Chronic and End-Stage Renal Disease and Indications for Renal Transplantation

5

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Introduction

Chronic kidney disease (CKD) is the ninth leading cause of mortality in the United States (USA) [1]. CKD is defined by changes in kidney structure or function, as evidenced by imaging abnormalities, albuminuria (≥30 mg/g), and/or a reduced estimated glomerular filtration rate (eGFR) of less than 60 ml/minute/1.73 m^2 for 3 months or more [2, 3]. The Kidney Disease Improving Global Outcomes (KDIGO) group classifies CKD by stage according to eGFR and albuminuria (see Table 5.1) [3]. Of note, end-stage renal disease (ESRD) is an administrative term in the United States, based on the conditions for payment for healthcare by the Medicare ESRD Program, specifically the level of eGFR and the occurrence of signs and symptoms of kidney failure necessitating initiation of treatment by replacement therapy. ESRD includes patients treated by dialysis or transplantation, irrespective of the level of GFR.

The progression between CKD stages is variable, however it generally takes years for one to reach stages 4 and 5. Rapid onset and progression is possible, such as with rapidly progressive glomerulonephritis and in cases where there is additional kidney injury, such as medication nephrotoxicity or sepsis. After reaching stages 5 with uremic symptoms or in cases of severe acute kidney injury, renal replacement therapy (RRT) is usually recommended. RRT includes continuous and intermittent dialysis modalities (i.e hemodialysis and peritoneal dialysis) and kidney transplantation. Continuous RRT can be done via continuous hemodialysis, hemofiltration, or hemodiafiltration; these interventions are done in acute situations, typically during treatment in intensive care unit. Many patients with CKD eventually require intermittent dialysis (often referred to as "dialysis"), which can be performed at a qualified center or at home (see Chap. 7 for further discussion of dialysis).

Albuminuria alone is an independent risk factor for CKD progression and is associated with increased mortality from cardiovascular disease [4–8]. Increasing stages of CKD carry an incremental risk of mortality [3]. Cardiovascular disease is the leading cause of death in CKD and remains so in patients who receive kidney transplants [9].

Patients with CKD, particularly those who have advanced to ESRD, utilize a disproportionate amount of healthcare resources. According to the United States Renal Data System (USRDS), Medicare expenditure for CKD approached $100 billion in 2015 and $34 billion of that amount was spent on care for patients with ESRD [10, 11]. Despite this, the awareness of CKD remains quite low among individuals who have the disease and the general population [10, 12]. Nearly half of patients with advanced stages of kidney disease are unaware of having CKD [12]. Patients may be aware of having diabetes or hypertension, and though they may have concurrent albuminuria and/or reduced eGFR, they often do not make the association that they have CKD. Many patients who present for transplantation report being unaware of having chronic kidney disease until they were near or had reached ESRD. Early referral from primary care providers to nephrology helps to bridge this gap and allows for patient education and dialysis planning. The general consensus is to refer patients with stage 3 CKD to nephrology. Early referral to nephrology allows for early referral to a kidney transplant center, which helps facilitate preemptive (i.e., transplant prior to needing dialysis) kidney transplantation. Transplanting patients just before they require dialysis is associated with better allograft and patient survival outcomes [13–15]. Given the extensive workup needed for kidney transplant (discussed later), early referral also allows patients time to complete required studies prior to transplantation.

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Table 5.1 Classification and prognosis of chronic kidney disease by GFR and albuminuria categories [3]

eGFR categories (ml/min/1.73m^2)			Albuminuria categories (mg/g)		
			A1 Normal to Midly increased	A2 Moderately increased	A3 Severely increased
			< 30 mg/g	30-300 mg/g	> 300 mg/g
G1	Normal or high	≥ 90			
G2	Mildly decreased	60-89			
G3a	Mildly to moderately decreased	45-59			
G3b	Moderately to severely decreased	30-44			
G4	Severly decreased	15-29			
G5	Kidney failure	<15			

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk

2012 KDIGO guidelines incorporate prognosis as predicted by accompanying albuminuria. Abbreviations: *eGFR* estimated glomerular filtration rate. Source: Adapted from: http://kdigo.org/home/guidelines/ckd-evaluation-management/

Epidemiology

According to the USRDS, the prevalence of CKD was 14.8% between 2011 and 2014 [10]. This number has been relatively stable over the past 2 decades and translates to approximately 30 million Americans with CKD. In 2015, the adjusted prevalence of patients on dialysis was 2128 persons per million/year, and there were 124,114 new ESRD cases with an adjusted incidence rate of 357 persons per million/year. Prevalent ESRD cases continue to rise due an aging population and increased patient survival on dialysis. In the United States, the vast majority of patients requiring renal replacement therapies are on hemodialysis compared to peritoneal dialysis and kidney transplantation. In 2015, among prevalent ESRD patients, 63.2% were on hemodialysis, 7.0% were on peritoneal dialysis, and 29.6% had received kidney transplants [10].

There are racial and ethnic differences in the prevalence and incidence of CKD. In 2015, the adjusted incidence rate ratio for ESRD compared to Caucasians was 3.0 for African Americans, 1.2 for American Indians/Alaska Natives, and 1.0 for Asians [10]. All groups experienced a decline in incidence rate over a 15-year period. The incidence rate ratio in Native Hawaiians/Pacific Islanders was 8.4; however, due to the significant discrepancy in this race designation in the US Census data versus USRDS, this data is inconclusive. In African Americans, the excess risk of ESRD is attributed to inheritance of apolipoprotein L1 (APO-L1) gene variants. Carrying two risk alleles confers a tenfold higher risk of ESRD from hypertension and a 17-fold higher risk from focal segmental glomerulosclerosis (FSGS) [16]. The APO-L1 risk alleles are found predominantly in people with West African Ancestry. Having one risk allele is reported to protect against *African Trypanosomiasis* similar to protection from Malaria seen in heterozygote carriers of the sickle cell gene [17].

Mortality among patients on dialysis decreased by 28% between 2001 and 2015. Adjusted mortality rates were 136, 166, and 29 per 1000 patient-years in ESRD, dialysis, and transplant patients, respectively [10]. In Medicare patients, the mortality rate among CKD patients is more than twice higher than that of patients without CKD at 109.8 per 1000 patient-years. CKD patients also experience higher rates of re-hospitalization compared to patients without CKD [10].

Etiologies of CKD

Diabetes and hypertension are the two leading causes of CKD in the United States and other developed countries [10]. The etiology of ESRD from diabetes and hypertension is often presumptive as it is not typical to obtain biopsies in these patients. Nonetheless, 40% of patients with CKD have diabetes and 32% have hypertension [10]. Advancing age is the largest predictor of low eGFR, while hypertension is the largest predictor of albuminuria [10]. Figure 5.1 shows the etiologies of incident ESRD based on data from USRDS [10].

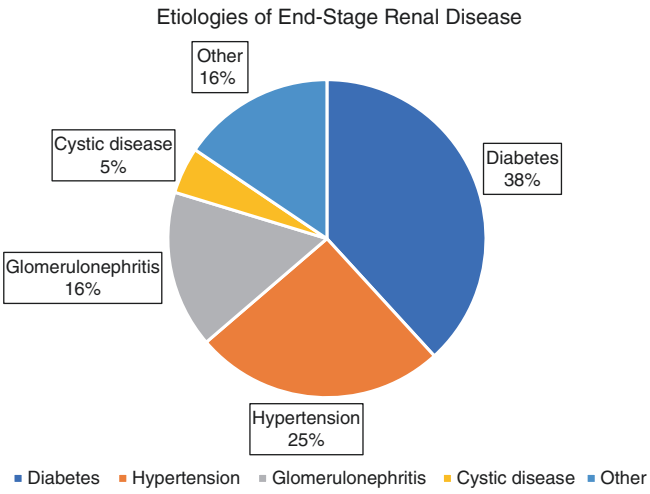

Fig. 5.1 Etiologies of incident ESRD according to 2015 USRDS data [10]

Table 5.2 Recurrence rates of kidney disease after transplant

Disease	Risk of recurrence	Risk of graft loss at 5–10 years
Primary FSGS	20–40%	20–30%
Membranoproliferative glomerulonephritis (MPGN) type I (monoclonal and polyclonal IgG)	20–60%	10–50%
MPGN type II (C3 glomerulopathy and dense deposit disease)	50–90%	10–50%
Membranous nephropathy	10–55%	20–50%
IgA nephropathy	50–60%	2–20%
Lupus nephritis	2–40%	15%
Anti-GBM disease	<5–50%	5%
Atypical hemolytic uremic syndrome	30–50%	>50%
Amyloidosis	25%	Rare
Primary hyperoxaluria	100%	80%

Glomerulonephritis or glomerular disease is the third leading cause of ESRD in the United States [10]. A study looking at the temporal and geographic trends in 21,374 biopsy-proven cases between 1986 and 2001 found that focal segmental glomerular sclerosis accounted for 25%; membranous nephropathy, 13%; lupus nephritis, 12.5%; IgA nephropathy, 10%; pauci-immune glomerulonephritis, 8%; minimal change disease, 5%; and membranoproliferative glomerulonephritis, 3% of cases of glomerular disease [18]. Glomerulopathies recur at variable time periods post-transplant and are an important cause of allograft loss/failure, particularly in living donor recipients [19].

It is important to know the cause of kidney disease due to the risk of disease recurrence in the transplanted kidney (see Table 5.2) [19–21]. This allows the transplant provider to counsel patients about their disease-specific risks. Some kidney diseases (e.g., primary FSGS and C3 glomerulopathies) can recur aggressively early and lead to allograft loss. The rates of disease recurrence and risk of graft loss reported in the litterature is variable based on different study design used and ascertainment and followup timeframes. This information is particularly important for patients with living donors.

Complications of Advanced Kidney Disease

Anemia

In advanced stages of kidney disease, anemia is caused by reduced erythropoietin production and shortened lifespan of red blood cells [22, 23]. The use of erythropoietin stimulating agents has greatly reduced the need for blood transfusions in the dialysis population [24]. Limiting sensitizing events is paramount in patients who are likely to need a kidney transplant. Sensitizing events (e.g., transfusions, pregnancies, prior transplants) increase the chance of developing panel reactive antibodies (PRA) to the general population. Patients with greater sensitization have smaller pools of available donors. Patients with PRA greater than 20% are considered sensitized, and those with PRA greater than 80% are considered highly sensitized. Previously patients who were considered highly sensitized had disproportionately long waitlist times. In December 2014, the US organ allocation rules changed to allow a sliding scale of points based on PRA. In addition, patients who are hypersensitized with PRA of 99 and 100 gained access to regional and national organ sharing, respectively.

Acid-base Imbalances

Patients with advanced stages of kidney disease tend to develop a chronic metabolic acidosis. Treatment of chronic metabolic acidosis with bicarbonate supplementation may mitigate uremic bone disease, malnutrition, and muscle wasting and may help slow the progression of kidney disease [3, 25–27]; however, the level at which supplementation should be initiated and whether to target a normal serum bicarbonate level is somewhat controversial in the nephrology community. The KDIGO group recommends treating chronic metabolic acidosis with bicarbonate supplementation to achieve serum bicarbonate levels above 22 mmol/L [3].

Electrolyte Imbalances

Hyperkalemia is the more common and feared electrolyte abnormality in patients with CKD as it may lead to fatal cardiac arrhythmias [28]. Chronic exposure to a high-potassium milieu raises the threshold at which cardiac arrhythmias occur, such that many dialysis patients adapt to serum potassium of greater than 6.0 mmol/l without the clinical consequences, levels that could pose a significant risk if acutely developed. As kidney disease progresses, patients are prone

to hyperkalemia due to oliguria, high-potassium diet, and/or the use of medications that induce a hypoaldosterone state (e.g., renin-angiotensin system blockers) [29].

Hyperkalemia is treated by adhering to a low-potassium diet, the use of potassium-binding resins (e.g., Kayexalate and Patiromer), discontinuing renin-angiotensin-aldosterone-system-blocking medications, and dialysis.

Hyponatremia is another common electrolyte abnormality in advanced CKD, and it is often caused by impaired free water excretion as eGFR declines. Hyponatremia may be confounded by a concurrent syndrome of inappropriate antidiuretic hormone secretion (SIADH) and/or hypervolemic states. It is important to decipher the exact etiology of hyponatremia and chronicity to determine appropriate treatment.

Mineral Bone Disease

Mineral bone disease (MBD) occurs from derangements in the phosphorus-calcium-parathyroid hormone axis that occur in advanced kidney disease [30]. Manifestations of MBD include osteitis fibrosa, osteomalacia, and adynamic bone disease. As kidney function declines, serum phosphorus rises and calcium decreases (due to decreased production of activated vitamin D by the kidney). The rise in phosphorus is initially mitigated by an elevated fibroblast growth factor (FGF)-23 level and then rising parathyroid hormone (PTH), both of which are phosphatonins [31]. The rise in PTH helps to normalize both phosphorus and calcium. This process leads to a development of secondary hyperparathyroidism. Treatment includes adhering to a low-phosphorous diet, taking phosphate binders with meals, and using active vitamin D analogs (e.g., calcitriol) and calcimimetics (e.g., Sensipar) [32, 33]. A selected number of patients with secondary hyperparathyroidism go on to develop tertiary hyperparathyroidism requiring parathyroidectomy. Some transplant centers require patients with uncontrolled hyperparathyroidism undergo parathyroidectomy prior to kidney transplantation. However, kidney transplantation alone may restore the calcium-phosphorous-PTH axis and lead to resolution of secondary hyperparathyroidism within several months. Patients with persistent hyperparathyroidism after kidney transplantation may then be referred for parathyroidectomy.

Hypertension and Volume Overload

Patients with advanced CKD are less adapt to changes in sodium and volume expansion. With development of oliguria or anuria, management of volume overload is quite challenging and may require near daily dialysis in some patients. Fluid restriction is paramount for reduction of intradialytic weight gains but is challenging for many patients. In these more challenging cases, longer (4 hours or more) and/or frequent (4 days a week or more) dialysis may be needed for volume management. To enable more aggressive ultrafiltration (fluid removal on dialysis), nocturnal dialysis or home hemodialysis modalities can accommodate longer or more frequent dialysis sessions in patients who can manage the timing, training, and equipment. Other treatment options include sodium restriction (< 2 grams per day), fluid restriction, and diuretics in patients who are not auric [3, 34].

Malnutrition

Malnutrition is a common consequence of advanced CKD [35]. Patients with CKD have diminished appetite and anorexia which is confounded by many dietary restrictions (e.g., sodium, potassium, phosphorus), and they lose amino acids in dialysate fluids. Renal dieticians are available in many kidney clinics and the US dialysis centers to help with frequent education and recommendations about diet.

Kidney Transplant Evaluation

Indications

Kidney transplant is an elective procedure and it is not without risks; nonetheless, it is the treatment of choice for stage 5 CKD/ESRD [20, 36]. Compared to dialysis, kidney transplantation improves quantity and quality of life. Unlike other solid organ transplants where the sickest patients get transplanted first, priority for kidney transplants is largely based on the waiting time and sensitization status.

Patients can receive transplants from a living donor or a deceased donor. The average waiting time for deceased donor kidney transplantation in the United States depends on geography, blood type, and sensitization status and ranges from 3 to 10 years, thus transplantation from an eligible living donor represents a much faster path [37]. Given the impact of dialysis vintage (i.e., length of time on dialysis) on outcomes, this is an important consideration. In December 2014, the United Network for Organ Sharing (UNOS) implemented a new kidney allocation system to improve equity and fairness for disadvantaged groups: highly sensitized patients, ethnic minorities, blood group B patients, and patients who experience late referral [38].

Timing of Referral

Patients with CKD are eligible for kidney transplant listing if they are on dialysis or if their eGFR is 20 ml/min/1.73 m^2

or less [38]. At this eGFR, patients are generally asymptomatic, and many do not develop symptoms that would require dialysis until eGFR falls below 12–15 mL/min/1.73m^2. The optimum timing for kidney transplant in patients who are not yet in ESRD is not defined. The goal is to wait for as long as possible such that the timing occurs right before uremic symptoms and complications develop. There is no survival (patient or graft) benefit to transplantation well in advance of the need for dialysis. The new kidney allocation system allows for backdating wait time to the dialysis start date [38]. This mitigates the disadvantage to patients who qualified for kidney transplantation but were referred late. A patient who had been on dialysis for 5 years at the time of referral would automatically get 5 years of waiting time.

Medical Evaluation

A comprehensive medical history, physical examination, laboratory and diagnostic studies (see Table 5.3), and psychosocial assessment are crucial in evaluating patients for kidney transplantation [39, 40]. The goal of the evaluation process is to detect conditions or disease that would make patients ineligible for transplantation. There are few absolute contraindications to kidney transplantation and these are represented in Table 5.4. In areas of the country where the waiting time is long, it is reasonable to undergo a limited workup to see if patients can be listed in their current state and defer the more extensive workup until the patient is closer to transplantation. In areas of the country with long waiting times, yearly updates and follow-up clinic visits closer to the time of transplant is often needed to ensure patients remain medically and psychosocially suitable for transplantation.

Table 5.3 Comprehensive workup for kidney transplantation. Limited life expectancy minimizes the potential benefit of transplantation

Blood type, complete blood count, comprehensive metabolic panel, coagulation studies
Infectious serologies: HIV, RPR, hepatitis B and C, varicella, EBV, CMV, gold quantiferon, and endemic fungi (e.g coccidioidomycosis, cryptococcus, and histoplasmosis) in applicable regions
Anti-A isoagglutinin titers should be measured in blood type B candidates who are willing to accept a kidney from an A2 or A2B donor
Chest X-ray
Cardiac screening with EKG, stress testing (pharmacologic echocardiography), myocardium perfusion scan or coronary angiogram as determined based on age and comorbid conditions
Age appropriate cancer screening as recommended by the USPSTF and cancer societies for the general population
Other testing determined based on clinical history, e.g., random drug screen in patients with a history of substance abuse

Table 5.4 Absolute contraindications to kidney transplantation

Active ischemic heart disease or severe cardiomyopathy
Severe peripheral vascular disease involving iliofemoral vessels
Active infection
Recent history of cancer other than non-melanoma skin cancers and carcinoma in-situ
Cirrhosis or advanced liver fibrosis (unless liver transplant candidate)
Primary oxalosis (unless liver transplant candidate)
Active psychosis
Active substance abuse or dependence
Incorrigible noncompliance
Body mass index (BMI) > 40
Lack of adequate social/caregiver support

Factors to Consider During the Evaluation Process

Age

There is no age limit for kidney transplantation; however, in general, patients over the age of 65–70 should be "well otherwise" (i.e., wow), with well-managed comorbidities. The benefits of transplantation should outweigh the risk of surgery, anesthesia, and chronic immunosuppression. With appropriate patient selection, those over the age of 70 do well with good long-term graft outcomes. Older patients or those with an expected post-transplant survival of around 5 years or more can be good candidates for deceased donor kidneys with a kidney donor profile index (KDPI) of 85% or higher, which can achieve satisfactory graft outcomes [41]. The KDPI is composed of ten donor factors (age, diabetes, hypertension, race/ethnicity, height, weight, creatinine, cause of death, donation after cardiac death (DCD) status, and hepatitis C status) and is a marker of organ quality. A KDPI of 85% percent has 85% higher expected risk of allograft failure compared to all kidney donors from the prior year. The estimated post-transplant survival is a score composed of four factors (diabetes, hypertension, prior transplant, dialysis vintage). Lower estimated post-transplant survival (EPTS) scores translate to higher post-transplant survival. Patients with scores of 20% or less primarily receive offers from KDPI kidneys of 20% or less. The KDPI and EPTS scores are used in the organ allocation system to help improve longevity matching, i.e., kidneys with the longest chance of survival go to the patient with the longest life expectancy [38].

Considering expected post-transplant survival in the evaluation process helps with counseling patients regarding staying on dialysis versus moving toward transplantation. Patients should be expected to survive longer than the half-life of a transplanted kidney. For older patients, it is also important to consider that the risk of death rises in the immediate postoperative period and is higher than in patients who are waitlisted for transplant. It takes about 3.5 years for the

mortality rate to drop below that of patients who remain on the waiting list [42]. Older patients may have acceptable quality of life on dialysis and may not experience a survival benefit with transplantation [43].

Cardiovascular Disease

The burden of cardiovascular disease is high in CKD patients [44, 45]. Noninvasive cardiac testing has limited utility in patients with CKD who have diabetes. Noninvasive testing (e.g., stress echocardiogram) is permissible in asymptomatic low-risk patients; however, higher-risk patients (i.e., those with diabetic nephropathy or long-standing diabetes, over the age of 50, with risk factors for coronary artery disease such as smoking, hypertension, hyperlipidemia, family history, or heart failure with reduced ejection fraction) should undergo coronary angiogram [46–48].

Cerebrovascular Disease

There is an increased risk of ischemic stroke in CKD after kidney transplantation [49]. Patients with history of ischemic stroke should undergo screening for carotid stenosis and repair. Patients with risk factors for stroke (e.g., hypertension, smoking, hyperlipidemia, transient ischemic attacks) or carotid artery bruits on physical examination should be evaluated. Patients with autosomal dominant polycystic kidney disease who have a family history of strokes, cerebral aneurysms, or chronic headaches should undergo screening to assess for cerebral aneurysms, and those who meet the size criteria should be repaired prior to kidney transplantation [50].

Peripheral Vascular Disease

The vascular physical examination is a crucial part of the kidney transplant evaluation. Kidney transplantation can be technically impossible in patients with severe vascular calcifications involving the iliofemoral system. Bilateral femoral and pedal pulses should be palpated. Patients with reduced or non-palpable pulses should have imaging to assess their vasculature (e.g., Doppler studies or non-contrast computed tomography (CT) of the abdomen/pelvis). Patients with severe distal stenosis are at risk for steal syndrome (i.e., shunting of blood flow leading to reduced distal perfusion) with a transplant and can risk limb loss, ulcer development, and/or poor wound healing. Patients with claudication symptoms should undergo evaluation and repair of flow-limiting stenosis.

Malignancy

All patients should undergo age-appropriate cancer screening as recommended by the United States Preventative Services Task Force (USPSTF) and professional cancer societies. Immunosuppression increases the risk for cancers in kidney transplant patients. Patients who have been treated for certain malignancies and remain disease-free for 2–5 years (depending on the type of cancer) may proceed to kidney transplantation (see Table 5.5) [51, 52].

Table 5.5 Cancer waiting period

Renal cell cancer	
Symptomatic < 5 cm	2 years
≥ 5 cm or invasive	5 years
Incidental (< 5 cm)	None
Wilms' tumor	2 years
Bladder	
In situ or noninvasive papillomas	None
Invasive	Inadequate evidence
Cervix	
In situ	None
Invasive	2–5 years
Uterus	2 years
Testis	2 years
Thyroid	2 years
Kaposi's and other sarcomas	2 years
Breast	2–5 years
Colorectal	2–5 years
Prostate	2 years
Liver	Contraindicated
Myeloma	Contraindicated
Lymphoma	2 years
Leukemia	2 years
Melanoma	5 years
In situ	2 years
Non-melanoma skin cancer	None
Lung	5 years

Adapted from Kasiske et al. [40] and Pham et al [36]

Hematologic Disease

Patients with a history of recurrent miscarriage, arterial/venous thrombosis, hemodialysis graft or fistula thrombosis, lupus, or a prior history of unexplained kidney allograft thrombosis should undergo a hypercoagulable workup [20, 37]. Hematology referral may be needed to assess thrombosis risk prior to transplantation. In addition, patients with monoclonal gammopathies or history of paraproteinemias may require hematology evaluation and recommendations regarding risk.

Obesity

Centers vary on their body mass index (BMI) cutoff point at which patients are required to lose weight prior to transplantation. Many centers consider a BMI over 35 kg/m^2 as an absolute contraindication to transplantation [20]. Obese patients are at increased risk for delayed graft function (defined as the need for dialysis in the first week of transplant), poor wound healing, and infections. Obesity is not associated with kidney transplant rejection, graft loss, or death.

Gastrointestinal Disease

Having recent gastrointestinal malignancy or cirrhosis that is not eligible for liver transplant are absolute contraindications to kidney transplant. Patients with evidence of advanced liver disease or cirrhosis should be referred to hepatology for liver transplant evaluation. For advanced stages of liver disease, combined liver-kidney transplant may be an option. Gastrointestinal ulcers should be under control as they may worsen with induction therapy and high-dose corticosteroids. Perforated visicus is a rare but feared complication of ulcers. Patients with chronic nausea and vomiting should be evaluated as these symptoms can worsen and cause patients to be unable to comply with transplant medications which could lead to rejection and allograft loss. In patients with chronic diarrhea and ESRD, hyperoxaluria (excess loss of oxalate in the urine that leads to calcium oxalate stones and crystal deposits) should be considered as a cause for ESRD and ruled out. If this diagnosis is missed, it can lead to rapid loss of a kidney transplant [20, 36]. Primary oxalosis is treated with combined liver and kidney transplantation.

Infection

Patients undergoing kidney transplant should be free of active infection before transplantation [20]. Patients with chronic viral infections like human immunodeficiency virus (HIV) may be transplanted if their disease is under good control. Transplants in patients with HIV should be done at centers with experience managing these patients. The new antiviral mediations for hepatitis C treatment yield excellent sustained viral clearance, making transplantation in this group permissible. This also opens up a pool of hepatitis C donors for hepatitis C positive recipients. Patients with latent tuberculosis should receive an adequate course of treatment (e.g., 9 months of isoniazid) before or after transplantation. For patients who did not complete their course prior to transplant, it is permissible to proceed and complete the course after transplant. Patients with poor dentition should see a dentist for deep cleaning and extractions as indicated prior to transplantation. Oral surgery in the early months post-transplant while immunosuppression is still intense is generally not advised. Although response to vaccination is poor in ESRD patients, live vaccines should be offered when indicated at this time, as they are contraindicated after transplantation.

Frailty

The prevalence of frailty rises with increasing stages of CKD [53–55]. Frailty is associated with increased length of stay, delayed graft function, higher risk of readmission, and mortality in kidney transplant patients [56–58]. Centers use various batteries to assess for frailty (e.g., sit-stand test, walking speed, test, grip strength, Fried criteria, short physical performance battery). Frail patients can undergo pre-transplant rehabilitation to improve outcomes post-transplant. Studies are being done to assess the impact of rehabilitation in kidney transplant recipients on their post-transplant outcomes and survival.

Psychosocial Evaluation

Potential kidney transplant recipients must be motivated to have a transplant. They should be able to understand the risks and benefits of the transplantation and chronic immunosuppression and be able to make an informed decision. Mental health professionals (i.e., social workers, psychiatrists, psychologists) play a crucial role in the evaluation of potential kidney transplant recipients. The goals of the psychosocial evaluation are to determine behavioral, social, and financial barriers to transplantation. This assessment elicits behaviors that may be risk factors for medical nonadherence after transplant. Social workers contact dialysis units to determine patients' adherence with their dialysis appointments and treatments. Many centers insist on absolute adherence with outpatient dialysis regimens in order to consider patients for transplantation. Patient's psychiatric or cognitive disease may require neuropsychiatric assessment and a referral to transplant psychiatry.

Patients who have low literacy concerns or difficulty understanding their medications are referred to pre-transplant education. Transplant centers require that one or two able adults serve as a caregiver(s) in the post-transplant phase. Caregivers help with medication reminders, transportation to appointments, and supervising the patient at home. Patients cannot name their proposed living donor (e.g., a spouse, child, or parent) as a caregiver.

Patients with alcohol or substance abuse may be required to undergo treatment rehabilitation and pass random alcohol and drug screening. Patients with diabetes, peripheral vascular disease, or other risk factors for cardiovascular disease are required to stop smoking to be eligible for transplantation.

Patients require adequate insurance for transplantation. ESRD patients qualify for Medicare based on the disease alone; however, coverage for prescriptions expires 3 years after transplant if the patient does not qualify for Medicare by age. Three years represents a crucial time in the field of kidney transplantation as patients who lose prescription coverage risk rejection and subsequent allograft loss. Many patients with ESRD are on disability. Kidney transplantation should improve quality of life to an extent of enabling patients to return to the workforce, if the patient desires. Patients who return to the workforce may gain insurance coverage with their employer.

Surgical Evaluation

As patients get closer to the top of the list, they may be seen by surgeons to ensure the transplant is technically feasible. Concerning factors from the initial evaluation include known peripheral vascular disease, symptoms of claudication,

history of amputation, and abnormal femoral and distal extremity pulses. These should prompt imaging of the iliofemoral system with a non-contrast CT scan evaluating for vascular calcification or ultrasound imaging evaluating for flow-limiting stenosis. Severe calcification of the iliofemoral system could make surgery technically infeasible.

Living Donation

About one third of kidney transplants in the United States come from living donors [59, 60]. The living donation rate has declined in recent years. Patients who receive living donors generally have immediate allograft function and a longer median survival of approximately 15 years compared to 10 years with deceased donors [59, 60]. Living donors must have a completely separate living donor advocate. Living donors should also undergo extensive medical, surgical, and psychosocial evaluation prior to living kidney donation [59, 60] (see Chap. 4 for more details).

Conclusions

CKD is an important cause of morbidity and the ninth leading cause of mortality in the United States. Diabetes and hypertension remain the most common causes of CKD in developed countries. Complications of advanced stages of CKD include anemia, chronic metabolic acidosis, electrolyte imbalances, volume overload, hypertension, and mineral bone disease. Kidney transplantation is the treatment of choice for patients with Stage 5 CKD and ESRD and leads to better health and cost-effective outcomes compared to dialysis. Nonetheless, kidney transplantation is an elective procedure with both short- and long-term risks and complications. The evaluation process requires the efforts of a multidisciplinary team to ensure appropriate candidate selection.

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