, 7]. In particular, obese patients with cardiovascular disease history should not go through the transplantation before an adequate amount of weight loss has been reached.

35.2.2.3 Diabetes Mellitus

Renal transplantation provides the survival benefit in diabetic patients with ESRD as compared to those diabetics on wait list. Pancreas transplantation provides glycemic control and improves the microvascular or macrovascular complications and quality of life of renal transplant recipients. Therefore, the pancreas transplantation should be considered as an alternative to insulin therapy for ESRD patients

Box 35.3. What the Guidelines Say You Should Do: Diabetes Mellitus

- Simultaneous kidney-pancreas transplantation or living donor renal transplantation is the treatment of choice for patients with type 1 diabetes mellitus who are suitable for renal transplantation [7].

with type 1 diabetes who have undergone, or plan to undergo, renal transplantation (Box 35.3). Patients who have a living kidney donor should consider undergoing renal transplantation before considering subsequent, cadaveric, pancreas transplantation [1, 7]. However, cardiovascular diseases are most frequent in diabetic patients and a thorough evaluation is recommended to exclude silent cardiovascular diseases prior to transplantation [2]. Similarly, as a complication of DM, neurogenic bladder is frequently seen in diabetic patients; therefore, a detailed urologic evaluation is recommended before transplant operation [2, 10].

35.2.2.4 Infections

The clinical preparation of a patient prior to transplantation should include exposure history, cultures for colonization, serologic tests, and administration of vaccines. Exposure to several microorganisms that may be activated by immunosuppressive agents after grafting and current latent infections and colonization should be investigated through a detailed history. Travel history for endemic infections (parasitosis, fungal infections, hepatitis viruses, mycobacterium, etc.); employment and hobbies that expose one to pets, soil, and toxins (psittacosis, endemic fungi, atypical mycobacteria); history of sexually transmitted diseases (especially HIV exposure); vaccinations and childhood illnesses; prior surgery such as splenectomy, portosystemic shunting, or sinus surgery; exposure to mycobacterial infection, especially mycobacterium tuberculosis; BCG vaccination; the results of previous tuberculin skin testing or interferon-gamma release assays; and drug and alcohol use should be questioned in each patient [8]. Transplant candidate vaccination is to be checked for hepatitis A, hepatitis B, pneumococcus, diphtheria, tetanus, pertussis, polio, varicella, measles, mumps, and rubella. Laboratory testing should be performed for past infectious exposures and active or latent infections. However, some tests should be applied to selected patients with high-risk factors. Routine and special tests for potential recipients are presented in Box 35.4. Screening for cytomegalovirus (CMV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), tuberculosis, *Treponema pallidum*, Epstein-Barr virus (EBV), human T-lymphotropic virus (HTLV), herpes simplex virus (HSV), toxoplasmosis, strongyloides, and varicella-zoster virus (VZV) is recommended for assessing the risk for posttransplant disorders and prophylactic strategies [7, 8]. Patients with HIV and hepatitis B and C should be evaluated by viral load testing. Testing for latent tuberculosis, or tuberculin skin testing (TST), is recommended despite anergy, which is the most common finding in those patients. Additionally, interferon-gamma release assays (IGRAs) may be useful in the detection of latent tuberculosis. X-ray chest films can also be helpful in determining prior exposure to tuberculosis. Transplant candidates,

Box 35.4. Recommended Laboratory Tests to Evaluate a Potential Renal Transplant Recipient [7, 8]

Urinalysis, urine culture
Serologic examination
Hepatitis A, B, and C
Tuberculosis (tuberculin skin testing or interferon-gamma release assays)
HIV
Cytomegalovirus (CMV)
Epstein-Barr virus (EBV)
Herpes simplex virus (HSV)
Varicella-zoster virus (VZV)
Syphilis (Venereal Disease Research Laboratory [VDRL] or rapid plasma reagin [RPR])
Human T-lymphotropic virus (HTLV)-I and HTLV-II
Urine and feces ova examination for parasites (if serology is positive)

Box 35.5. What the Guidelines Say You Should Do: Infections

- All potential transplant recipients should be tested for prior exposure to viral infections [7].
- HIV per se is not a contraindication for kidney transplantation [6].

who have a history of tuberculosis exposure or recent TST conversion or positive IGRA and who have no clinical or radiologic evidence of active disease should receive antituberculosis prophylaxis. If donor has a history of untreated tuberculosis, prophylaxis should be administered to recipients of transplants [7, 8] (Box 35.5).

35.2.3 Pulmonary Evaluation

There is limited information about optimal pretransplant evaluation of patients with pulmonary diseases. However, the evaluation should be similar to that for the general population who undergo other types of surgery. The 2005 Canadian Society of Transplantation consensus guidelines suggest that patients with home oxygen therapy requirement, uncontrolled asthma, and severe chronic obstructive pulmonary disease/pulmonary fibrosis/restrictive disease should not be candidates for transplantation. Predictive value of FEV1 <25 %, PO_2 room air <60 mmHg with exercise desaturation SaO_2 <90 %, >4 lower respiratory tract infections in the last 12 months, and moderate disease with progression are the criteria for severity of pulmonary disease [2]. The pulmonary complications in smoking patients have been reported to be increased over that of nonsmoker patients. Thus, smoking cessation should be strongly recommended to patients who smoke before transplantation [6].

35.2.4 Cardiovascular Diseases

Patients with ESRD have high prevalence of cardiovascular disease. It is important to optimize the cardiovascular status of the transplant recipient before surgery because of high perioperative risk and posttransplant complications. The stress of surgery and anesthetic agents can stimulate various cardiac events. In addition, perioperative cardiac complications may cause delayed graft function [11]. Interventions such as coronary angioplasty/stenting or coronary artery bypass surgery could also affect the allograft. Therefore, transplant recipients should be evaluated for cardiovascular risk and cardiac interventions prior to transplantation [5, 11] (Box 35.6).

Box 35.6. What the Guidelines Say You Should Do: Cardiovascular Evaluation

- Noninvasive stress testing may be considered in kidney transplantation candidates with no active cardiac conditions based on the presence of multiple coronary artery disease risk factors regardless of functional status [5].
- Kidney transplantation candidates who have a left ventricular ejection fraction less than 50 %, evidence of ischemic left ventricular dilation, exercise-induced hypotension, angina, or demonstrable ischemia in the distribution of multiple coronary arteries should be referred to a cardiologist for evaluation and long-term management [5].

A careful history and physical examination are recommended to recognize active cardiac diseases. In addition, a preoperative resting 12-lead ECG is recommended for potential renal transplantation recipients with or without known cardiovascular diseases. Noninvasive stress testing such as exercise testing or thallium perfusion scintigraphy/dobutamine echocardiography for patients with limited mobility should be considered in asymptomatic patients with multiple cardiovascular risk factors including diabetes mellitus, prior cardiovascular disease, more than 1 year on dialysis, left ventricular hypertrophy, age greater than 60 years, smoking, hypertension, and dyslipidemia [5]. Echocardiography may be considered to identify valvular disease, cardiomyopathy, or systolic/diastolic dysfunction and

pulmonary hypertension [5]. If initial evaluation reveals that transplant candidates have cardiac failure or exercise-induced angina or hypotension or ischemia, those patients should be referred for further cardiological evaluation. Coronary angiography is recommended in patients with strong evidence of ischemic heart disease [5, 8]. Coronary revascularization by surgery or via angioplasty with stent placement should be considered before transplantation. However, the routine prophylactic coronary revascularization is not recommended for patients with stable coronary artery disease [5, 8].

Transplant candidates should be carefully assessed for peripheral vascular disease which may lead to technical complications during transplant surgery. In addition to physical examination of pulse and evaluation of arterial murmurs, abdominal X-ray study is also recommended. A Doppler ultrasonographic study is indicated for patients with signs of arterial occlusion and vascular calcifications. Angiography may be considered in patients with severe peripheral vascular disease for vascular repair before transplantation [10]. Cerebrovascular disease may also be an important cause of morbidity and mortality in patients after transplantation. If transplant candidates are presented with signs or symptoms or vascular calcifications in X-ray study, Doppler ultrasonographic evaluation of supra-aortic trunk is indicated to complete evaluation. Patients with a history of transient ischemic attack should be referred for further neurological evaluation. If carotid surgery is required, it should be applied before transplantation [10].

35.2.5 Malignancies

Active malignancy is an absolute contraindication to transplantation [6]. This contraindication is linked with short survival and/or progression or de novo development of malignancy by immunosuppressive therapy. For patients with a history of malignancy, close consultation with oncology is essential. Minimum disease-free waiting time is required for almost all cancers before transplantation. Waiting time depends on the type of tumor and changes between 1 and 5 years [4, 8, 10, 12] (Table 35.1). For potential transplant recipients, screening is

Table 35.1 Waiting time for neoplastic diseases before transplantation [4, 8, 11, 12]

Neoplastic disease	Waiting time
Incidental renal cancer	No
Bladder cancer (noninvasive papilloma)	No
In situ cervical carcinoma	No/2 years
Basal cell tumor	No/2 years
Squamous cell carcinoma (skin)	No/2 years
Wilms tumor	2 years
Renal cancer if < 5 cm	2 years
Breast carcinoma (stage 0–2)	2–5years
Melanoma (in situ)	2–5years
Bladder carcinoma (invasive)	2 years
Uterine body cancers	2 years
Testicular cancer	2 years
Thyroid cancer	2 years
Lymphoma	2–5 years
Colorectal carcinoma	
Duke A or B1	2–5 years
Duke C	2–5/>5 years
Duke D	2–5/contraindicated
Invasive cervical carcinoma	>5 years
Renal cell carcinoma if >5 cm	>5 years
Breast carcinoma (stages III–IV)	>5 years/contraindicated
Melanoma invasive	>5 years
Multiple myeloma	Contraindicated

Table 35.2 Screening procedures for cancer before transplantation

Organ	Procedure
Renal	Native renal ultrasound to assess for acquired cystic disease or masses
Lung	Chest X-ray
Hematologic	Complete blood count Leukocyte formula Erythrocyte sedimentation rate Immunofixation electrophoresis (>60 years of age)
Colorectal	Abdominal ultrasonography Colonoscopy if >50 years of age
Prostate	PSA for male >50 years of age
Cervical	Pap smear
Breast	Mammogram for women >40 years of age or with family history of breast cancer

Box 35.7. What the Guidelines Say You Should Do: Malignancies

- Current or active malignancy was absolutely contraindicated for wait-listing in adults and children because of "the risk of dissemination and fatal outcome" with exceptions made for small or superficial skin, prostate, or bladder cancers [4].
- Renal transplantation should only be considered in potential recipients with previous malignancy (excluding non-melanoma skin cancer) if there is no evidence of persistent cancer [7].
- Patients with current or previous cancer should be discussed with an oncologist and considered on a case-by-case basis [6].

recommended for renal, colorectal, prostate, cervical, and breast cancer prior to transplant [8, 10, 11] (Table 35.2) (Box 35.7).

35.2.6 Urologic Disorders

Urinary tract pathologies are observed in up to 25 % of all ESRD patients; therefore all potential renal transplant recipients should be evaluated for the presence of urologic disorders [13]. Congenital or acquired anomalies of urinary system should be treated before transplantation. Detailed clinical history and physical examination, microscopic urine sediment examination, and abdominal ultrasound are basic instruments of urologic evaluation. Additional complementary urodynamic studies may be helpful to assess the recurrent urinary infections, micturition dynamics, and residual diuresis. Augmentation cystoplasty and urinary diversion procedures may be required in some patients with dysfunctional bladder. Similarly, prostate resection before transplantation may be necessary in some male transplant recipients with outflow tract obstruction due to prostate hypertrophy. Pretransplant native nephrectomy is not recommended for all patients with autosomal dominant polycystic kidney disease (ADPKD). Recurrent infection, bleeding and/or intractable pain, and enormously enlarged kidneys may be indications for unilateral or bilateral nephrectomy [10, 13].

35.3 Causes of Kidney Disease

Certain kidney diseases have a chance to recur in the posttransplantation period. Although the incidence of recurrence and graft loss are heterogeneous, the reported recurrence rates of kidney diseases after renal transplantation are presented in Table 35.3 [8, 10, 14]. Despite the high risk for some kidney diseases to recur, recurrence rarely causes early graft loss. Therefore, transplantation is generally not contraindicated; however, a waiting time period is recommended for diseases with a high recurrence risk. In patients with antiglomerular basement membrane disease, lupus nephritis, vasculitis, and thrombotic microangiopathy, transplantation is recommended after the disease becomes inactive for 6–12 months on minimum or no immunosuppression [6, 7].

35.3.1 Gastrointestinal Disorders

The potential transplant recipients should be evaluated for gastrointestinal disorders prior to transplantation. Peptic ulcer disease may be aggravated after transplantation; therefore candidates with

Table 35.3 Recurrence and graft loss rate of primary renal disease after transplantation [8, 10, 14]

Disease	Recurrence %	Graft loss %
FSGS	20–40	20–50
IgA nephropathy	20–60	45–70
Membranous GN	10–30	10–50
MPGN type I	20–65	15
MPGN type II	50–100	30
Systemic lupus erythematosus	5–54	7
ANCA-associated vasculitis	9–36	7–30
AA amyloidosis	14	Frequent
Anti-GBM disease	Infrequent	Frequent
Cryoglobulinemia	50	Frequent
Fibrillary glomerulonephritis	43	Frequent
Hemolytic uremic syndrome	60	73
Henoch-Schonlein purpura	15–35	11–13

peptic ulcer should be treated until the lesions disappeared by endoscopic examination before transplantation. In addition, H2 receptor antagonists or proton pump inhibitors should be admitted to all candidates for prophylaxis in the posttransplant period [15]. Cholecystitis or diverticulitis may cause serious morbidity and mortality in immunosuppressed patients [8, 10]. Therefore, transplant candidates should be evaluated by ultrasonography and colonoscopy for the presence of cholelithiasis or diverticulosis. If a potential transplant recipient has cholelithiasis, it may be an indication for cholecystectomy. Similarly, presence of diverticulitis history in a transplant candidate with diverticulosis should be considered as an indication for segmental sigmoidectomy prior to transplantation [8, 10].

35.3.2 Hematologic Disorders

Hematologic pretransplantation workup includes complete blood count, measurement of partial thromboplastin time, and international normalized ratio (INR). Coagulation disorders may cause posttransplantation thrombosis, thereby graft loss. If transplant candidates have history of recurrent miscarriage, arteriovenous thrombosis, hemodialysis graft or fistula thrombosis, lupus, and prior graft thrombosis, they should be screened for activated protein C resistance ratio or factor V Leiden mutation, antiphospholipid antibody, lupus anticoagulation, protein C or protein S deficiency, antithrombin III deficiency, and homocysteine levels. Hypercoagulability is not a contraindication for transplantation; however, anticoagulation therapy is recommended for patients in the perioperative period [8, 9].

35.4 Psychiatric/Psychosocial Evaluation

A psychosocial state of transplant candidates should be evaluated by an experienced competent individual before transplantation. Cognitive impairment, mental illness, nonadherence to therapy, and drug or alcohol abuse are potential problems that might adversely affect the outcome of transplantation. Cognitive impairment is not an absolute contraindication to kidney transplantation. Some individuals with irreversible cognitive impairment may be acceptable candidates for transplantation in the presence of a reliable primary support person who will take charge of administering immunosuppressive medications and monitor compliance with medical follow-up. Patient nonadherence to therapy is a contraindication to kidney transplantation. Renal transplantation should be delayed until patients have demonstrated adherence to therapy for at least 6 months. Alcohol and substance abuse can interfere with a patient's ability to adhere to therapy after renal transplantation. Patients with alcohol and/or substance abuse need to be adequately treated before transplantation. Renal transplantation should be delayed until the patient has demonstrated freedom from substance abuse for at least 6 months. Individuals with a significant mood or anxiety disorder, psychosis, substance abuse, or

a severe personality disorder should be referred for psychiatric diagnoses, treatment, and follow-up to reduce barriers to transplantation. However, active affective disorders are contraindications to transplantation, depression in ESRD can be readily treated, and case reports also demonstrate the successful transplantation in patients with major psychoses, if adequate support and supervision is provided [1, 2].

35.5 Immunologic Evaluation

Pretransplant immunologic evaluation involves a number of immunologic tests before transplantation (Box 35.8). Besides the blood antigens (ABO), human leukocyte antigens (HLAs) are the strongest transplantation antigens and can stimulate a primary immune response. Antibodies against HLA are found in patients who have been immunized by pregnancy, blood transfusion, or a prior HLA-mismatched allograft. The presence of HLA antibodies is associated with antibody-mediated rejection in the early period of transplantation. Patients with HLA antibodies have increased risk of delayed graft function and rejection in the perioperative period. However, in recent years, patients were successfully transplanted with immunologically incompatible grafts (HLA or ABO incompatible) using various desensitization protocols that reduce the preexisting antibody levels in transplant recipients. An increased degree of HLA antigen mismatching is associated with a greater risk of chronic graft loss and short graft survival, although not early rejection. Therefore, tests for blood and HLA typing and for antibodies to lymphocyte antigens are recommended to potential transplant recipients before transplantation [6, 16–18] (Box 35.9).

Box 35.8. Immunologic Tests Before Transplantation

For Patients on Wait List

Blood antigens (ABO) typing
Human leukocyte antigen (HLA) typing
HLA antibody detection
PRA
Donor-specific antibody (DSA) determination by single-antigen bead assays

For Patients with a Known Potential Donor

Crossmatches by CDC, ELISA, flow cytometry, Luminex

Box 35.9. What the Guidelines Say You Should Do: Immunologic Evaluation

- High immunologic risk is indicated when there are high titers circulating antibodies specific for mismatched donor HLA antigens present at the time of transplantation [18].
- A patient's HLA alloantibody profile must be assessed to delineate the antigens regarded as unacceptable for transplant [18].
- A pretransplant crossmatch should be performed for all patients unless a program exists for identifying those individuals who can confidently be defined as sensitized.
- Patients with no detectable HLA-specific antibodies can be transplanted on the basis of a negative virtual crossmatch (vXM) without waiting for a crossmatch test to be performed [18].
- Serum samples of patients in wait list must be sent to the histocompatibility laboratory no less than three monthly for routine antibody monitoring and also following transfusion of any blood products [18].
- ELISA technology is more sensitive than complement-dependent cytotoxicity (CDC), whereas Luminex bead technologies are more sensitive than both CDC and flow cytometry, enabling the detection of low levels of HLA-specific antibody [17].

Panel-reactive antibody (PRA) defines the presence of HLA antibodies and sensitization against the potential donors. Complement-dependent cytotoxicity (CDC) and the enzyme-linked immunoabsorption (ELISA), flow cytometry, and Luminex-based assays can be used to determine the PRA. When a potential donor is known, a test called crossmatch (XM) which evaluates for any evidence of preformed antibodies with specificity for potential donor is recommended for prevention of hyperacute or acute antibody-mediated rejection. Different techniques included CDC with antihuman globulin (AHG) or dithiothreitol (DTT) and flow cytometry and ELISA and Luminex are available assays which differ in their degree of sensitivity. Recently, a highly sensitive screening technique as single-antigen bead assay has been introduced. This technique can provide virtual crossmatch and immunologic risk assessment for transplant recipients before transplantation. HLA antibody screening and donor-specific antibody (DSA) determination should be regularly performed by PRA tests or single-antigen bead assays especially in highly sensitized patients. CDC T- and B-cell AHG crossmatch are usually recommended for all allograft recipients in many centers. When CDC XM is positive, the process should be repeated with addition of DTT. CDC-positive/DTT-negative test should not prevent transplantation. The result of a CDC-positive/DTT-positive test is a contraindication to transplantation unless donor-specific antibodies (DSAs) can be reduced with desensitization protocols. Flow cytometry can be used as a crossmatch test and is routinely performed in some centers; however, T- and B-cell flow crossmatch are recommended for highly sensitized potential recipients with a history of a positive PRA or with a previous transplant history in others. Despite that the setting of a positive flow crossmatch with negative CDC XM is associated with increased risk for acute antibody-mediated rejection, it is not a contraindication to transplantation. Similarly, if DSA positivity is present in single-antigen bead assay but the CDC XM is negative, this should be interpreted as an increased immunologic risk; however, it is not an absolute contraindication to transplantation especially after elimination of DSA by desensitization [6, 16–18].

35.6 Follow-Up in the Wait List

Transplant candidates on wait list should be ready for transplantation at any time. Therefore, dialysis nephrologists and potential transplant recipients themselves must inform the transplant programs about major developments in the patient's health that could be relevant to their transplant candidacy. Standard health maintenance screening is required, together with the routine updating of serologic and other blood test results that may be relevant to the pre- and/or posttransplant management. Patients considered to be low risk on wait list should be reevaluated at least every 2 years. Annual screening for coronary artery disease (CAD) is required for patients accepted to be at high risk because of previously documented CAD, diabetes mellitus, advanced age, or obesity. Patients with obesity are frequently requested or required to lose weight in order to be listed on the wait list or maintain their active status. Those patients should be also encouraged to engage in frequent physical activity [2, 19]. Patients on wait list may be sensitized by the development of antibodies against histocompatibility antigens as a result of blood transfusion, pregnancy, and prior failed transplants. A patient's HLA alloantibody profile must be assessed to delineate the antigens regarded as unacceptable. Therefore, pretransplant samples should be obtained and tested at three monthly intervals and after known sensitizing events [18] (Box 35.10).

Box 35.10. Relevant Guidelines

1. *American Society of Transplantation Guideline*: The evaluation of renal transplantation candidates: clinical practice guidelines. Am J Transplant. 2001;suppl 1:5–95 [1]. https://www.unitedhealthcareonline.com
2. *Canadian Society of Transplantation Guideline*: Consensus guidelines on eligibility for kidney transplantation. CMAJ. 2005;173:S1 [2]. https://www.cst-transplant.ca
3. *UK Renal Association Guideline*: Clinical practice guideline on the assessment of the potential kidney transplant recipient. Nephron Clin Pract. 2011;118:c209 [7]. https://www.renal.org/guidelines
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7. *The European Renal Best Practice* (*ERBP*) *Guideline*: Management of donor and recipient of kidney transplant in the peri-operative phase (including preparation and acceptance of living donors). Nephrol Dial Transplant 2013;28: ii1–71[6]. https://www.european-renal-best-practice.org

Before You Finish: Practice Pearls for the Clinician

- Advanced age is not a contraindication to transplantation.
- Kidney transplantation is not beneficial in potential RTR with BMI greater than or equal to 41 kg/m^2.
- Renal or combined kidney-pancreas transplantation provides significant survival advantage to diabetic patients.
- Cardiac interventions such as coronary angioplasty/stenting or coronary artery bypass surgery to transplant recipients with coronary artery disease should be performed before transplantation.
- Regardless of no clinical or radiologic evidence of active tuberculosis, potential RTRs, who have a history of tuberculosis exposure or recent TST conversion or positive IGRA, should receive antituberculosis prophylaxis.
- Minimum disease-free waiting time is required for almost all cancers before transplantation.
- Pretransplant native nephrectomy is not recommended for all patients with autosomal dominant polycystic kidney disease.
- Despite the high risk for some kidney disease to recur, recurrence rarely causes early graft loss.
- Hypercoagulability is not a contraindication for transplantation; however, anticoagulation therapy is recommended for patients in perioperative period.
- The result of a CDC-positive/DTT-positive test is a *contraindication* to transplantation unless donor-specific antibodies (DSAs) can be reduced with desensitization protocols.

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