

Summary of the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation

Steven J. Chadban, BMed, PhD,^{1*} Curie Ahn, MD, PhD,² David A. Axelrod, MD, MBA,³ Bethany J. Foster, MD, MSCE,⁴ Bertram L. Kasiske, MD,⁵ Vijah Kher, MD, DM,⁶ Deepali Kumar, MD, MSc,⁷ Rainer Oberbauer, MD, PhD,⁸ Julio Pascual, MD, PhD,⁹ Helen L. Pilmore, MD,¹⁰ James R. Rodrigue, PhD,¹¹ Dorry L. Segev, MD, PhD,¹² Neil S. Sheerin, BSc, PhD,¹³ Kathryn J. Tinckam, MD, MMSc,⁷ Germaine Wong, MD, PhD,¹⁴ Ethan M. Balk, MD, MPH,¹⁵ Craig E. Gordon, MD, MS,¹⁶ Amy Earley, BS,¹⁷ Valerie Rofeberg, ScM,¹⁵ and Gregory A. Knoll, MD, MSc^{18*}

Abstract: The 2020 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation is intended to assist health care professionals worldwide who evaluate and manage potential candidates for deceased or living donor kidney transplantation. This guideline addresses general candidacy issues such as access to transplantation, patient demographic and health status factors, immunological and psychosocial assessment. The roles of various risk factors and comorbid conditions governing an individual's suitability for transplantation such as adherence, tobacco use, diabetes, obesity, perioperative issues, causes of kidney failure, infections, malignancy, pulmonary disease, cardiac and peripheral arterial disease, neurologic disease, gastrointestinal and liver disease, hematologic disease, and bone and mineral disorder are also addressed. This guideline provides recommendations for evaluation of individual aspects of a candidate's profile such that each risk factor and comorbidity are considered separately. The goal is to assist the clinical team to assimilate all data relevant to an individual, consider this within their local health context, and make an overall judgment on candidacy for transplantation. The guideline development process followed the Grades of Recommendation Assessment, Development, and Evaluation (GRADE) approach. Guideline recommendations are primarily based on systematic reviews of relevant studies and our assessment of the quality of that evidence. The strengths of recommendations are provided in the full report. Limitations of the evidence are discussed with differences from previous guidelines noted and suggestions for future research are also provided.

Keywords: albuminuria; adherence; bone and mineral metabolism; candidates; CKD-MBD; clinical practice guideline; cancer; cardiac disease; compatibility; diabetes mellitus; end-stage kidney disease; evidence-based recommendation; gastrointestinal disease; genetic kidney disease; hematuria; hematological disorders; HLA; immunological assessment; infectious diseases; KDIGO; kidney transplantation; liver disease; malignancy; mineral and bone disorder; neurologic disease; obesity; pediatric; perioperative; peripheral arterial disease; pulmonary disease; psychosocial; systematic review; tobacco

(*Transplantation* 2020;104: 708–714).

Received 6 January 2020.

¹ Royal Prince Alfred Hospital and Charles Perkins Centre, University of Sydney, Sydney, Australia.

² Seoul National University, Seoul, South Korea.

³ University of Iowa, Iowa City, IA, USA.

⁴ The Montreal Children's Hospital, McGill University Health Centre, Montreal, Canada.

⁵ Hennepin County Medical Center, Minneapolis, MN, USA.

⁶ Medanta Kidney and Urology Institute, Haryana, India.

⁷ University Health Network, University of Toronto, Toronto, Canada.

⁸ Medical University of Vienna, Vienna, Austria.

⁹ Hospital del Mar, Barcelona, Spain.

¹⁰ Auckland City Hospital, Auckland, New Zealand.

¹¹ Beth Israel Deaconess Medical Center, Boston, MA, USA.

¹² Johns Hopkins University School of Medicine, Baltimore, MD, USA.

¹³ Newcastle University, Newcastle, UK.

¹⁴ University of Sydney, Sydney, Australia.

¹⁵ Center for Evidence Synthesis in Health, Brown University School of Public Health, Providence, RI, USA.

¹⁶ Tufts Medical Center, Boston, MA, USA.

¹⁷ Evidera, Waltham, MA, USA.

¹⁸ The Ottawa Hospital and Ottawa Hospital Research Institute, Ottawa, Canada.

*Guideline Work Group Co-Chairs.

S.J.C and G.A.K contributed to the first draft of the manuscript and have led all subsequent revisions and integrated comments and suggested changes from the entire authorship. All other authors participated in the writing of the KDIGO guideline from which this review article is based.

The need for this guideline originated from the Kidney Disease: Improving Global Outcomes (KDIGO) Executive Committee in consultation with The Transplantation Society and other organizations. A proposed scope of the guideline was developed by the Work Group Co-Chairs with KDIGO staff. The draft scope of work was distributed for international public review in March 2016 and was subsequently revised and finalized based on comments and suggestions received. The Work Group Co-Chairs met with the Evidence Review Team (ERT) to outline key questions amenable to formal evidence review and to determine the literature search strategy. The search was conducted by the independent ERT and two face-to-face guideline Work Group meetings were subsequently held. A draft of this guideline underwent public review in October 2018 and was further revised by the Work Group.

This guideline seeks to inform the evaluation and management of possible candidates for kidney transplantation alone, from either a deceased or living donor, and does not address candidates for combined kidney transplantation with another organ. It covers the time period from the first consideration of the need for kidney replacement therapy to kidney transplant surgery. Adult and pediatric candidates are considered. Education of the candidate and their family is beyond the scope of this guideline; however, we do wish to highlight the essential role of patient education as a requirement to enable shared-decision making and consent regarding the decision to proceed to transplantation or not. We have attempted to be as comprehensive as possible in addressing all clinically relevant conditions that may impact transplant candidacy, but given the rapidly evolving nature of medicine we acknowledge the likelihood of omissions.

The ERT searched Medline, EMBASE, and the Cochrane Library to identify relevant systematic reviews, randomized controlled trials, and observational studies published through August 2017 with supplemental searches performed in May 2019. A total of 45,914 citations were screened based on *a priori* criteria for eligible evidence and of these, 762 were selected for consideration for inclusion. After review of the full-text articles, 190 were included. As reported in the full guideline,¹ recommendations with supporting evidence identified by the systematic review were graded on the strength of recommendation (1 or 2) and on the strength of evidence (A, B, C or D for strong, moderate, weak and very weak, respectively) in accordance with the Grades of Recommendation Assessment, Development and Evaluation (GRADE) criteria.

The guideline Work Group made all recommendations needed to inform cohesive patient care while also explicitly identifying which recommendations were supported

by systematic evidence review and which were not. Recommendations for topics that are not addressed in the formal evidence review were based on other published evidence, newly generated evidence, and Work Group consensus; these guideline statements were “not graded.” They should not be interpreted as being stronger recommendations than Level 1 or 2 recommendations.

This summary provides a brief overview of the guideline recommendations organized by chapters as they appear in the full guideline.¹

SECTION 1: ACCESS TO TRANSPLANTATION

- ✓ All patients with chronic kidney disease (CKD) G4-G5 (glomerular filtration rate [GFR] < 30 ml/min/1.73 m²) who are expected to reach end-stage kidney disease (ESKD) should be informed of, educated about, and considered for kidney transplantation
- ✓ Refer potential kidney transplant candidates for evaluation at least 6 to 12 months before anticipated dialysis initiation to facilitate identification/work-up of living donors and plan for possible pre-emptive transplantation
- ✓ Pre-emptive transplantation with a living kidney donor is the preferred treatment for transplant-eligible CKD patients

As transplantation on average affords superior survival and quality of life at lower cost compared to dialysis, we suggest all potentially suitable candidates should be referred for assessment. Since candidacy assessment (and living donor work-up when available) may take weeks to months, we recommend sufficiently early referral to enable pre-emptive transplantation whenever possible.

For patients with a kidney diagnosis or comorbid illness that may render transplantation futile or more dangerous than dialysis, assessment by disease-specific experts should be sought. Amyloidosis, myeloma and other gammopathies as a cause of ESKD are examples where expert assessment is required and transplantation considered only if experts are supportive, typically following potentially curative therapy. Transplant assessment should generally be deferred in the presence of active infection, other than hepatitis C virus (HCV), or active cancer, other than localized non-melanoma skin, prostate or asymptomatic kidney cancers (< 1 cm diameter). In people with active cancer, candidacy may be considered once potentially curative therapy has been completed and remission achieved. Severe, symptomatic cardiac, respiratory, or liver disease may also warrant specialist assessment and management followed by transplant assessment only if the treating specialist is supportive. The presence of progressive neurodegenerative disease, ongoing substance abuse or unstable psychiatric

S.J.C acknowledges receiving research operating grant support. G.A.K received support from the Canadian Institutes of Health Research.

The guideline upon which this manuscript is based was funded by KDIGO with contributions from The Transplantation Society.

Correspondence:

Steve J. Chadban, Department of Renal Medicine, Royal Prince Alfred Hospital, Missenden Road, Camperdown, NSW 2050, Australia. (Steve.Chadban@health.nsw.gov.au).

Greg A. Knoll, Division of Nephrology, The Ottawa Hospital, Riverside Campus, 1967 Riverside Drive, Ottawa, ON, Canada K1H 7W9. (gknoll@toh.ca).

Copyright © 2020 KDIGO. Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

ISSN: 0041-1337/20/1044-708

DOI: 10.1097/TP.0000000000003137

disease that may compromise transplant outcomes may also preclude or delay assessment of candidacy.

Determination of transplant candidacy is necessarily multifaceted, often involving assessment and synthesis of a range of physical, psychological and behavioral issues. This should be undertaken by a multidisciplinary team including at least a transplant physician, a transplant surgeon, a health care worker experienced in psychosocial assessment, and other professionals as deemed necessary and where available. Patient education and participation in the decision-making process is essential, and where a patient is deemed unsuitable for transplantation, access to a second opinion should be provided.

SECTION 2: AGE

- ✓ Do not exclude patients from kidney transplantation because of age alone but rather consider the context of other comorbidities, including frailty, that may impact outcome when deciding about suitability for kidney transplantation

The survival advantage of transplantation over dialysis persists in the elderly, even in studies evaluating preferential allocation of lesser quality kidneys to older recipients. Given the increasing numbers of older candidates listed for transplantation in many centers, further evidence on the outcomes of transplantation in the elderly, including duration of hospitalization, cost, quality of life and survival are warranted. Development of predictive tools which incorporate multi-morbidity and frailty in addition to age may also improve our ability to assess candidacy, advise patients, and improve outcomes of transplantation.

SECTION 3: PEDIATRIC ISSUES

- ✓ Perform neurocognitive assessment in pediatric candidates who experienced ESKD before the age of 5 years and an academic assessment of those who are experiencing difficulties at school

Abnormalities in cognitive function and academic performance are common in pediatric kidney transplant recipients. Their recognition prior to transplantation may guide expectations for clinicians and caregivers, enable appropriate intervention and support pre- and post-transplantation and assist with pediatric-to-adult transition.

SECTION 4: PSYCHOSOCIAL ASSESSMENT

- ✓ A psychosocial assessment should be performed in all candidates by a health care professional experienced in the psychosocial aspects of kidney transplantation
- ✓ Pre-transplant counseling and services should be offered to candidates with a diagnosable psychiatric or psychological condition, substance use disorder or nonadherence

The primary goal of the psychological assessment is to identify any areas requiring management or support prior to or after transplantation. Transplantation should be deferred in the presence of severe, ongoing psychological disorders, including substance abuse that would likely compromise transplantation outcomes. In such cases, candidacy may be re-evaluated following successful

intervention. Less severe psychological disorders are very common among candidates. Identification may enable provision of appropriate monitoring and support at the time of transplantation and during longer term follow-up, rather than exclusion from candidacy. Further evidence is required as to who should perform the psychological assessment, how it should be performed, and whether clinician rating scales should be used.

SECTION 5: ADHERENCE

- ✓ Assess adherence and adherence barriers pre-transplantation. Appropriate adherence-based education, counseling pre-transplant and post-transplant surveillance should be provided
- ✓ Candidates with a history of nonadherence from kidney transplantation should not be excluded except for those with ongoing, health-compromising nonadherent behavior despite education counseling

Non-adherence to immunosuppression is strongly associated with development of rejection, particularly antibody mediated, and resultant premature graft failure. However, pre-transplant non-adherent behaviors are only weakly associated with post-transplant outcomes. Identification of non-adherent behavior pre-transplant may enable efforts to determine barriers to adherence, provide counseling and increase post-transplant monitoring, but in most cases should not preclude candidacy.

SECTION 6: TOBACCO

- ✓ Assess candidates for past and present use of tobacco products. All candidates should avoid tobacco products before and indefinitely after transplantation
- ✓ Chest computed tomography (CT) for current or former heavy tobacco users (≥ 30 pack-years) to screen for occult lung cancer is suggested and chest radiograph for other candidates

High quality evidence indicates that smokers incur increased risks of perioperative respiratory complications and post-transplant cardiovascular events, cancer and premature mortality. As smoking cessation programs are proven to be more effective than simple advice to quit, smokers should be referred to such programs. Recent studies have provided evidence of superiority of CT over chest radiograph in screening heavy smokers for occult lung cancer, which if found would warrant treatment prior to any further consideration of candidacy for transplantation.

SECTION 7: SURGICAL ISSUES INCLUDING OBESITY

- ✓ Candidate assessment of body habitus, frailty, and medical conditions that could inhibit wound healing, should be performed. Candidates should not be excluded from transplantation solely because of obesity
- ✓ Candidates should not be excluded because of their need for anticoagulation, antiplatelet therapy, or a history of heparin-induced thrombocytopenia
- ✓ Assess vascular anatomy and patency for patients with significant peripheral arterial disease, prior transplant procedures, venous dialysis catheters, pelvic surgery, or deep venous thrombosis

- ✓ Evaluate native kidney size in patients with polycystic kidney disease. Staged or simultaneous native nephrectomy and transplantation may be considered for candidates with a painful, recurrently infected, or potentially malignant polycystic kidney, or if the patient has insufficient room for a transplant

Patients with BMI ≥ 35 kg/m² should be considered for interventions such as dietary counseling or bariatric surgery prior to transplantation. Those with BMI ≥ 40 kg/m² should be approached with caution since there is increased risk for post-operative complications (eg, delayed wound healing).

Risks of perioperative bleeding are increased in patients receiving anticoagulants or antiplatelet agents. Excessive perioperative bleeding may prolong surgery, require transfusions, re-operation and prolonged hospitalization, and may be life-threatening. Pre-transplant knowledge of such therapies will enable proper surgical planning. Use of direct-acting oral anticoagulants or dual antiplatelet therapy incurs the greatest bleeding risks and listing of patients requiring such therapy should only be considered in centers with surgical experience of these agents, and in consultation with hematology and cardiology experts as appropriate.

SECTION 8: DIABETES

- ✓ Candidates with diabetes mellitus, type 1 or type 2, should not be excluded from kidney transplantation
- ✓ Testing for abnormal glucose metabolism by oral glucose tolerance test is suggested in candidates who are not known to have diabetes

Simultaneous kidney-pancreas transplantation provides superior outcomes over kidney alone transplantation for appropriate candidates with type 1 diabetes. Such patients should be referred to a center providing simultaneous kidney-pancreas transplantation when available.

Type 2 diabetes is the most common cause of ESKD worldwide. Survival after transplantation is inferior for those with type 2 diabetes compared to other causes of ESKD. However, transplantation provides a survival advantage over dialysis for most patients with type 2 diabetes. Determining transplant candidacy in patients with type 2 diabetes is therefore a major challenge, typically involving the synthesis of multiple comorbidities all of which may impact transplant management and post-transplant outcomes. Candidacy should not be excluded by diabetes *per se*, but determined after full consideration of comorbid status.

New-onset diabetes is common after transplant and incurs increased risks of cardiovascular events and death. Risk of developing diabetes may be influenced by modifiable factors including choice of immunosuppression. Detection of impaired glucose tolerance by oral glucose tolerance testing prior to transplantation is more predictive of diabetes than fasting blood glucose or HbA1c, so such testing may be considered during candidate assessment to inform risk and management.

SECTION 9: CAUSE OF END-STAGE KIDNEY DISEASE

- ✓ Cause of ESKD in candidates should be determined where possible to inform risks and management after kidney transplantation
- ✓ Candidates with primary focal segmental glomerulosclerosis (FSGS), membranous nephropathy, IgA nephropathy,

IgA vasculitis, immune complex-mediated membranoproliferative glomerulonephritis, C3 glomerulopathy, lupus nephritis, antiphospholipid syndrome, ANCA-associated vasculitis, anti-GBM disease, hemolytic uremic syndrome (HUS), atypical HUS, fibrillary or immunotactoid glomerulonephritis, correctable hyperoxaluria, or those with cystinosis, Fabry disease, sickle cell disease, sarcoidosis, Alport syndrome, systemic sclerosis or AA amyloidosis with no severe extrarenal disease, should not be excluded from transplantation. However, the risk of recurrence should be considered and discussed with the candidate

- ✓ Candidates with multiple myeloma, light chain deposition disease (LCDD), heavy chain deposition disease (HCDD), light and heavy chain deposition disease (LHCDD), or AL amyloidosis should be excluded from kidney transplantation unless they have received a potentially curative treatment regimen and are in stable remission

Recurrent disease is a significant cause of graft failure. However, post-transplant outcomes remain superior to dialysis for the vast majority of people with glomerulonephritis or metabolic diseases that may recur in the allograft. Risk of recurrence and its timing, impact on graft survival and options for prevention, early detection and treatment vary enormously between different diseases. Defining the cause of kidney failure is an essential prerequisite for optimal risk evaluation, patient education and transplant management of candidates with a disease that may recur.

SECTION 10: INFECTIONS

- ✓ Delay kidney transplantation until active infections (bacterial, fungal, viral [except HCV], parasitic) are treated
- ✓ Asymptomatic colonization with bacterial, viral, parasitic or fungal organisms should not preclude transplantation
- ✓ Screen all candidates for infections including human immunodeficiency virus (HIV), HCV, hepatitis B virus (HBV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus (HSV), varicella-zoster virus (VZV), measles, mumps, and rubella (MMR), human T-cell lymphotropic virus (HTLV) and syphilis. Screening for hepatitis D virus (HDV), strongyloides, Chagas disease, tuberculosis (TB), and malaria may be considered in endemic areas
- ✓ Vaccination series recommended for the general and immunocompromised local populations should be completed prior to kidney transplantation. Live attenuated vaccines should be completed at least 4 weeks prior to transplantation
- ✓ Vaccination can be considered for candidates who, due to age, direct exposure, residence or travel to endemic areas are at increased risk for specific diseases such as rabies, tick-borne meningoencephalitis, Japanese encephalitis (inactivated), Meningococcus, *Salmonella typhi* (inactivated) and yellow fever

Infection is a common cause of morbidity and mortality among kidney transplant recipients, particularly in low and middle-income countries. Measures to minimize the risk of infective complications are therefore warranted; however, such measures are greatly influenced by local epidemiology and resources.

Active infections may be accelerated by transplant immunosuppression, therefore diagnosis and treatment prior to transplantation is rational. Cure of infection prior to transplantation is ideal; however, control of infection prior to transplantation coupled with ongoing therapy designed to achieve a post-transplant cure is acceptable

for selected infections, such as peritoneal dialysis exit-site infection. Screen-detected infections, such as occult TB and strongyloides, do not preclude transplantation but may be an indication for treatment to prevent post-transplant disease, subject to local practice patterns and epidemiology. Colonization with multi-resistant organisms is a growing concern which should be used to guide antibiotic choices and strategies to limit spread, rather than to preclude transplantation.

The absence of protective immunity may pose risks of viral infection post-transplant that may be ameliorated by pre-transplant vaccination, particularly in the case of HBV and varicella. The absence of pre-transplant immunity to CMV and EBV carries implications for post-transplant infection and cancer risks and guides prophylactic and immunosuppressive strategies. The presence of infection with HCV, HBV or HIV should not preclude transplantation, but must be known to enable optimal transplant planning and use of antiviral therapies.

SECTION 11: MALIGNANCY

- ✓ All candidates should undergo routine cancer screening, as per local guidelines for the general population
- ✓ Candidates at increased risk for renal cell carcinoma, bladder carcinoma and hepatocellular carcinoma should be screened
- ✓ Candidates with active malignancy should be excluded from kidney transplantation, except for those with indolent and low-grade cancers such as prostate cancer (Gleason score \leq 6), superficial non-melanoma skin cancer and incidentally detected renal tumors (\leq 1 cm in maximum diameter), until in remission following potentially curative therapy
- ✓ Timing of kidney transplantation after potentially curative treatment for cancer is dependent on the cancer type and stage at initial diagnosis. Decisions about transplantation for candidates in remission from cancer should be made collaboratively with oncologists, transplant nephrologists, patients, and their caregivers

Previous guidelines vary in their recommendations for candidates with cancer, most of which are based upon observational registry data and expert opinion. Patients with certain cancers, particularly metastatic melanoma and advanced breast cancer, have traditionally been excluded from transplantation due to low prospects for cure and propensity for late recurrence. Transplant candidacy has been recommended for people with more curable types of cancer, but only after complete remission has been achieved and sustained for an arbitrary period of 2-5 years following receipt of potentially curable therapy. Recent observational data from Norway demonstrating excellent short- and medium-term post-transplant survival following re-listing one year after potentially curative therapy has challenged this dogma. Such data, coupled with recent major advances in genetic diagnosis and therapy in oncology, create great uncertainty in attempting to guide the assessment of the candidate with prior cancer. Data on performance characteristics of screening tests for cancer in people with ESKD, and in risk prediction for outcomes on dialysis versus after transplantation in the context of prior cancer are urgently required in order to advance this field.

SECTION 12: PULMONARY DISEASE

- ✓ Assess candidates with lung disease in collaboration with a pulmonary specialist to determine suitability for transplantation. Pulmonary function testing is recommended in candidates with impaired functional capacity, respiratory symptoms, or known pulmonary disease
- ✓ All candidates should avoid tobacco products before and indefinitely after transplantation
- ✓ Patients with irreversible, severe obstructive or restrictive lung disease should be excluded from kidney transplantation

Candidates with severe, irreversible lung disease and ESKD are at high risk of premature post-transplant death but may benefit from combined kidney-lung or heart-lung transplantation. Such candidates should be referred to centers specialized in multiorgan transplantation where available.

SECTION 13: CARDIAC DISEASE

- ✓ Evaluate all candidates for the presence and severity of cardiac disease with history, physical examination, and electrocardiogram. Patients with signs or symptoms of active cardiac disease should undergo assessment by a cardiologist and be managed according to current local cardiac guidelines prior to further consideration for a kidney transplant
- ✓ Asymptomatic candidates at high risk for coronary artery disease (CAD) (eg, diabetes, previous CAD) or with poor functional capacity should undergo non-invasive CAD screening. Asymptomatic candidates who have been on dialysis for at least two years or have risk factors for pulmonary hypertension should undergo echocardiography. Cardiac imaging should be performed in patients with systemic amyloidosis to ascertain cardiac involvement and severity
- ✓ Candidates with *uncorrectable*, symptomatic NYHA III/IV heart disease [severe CAD; left ventricular dysfunction (ejection fraction $<$ 30%); severe valvular disease] should be excluded from kidney transplantation unless there are mitigating factors
- ✓ Candidates who have had a myocardial infarction should be assessed by a cardiologist to determine whether further testing is warranted and when they can safely proceed with kidney transplantation
- ✓ Cardioprotective medications, including aspirin, β -blockers, and statins, should be continued during waitlisting and at time of transplantation, according to local guidance

Cardiovascular disease is the most common cause of death among patients on dialysis and after transplantation. The incidence of major cardiac events is maximal during the first month after transplantation, associated with the stresses of surgery, fluid resuscitation and high-dose immunosuppression. Pre-transplant assessment has therefore traditionally focused on strategies to prevent events during this period, based upon regularly screening candidates for asymptomatic CAD. Non-invasive screening tests, including exercise stress test, stress echocardiography and MIBI (^{99m}Tc -methoxy-isobutylisonitrile), are only moderately predictive of significant CAD and CAD-related events in the ESKD population. Revascularization of asymptomatic CAD does not reduce risks of mortality for people with type 2 diabetes nor in those undergoing major vascular surgery. There are no contemporary data in ESKD to determine whether

revascularization is helpful or harmful overall; however, the risks of revascularization in ESKD are higher than for the general population.

Given these uncertainties, we have recommended screening candidates deemed to be at high risk for CAD at time of evaluation, in order to guide medical management and inform risk. However, we have not recommended exclusion of candidates with asymptomatic CAD from transplantation. We eagerly await contemporary evidence on the risks and benefits of screening for CAD at transplant evaluation, at regular intervals while waiting for a transplant, and on the utility of coronary revascularization for asymptomatic CAD in ESKD.

Candidates with known CAD should be managed in collaboration with a cardiologist familiar with transplantation. For candidates with recent revascularization or infarction, risks of complications including further ischemic events or arrhythmia are maximal soon after the event and diminish with time. The minimum waiting period before it is safe to undergo kidney transplantation after an event is not well established and should be decided by weighing the risk of vascular events, particularly if transplant listing will require a reduction in antiplatelet therapy, with the risks of delaying access to transplantation.

SECTION 14: PERIPHERAL ARTERIAL DISEASE

- ✓ Evaluate all candidates for presence and severity of peripheral arterial disease (PAD) with history and physical examination. Those without clinically apparent PAD, but who are at high risk for PAD, should undergo non-invasive vascular testing
- ✓ Candidates with clinically apparent PAD should be seen in consultation with a vascular surgeon. Patients with clinically apparent PAD or abnormal noninvasive testing should undergo non-contrast CT imaging of the abdomen/pelvis to evaluate arterial calcification and improve operative planning
- ✓ Candidates with non-healing extremity wounds with active infection should delay transplantation until the infection is resolved. Patients with severe aorto-iliac disease or distal vascular disease should not be excluded from kidney transplantation but risk of progression after transplantation should be considered and discussed with the patient

SECTION 15: NEUROLOGIC DISEASE

- ✓ Assess mental status in candidates with known or suspected cognitive impairment. Candidates with non-progressive intellectual, developmental, or cognitive disability should not be excluded from transplantation
- ✓ Candidates with peripheral neuropathy should not be excluded from kidney transplantation. If such neuropathy can be attributed to uremia, urgent access to transplantation may be considered
- ✓ A suggested waiting time of at least 6 months before kidney transplantation is advised for those who experienced a stroke and 3 months for those with a transient ischemic attack
- ✓ We do not recommend screening asymptomatic candidates for carotid stenoses
- ✓ Screening candidates with autosomal dominant polycystic kidney (ADPKD) disease for intracranial aneurysms may be warranted only if they are at high risk due to prior history of or a family history of subarachnoid hemorrhage

SECTION 16: GASTROINTESTINAL AND LIVER DISEASE

- ✓ Evaluate all candidates for the presence of gastrointestinal disease, including liver disease, with a targeted history and physical examination
- ✓ Candidates with a history of peptic ulcer disease, diverticulitis, acute or chronic pancreatitis, asymptomatic cholelithiasis, or inflammatory bowel disease, should not be excluded from kidney transplantation. For such candidates, delay kidney transplantation until symptoms have resolved
- ✓ Screen kidney transplant candidates for liver disease with a total bilirubin, alanine aminotransferase (ALT), international normalized ratio (INR), and albumin. In the presence of acute hepatitis of any cause, delay kidney transplantation until resolution and a long-term strategy for managing liver disease has been implemented
- ✓ Candidates with cirrhosis or suspected cirrhosis should be referred to a specialist with expertise in combined liver-kidney transplantation for evaluation. We recommend screening for hepatocellular carcinoma in candidates with cirrhosis prior to transplantation using techniques and frequency as per local guidelines

Little evidence exists to support recommendations made in previous guidelines regarding screening asymptomatic candidates for peptic ulcer disease, prophylactic cholecystectomy for candidates with asymptomatic gallstones, prophylactic resection of diverticular disease, or exclusion of candidates with prior pancreatitis from transplantation.

SECTION 17: HEMATOLOGIC DISORDERS

- ✓ Routinely screening for thrombophilia in candidates is not recommended. Screening for thrombophilia should be limited to those who have experienced a venous thromboembolic event, recurrent arteriovenous access thromboses, non-atherosclerotic arterial thrombosis, or family history of venous thromboembolism to identify candidates at higher risk of graft thrombosis
- ✓ Testing for antiphospholipid antibodies (APLAs) may be warranted in patients with systemic lupus erythematosus (SLE) or features of antiphospholipid syndrome (APS)
- ✓ Evaluate transplant suitability of patients with significant cytopenias based on cause and severity, in consultation with a hematologist
- ✓ Candidates with monoclonal gammopathy of undetermined significance (MGUS) or smoldering multiple myeloma should not be excluded from transplantation but a greater risk for post-transplant lymphoproliferative disease (PTLD) and transformation to multiple myeloma, respectively, should be considered and discussed with the patient
- ✓ Patients with leukemia or lymphoma should avoid transplantation until they have received potentially curative therapy, achieved remission and remained cancer free for a period to be determined with their hematologist/oncologist
- ✓ Decisions about kidney transplantation in patients with myelodysplasias, chronic leukemia, chronic/low-grade lymphomas, or prior history of hematological malignancy should be made after consultation with a hematologist

Research into optimal strategies for anticoagulation intra- and perioperatively for candidates with a demonstrated thrombophilia is required. The use of direct-acting oral anticoagulants is rapidly increasing in clinical practice but presents significant difficulties for candidate management at the time of transplantation, due to our current inability to reliably reverse their effects. Our

guideline differs from others in avoiding recommended “waiting times” between completion of potentially curative therapy for hematological cancers and subsequent kidney transplantation. Research is required to validate the approach of transplanting once the transplant clinicians and hematologists agree that a stable remission has been achieved.

SECTION 18: BONE AND MINERAL METABOLISM

- ✓ Measure serum parathyroid hormone (PTH) at the time of transplant evaluation
- ✓ Transplantation for patients with severe hyperparathyroidism should be delayed until they have been adequately treated as per KDIGO CKD-MBD Guideline²

Severe hyperparathyroidism may compromise outcomes through post-transplant hypercalcemia and graft dysfunction. Correction prior to transplantation is therefore advisable. Transplant recipients may experience bone demineralization and are at increased risk of fracture; however, proven strategies to prevent post-transplant fracture are lacking.

SECTION 19: IMMUNOLOGICAL ASSESSMENT

- ✓ Communicate all sensitizing events or clinical events that can impact panel reactive antibody (PRA) to the human leukocyte antigen (HLA) laboratory
- ✓ Perform HLA antibody testing at transplant evaluation, at regular intervals prior to transplantation and after a sensitizing event or a clinical event that can impact PRA

- ✓ HLA antibody testing should be performed using solid phase assays and HLA typing should use molecular methods, optimally at all loci. Routine testing for non-HLA or complement-binding HLA antibodies is not suggested
- ✓ Candidates should be informed about their access to transplantation based on blood type and histocompatibility testing results

The presence of donor specific antibodies, particularly when directed against HLA molecules, is a key risk factor for rejection and consequent graft failure, and is therefore both a key barrier to transplantation and an important piece of information required by clinicians to minimize risk of adverse outcomes.

ACKNOWLEDGMENTS

The authors and KDIGO gratefully acknowledge the financial support from The Transplantation Society which helped make this guideline possible.

REFERENCE

1. Kidney Disease: Improving Global Outcomes (KDIGO) Kidney Transplant Candidate Work Group. KDIGO Clinical Practice Guideline on the Evaluation and Management of Candidates for Kidney Transplantation. *Transplantation*. 2020; 104(4)(suppl):S1–S103.
2. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). *Kidney Int Suppl*. 2017;7:1–59.