REVIEW ARTICLE

Cardiovascular disease and kidney transplantation-evaluation of potential transplant recipient

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KEY WORDS

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ABSTRACT

Cardiovascular evaluation of a potential kidney transplant recipient remains controversial. The burning issue is the lack of clear guidelines as well as the fact that patients with a low probability of cardiovascular disease undergo numerous unnecessary screening procedures and false-positive results are common. In general, the standard procedure involves clinical data collection, physical examination, electrocardiography, chest-X ray, measurement of the lipid profile and fasting glycemia, cardiac ultrasonography, followed by coronary angiography. An exercise tolerance test is not recommended because it has low sensitivity and is difficult to perform and interpret. Cardiac ultrasonography should be performed after a hemodialysis session to avoid an effect on hypervolemia. All noninvasive diagnostic imaging and isotope tests are usually of limited value and, to a large extent, are facility- and operator-dependent. Coronary angiography should be considered in patients with positive exercise tolerance test results and a history of acute coronary syndrome, unstable coronary artery disease, and high cardiovascular risk. However, a decision regarding therapy, ie, percutaneous coronary intervention, stenting (type of stent), or coronary artery bypass grafting should be made during the meeting of a cardiac team. The guidelines also discuss cardiac contraindications to kidney transplantation. It should be stressed that a patient scheduled for a kidney transplant is sick at the time of evaluation and that his or her condition may change after several years on the waiting list. Therefore, cardiac reevaluation may be needed. Preemptive transplantation as well as short dialysis therapy before transplantation (<6 months) are associated with better patient and graft survival and thus with lower incidence of cardiovascular complications and better quality of life. The current review discusses the available guidelines on the evaluation of the potential kidney transplant recipient.

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Cardiovascular disease and kidney disease Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in patients on renal replacement therapy, including kidney transplant recipients.[1] Death from CVD is also the most common cause of graft loss.[2] Mortality associated with kidney transplantation decreased significantly in the 1960s and 1980s owing to a reduction in the incidence of infection-related deaths,[2] while cardiovascular mortality increased. Nowadays, from 50% to 60% of deaths can be directly attributed to CVD, with an incidence of ischemic heart disease being approximately 1 per 100 person-years at risk.[3] In contrast, some older studies reported that between 17% and 50% of deaths in kidney transplant recipients were due to CVD.[4] Moreover, CVD is the most common cause of death in kidney allograft recipients with a functioning graft, and accounts for 30% of overall graft loss from death, with the greatest rates in

the first months after transplantation.[5] It should also be stressed that kidney transplant recipients have a lower risk of fatal and nonfatal cardiovascular events compared with dialyzed patients on the waiting list, but a much higher risk compared with the general population.[6-10] CVD and kidney disease seem to be lethally synergistic and both approach the level of an epidemic. Patients with CVD often have impaired kidney function, while on the other hand, CVD is the best single predictor of mortality in patients with chronic kidney disease (CKD).[11] The risk in a patient with moderately impaired renal function is comparable in magnitude to that of a patient with diabetes mellitus.[12] Even a very successful kidney transplantation would transfer patients from stage 5 CKD into stage 2, very rarely into stage 1, but, in the majority of cases, into stage 3 of CKD.[13] Sarnak and Levey[14] reported that differences in death rates range from an approximately 120-fold difference between patients aged 25 to 34 years, to a 15-fold difference between patients aged 55 to 64 years, and to as much as a 3-fold difference in patients older than 85 years. In general, morbidity and mortality in dialyzed patients is so high that a 5-year survival in patients older than 64 years is worse than that in nondialyzed patients suffering from malignancies. This dramatic difference in cardiovascular deaths between the general population and dialyzed patients has raised the question of whether patients with chronic renal failure have a unique susceptibility to CVD, whether progression of atherosclerosis is accelerated, and whether there are particular factors predisposing to CVD in this population.[15] Importantly, apart from traditional risk factors for CVD established in the Framingham Heart Study (age, male sex, hypertension, elevated low-density lipoprotein cholesterol and reduced high-density lipoprotein cholesterol levels, diabetes mellitus, smoking, physical inactivity, menopause, stress, and positive family history), kidney allograft recipients also have nontraditional risk factors related to immunosuppressive agents or to CKD. An exacerbation of traditional risk factors encountered in the general population induced by immunosuppressive drugs also contribute to enhanced CVD risk in kidney allograft recipients.[16] In several studies, the traditional risk factors such as advanced age, diabetes mellitus, male sex, cigarette smoking, hypertension, and elevated serum cholesterol levels were independently associated with posttransplant atherosclerotic CVD.[16-19] Nontraditional risk factors contributing to CVD include reduced kidney function following transplantation, dialysis vintage before transplantation, rejection, hyperhomocysteinemia, elevated levels of lipoprotein(a), C-reactive protein, and interleukin 6, proteinuria, and low physical activity.[16,20-24] Some studies also stressed that the presence of vascular calcifications detected on radiography prior to transplantation (a common finding) is also associated with increased cardiovascular and all-cause mortality after transplantation.[25,26] However, from the clinical perspective, we should emphasize that our potential kidney transplant recipients are older and have more comorbidities such as diabetes, chronic heart failure, coronary artery disease (CAD), previous myocardial infarction, previous stroke, peripheral vascular disease, vascular calcifications with longer dialysis vintage, and secondary hyperparathyroidism. According to the Health Resources and Services Administration Organ Procurement and Transplant Network Database in 2011, 62% of kidney transplantation candidates were older than 50 years of age compared with 28.7% of kidney transplantation candidates in 1991.[5] Thus, a marked shift in the age composition of transplant wait lists toward older adults are also raising the average medical complexity and comorbidity burden among listed candidates. Therefore, appropriate testing of potential kidney transplant recipients, including cardiac testing, remains the most burning issue.

Cardiac evaluation of kidney transplant recipients It is important to evaluate the presence and severity of coronary disease, heart failure, valvular disease, and arrhythmias before transplantation. The goals of cardiac evaluation include determining transplant candidacy and identification of patients who might benefit from preoperative cardiac intervention (eg, percutaneous coronary intervention [PCI], coronary artery bypass grafting [CABG]), and aggressive risk factor modification to decrease perioperative and posttransplant CV events. This is particularly important in diabetic patients as they are at a very high risk of CVD.[27,28] Typically, the evaluation starts with a detailed anamnesis, careful physical examination, electrocardiogram, and chest radiograph.[29-33] The diagnosis of CAD is extremely difficult in dialysis patients. Electrocardiography (ECG) is the basic method used to select candidates for invasive diagnostics. The value of ECG is limited because of relatively low sensitivity and specificity. In our previous study, we found a high percentage of pathological changes such as left ventricular hypertrophy and ST-T interval abnormalities.[34] Survival of hemodialyzed diabetic patients was not inferior to that in nondiabetics; however, morbidity was significantly higher owing to adverse cardiac events.[35] After comparing all analyzed features on ECG between diabetic and nondiabetic patients, we did not reveal any significant differences.[36] Based on the findings of this initial assessment, noninvasive testing is usually performed in candidates for kidney transplantation with the signs and symptoms of heart disease, previous history of CAD (such as myocardial infarction), signs and symptoms of heart failure, diabetes, and/or multiple major risk factors for heart disease.[37,38] Risk factors for CVD include increased age (>45 years in men and >55 years in women), presence of hypertension, dyslipidemia, or diabetes, positive family history of CVD, peripheral vascular disease, current smoking or a history of smoking,

prolonged duration of CKD, and dialysis vintage longer than 1 year.[5,10,39]

Guidelines and position papers developed by national organizations can serve as useful tools for informing cardiac evaluation practices before noncardiac surgery. However, the discrepancies among the existing guidelines and the unique clinical characteristics of patients with end-stage organ failure raise questions about the applicability of the available recommendations to transplantation candidates.

Two clinical practice guidelines, ie, the 2001 American Society of Transplantation guidelines[31] and the 2000 European Renal Association-European Dialysis Transplant Association "European Best Practice Guidelines",[40] are now more than 10 years old, were based on expert consensus panels, and were not based on the systematic review of the existing evidence.

The 2005 Canadian Society for Transplantation Guidelines suggested that the following patients with known coronary heart disease may be eligible for kidney transplantation: asymptomatic low-risk patients; asymptomatic patients with negative noninvasive testing results; patients on appropriate medical therapy with angiographic results showing noncritical disease; and patients in whom successful interventions have been performed.[32] The guidelines also recommend to reevaluate patients with CAD on a regular basis, which includes a medical history, physical examination, ECG, and noninvasive testing. They recommend to reevaluate high-risk patients annually, and others—when symptoms appear. They also stress that a repeat angiogram may be considered in patients with known CAD before transplantation if waiting time has been prolonged and it is known that a transplant is likely within the next year. In addition, they recommend that all high-risk patients on the wait list should receive aggressive therapy aimed at risk-factor reduction. The 2005 National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF/KDOQI) guidelines for CAD in dialysis patients recommend for kidney transplantation candidates with normal cardiac stress testing results at listing an annual testing in those with diabetes mellitus, testing every 2 years in those with ischemic heart disease or peripheral vascular disease, and testing every 3 years in others.[12]

In 2005, the National Kidney Foundation published the "Clinical Practice Guidelines for Cardiovascular Disease in Dialysis Patients" within the NKF/KDOQI.[12] In the section on CAD, a rather aggressive screening of patients with end-stage renal disease (ESRD) as part of the evaluation to determine candidacy for renal transplantation is suggested, although the statements were rated Level of Evidence C, which means based on either weak evidence or the opinions of the working group. The NKF/KDOQI recommends that any patient on the kidney transplant wait list with a history of diabetes mellitus or known CAD undergo noninvasive stress testing at baseline and then subsequently every 12 months until transplantation. Similarly, potential kidney transplant recipients deemed as high risk per the Framingham criteria (≥2 traditional risk factors, left ventricular ejection fraction ≤40%, or peripheral vascular disease) should undergo cardiac evaluation at baseline and then subsequently every 12 months until transplantation. The fundamental basis of the latest "Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery" developed by the American College of Cardiology/American Heart Association in 2008 is grounded in the understanding of the role of coronary revascularization before noncardiac surgery.[29] The guidelines suggest consideration of further cardiac evaluation in symptomatic patients but do not encourage further testing in patients who have no cardiac symptoms with a functional capacity of 4 metabolic equivalent tasks or more, regardless of the diabetic status, history of CAD, or other traditional cardiac risk factors. This recommendation was based on the 2 recent randomized trials that did not show benefit of revascularization (either PCI or CABG) in asymptomatic CAD before major vascular surgery.[41-43] Fortunately, in 2012, expert consensus document "Cardiac Disease Evaluation and Management Among Kidney and Liver Transplantation Candidates a Scientific Statement From the American Heart Association and the American College of Cardiology Foundation Endorsed by the American Society of Transplant Surgeons, American Society of Transplantation, and National Kidney Foundation" was published to help with cardiac testing in potential kidney transplant recipients and aid nephrologists and cardiologists who deal with this particular population of patients in their everyday practice.[44] Routine screening for CAD in asymptomatic patients with ESRD is usually done only for renal transplant candidates.[2] Clinical evaluation as well as noninvasive screening tests for CAD have numerous limitations. It is unclear which noninvasive test is optimal.[39] Thus, there is a place for a novel, noninvasive first-line test in CAD that could be safely used in patients with ESRD. Early detection of abnormalities in the cardiac structure and function may be important to allow timely and appropriate cardiac interventions. Echocardiography is a noninvasive cardiac imaging test, which is widely available and provides invaluable information on cardiac morphology and function. However, it has limitations in that it is operator-dependent, and image quality can vary depending on the operator's experience and the patient's acoustic window. Hemodialysis patients undergo regular hemodynamic changes that also may affect echocardiographic findings.[45]

Myocardial contrast echocardiography (MCE) is a bedside technique recently applied for the assessment of myocardial perfusion as well as in patients with ESRD.[46-48] Real-time MCE was also evaluated as a tool to select candidates for coronary revascularization among patients with ESRD

and to assess the rate, results of revascularization, and mortality in this particular population.[47,48] As reported previously, revascularization did not improve patient's survival.[49] Moreover, there was no significant difference between the overall 3-year mortality among those who underwent invasive procedures and mortality in the group with significant CAD treated conservatively. This study indicated that if the patient has perfusion defects on MCE, there is high probability that this patient has significant CAD and that perfusion defect on MCE was associated with revascularization (PCI and CABG) in a multivariate analysis. Thus, MCE was a safe and uncomplicated method useful for the selection of candidates for coronary revascularization among ESRD patients. However, the use of the frame count method to assess coronary blood flow in patients with ESRD might help in the evaluation of a potential kidney transplant recipient.[50] Herzog[51] suggested a lower accuracy for the detection of CAD in dialysis patients using stress nuclear or echocardiographic imaging techniques, compared with the general population. From the clinical perspective, echocardiography should be performed after a hemodialysis session, optimally in the euvolemic state. Left ventricular hypertrophy is frequently seen in hemodialysis patients. Tomaszuk-Kazberuk et al.[34] reported that patients with ESRD and diabetes have significantly larger left atrial size, thicker left ventricular walls, and higher ferritin levels than those without diabetes. The limitation of the stress test is its difficulty in achieving target metabolic activity and heart rate limit. Stress testing is usually discontinued, mainly owing to fatigue, and is thus considered nondiagnostic. Therefore, simpler and clinically more relevant methods to assess the cardiac status in potential kidney allograft recipients should be considered. Reilly et al.[52] reported that patients referred for evaluation before major noncardiac procedures were asked to estimate the number of blocks they could walk and flights of stairs they could climb without experiencing cardiac symptoms. Those who could not walk 4 blocks and climb 2 flights of stairs were considered to have poor exercise tolerance and were found to have twice as many perioperative cardiovascular complications as those with a better functional status. However, in a recently published scientific statement by the American Heart Association and the American College of Cardiology Foundation: endorsed by the American Society of Transplant Surgeons, American Society of Transplantation, and National Kidney Foundation, it has been suggested that both dobutamine stress echocardiography and thallium myocardial perfusion scan have moderate sensitivity and specificity among kidney transplant candidates.[44] However, magnetic resonance imaging and computed tomography do not allow to differentiate localized calcifications due to atherosclerotic lesions from diffuse, intraarterial calcium deposits typical for CKD. At present, also a computed tomography scan is not recommended for the diagnosis of CAD in dialysis patients because the correlation between coronary calcification and luminal diameter in dialysis patients is less certain than in the general population, since vascular calcification in this population is often the result of medial calcification rather than atherosclerosis.[44] As in the case of echocardiography, scintigraphy is also operator-dependent and image quality can vary depending on the operator's experience and data are scarce in this population. Experience with cardiac magnetic resonance imaging in dialysis patients is very limited. Therefore, the optimal choice of a cardiac test for potential kidney transplant recipients is generally based on the expertise of a given medical center.

Patients with CKD may potentially benefit from CABG and PCI although both methods are associated with lower procedural success and increased periprocedural complications in patients with CKD.[53] Coronary angiography may be required in patients, including those with diabetes, with positive noninvasive test results, previous history of myocardial infarction, unstable angina, and/or high risk of heart disease.[30,33,37] The decision to perform angiography and possible revascularization (PCI or CABG) is usually made by the heart team including a cardiologist or invasive cardiologist and a cardiac surgeon.

There are currently no definitive data for or against screening for myocardial ischemia among kidney transplantation candidates without active cardiac conditions. Moreover, the next question arises of whether screening in asymptomatic patients with diabetes mellitus without known CAD is necessary to justify more aggressive medical therapy or to identify patients who should be considered for invasive therapy such as revascularization. Kasiske et al.[54] retrospectively reviewed the records from all adult patients (n = 514) placed on the deceased donor kidney transplantation waiting list at a single center between January 1992 and June 2000. During this time, there was a consistent policy for high-risk patients to undergo noninvasive stress testing or coronary angiography or both. They found that among low-risk patients who were not screened, the incidence of a cardiovascular event after being placed on the waiting list was extremely low (0.5%, 3.5%, and 5.3% at 1, 3, and 5 years, respectively) before and after transplantation. In a high-risk group, screening led to prophylactic angioplasty and bypass surgery in 6.2% and 3% of the patients, respectively. They concluded that risk-stratified strategy effectively avoided unnecessary screening studies in over 40% of the patients, a group in whom the risk of adverse events was low. Therefore, according to a recent expert consensus report from 2012, "noninvasive stress testing may be considered in kidney transplantation candidates with no active cardiac conditions based on the presence of multiple CAD risk factors regardless of functional status" and "routine noninvasive screening of patients

with diabetes mellitus either for peritransplantation cardiac evaluation or for long-term care is not justified by existing evidence".[44] However, it is still evidence level C.

The most recent European Best Practice Guidelines (ERBP) Guideline on the Management and Evaluation of the Kidney Donor and Recipient/European Renal Best Practice Transplantation Guideline Development Group published in 2013 recommend that "basic clinical data, physical examination, resting ECG and chest-X ray are a sufficient standard work-up in asymptomatic low risk kidney transplant candidates".[37] The group also recommend "performing a standard exercise tolerance test and cardiac ultrasound in asymptomatic high risk patients (older age, diabetes, history of CVD). In patients with a true negative test, further cardiac screening is not indicated".[37] In addition, further cardiac investigation for occult CAD with noninvasive stress imaging (myocardial perfusion or dobutamine stress echocardiography) in kidney transplant candidates with high risk and a positive or inconclusive exercise tolerance test result is recommended; however, all these recommendations are still evidence level C, while the last one (coronary angiography in renal transplant candidates with a positive test for cardiac ischemia) is level D, namely, expert opinions only. The ERBP group suggests to follow the current cardiovascular guidelines as an expert opinion as well.

The KHA-CARI Guideline: Recipient Assessment for Transplantation, published in 2013, took a very concise and pragmatic approach and listed the risk factors for cardiovascular screening such as older age, diabetes mellitus, abnormal echocardiogram, previous ischemic heart disease or congestive heart failure, increased duration of dialysis, and smoking status.[33] They suggested that kidney transplant candidates with low-risk of CVD do not require stress testing for CAD, while kidney transplant candidates with a moderate or high clinical risk of CVD should undergo cardiac stress testing before transplantation.[33] They also recommend that coronary angiography be considered in kidney transplant candidates with abnormalities on screening procedures and suggest that the benefit of revascularization before transplantation be reviewed on an individual basis.

There are still no clear guidelines as to which patients to screen and what the optimal frequency for repeat noninvasive stress testing in patients awaiting renal transplantation should be. According to the most recent recommendations, issued in 2012, "the usefulness of periodically screening asymptomatic kidney transplantation candidates for myocardial ischemia while on the transplant waiting list to reduce the risk of MACEs [major adverse cardiac events] is uncertain". This is still evidence level C.[44]

In 2014, 2 other guidelines, which may be at least partially relevant to the cardiac evaluation of potential kidney transplant recipients, were published by the European Society of Cardiology.[55,56] The new European Society of Cardiology (ESC) and the European Society of Anaesthesiology Guidelines on noncardiac surgery, released in 2014, assessed the surgical risk of patients undergoing kidney transplantation as intermediate (1%–5%).[55]

Preoperative noninvasive testing aims to provide information on 3 cardiac risk markers: left ventricular dysfunction, myocardial ischemia, and heart valve abnormalities, all of which are major determinants of adverse postoperative outcome. Noninvasive testing should be considered not only for coronary artery revascularization but also for patient counseling, change of perioperative management in relation to the type of surgery, anesthetic technique, and long-term prognosis. Thus, in kidney transplant recipients, resting ECG is recommended (IC), while standard echocardiography is not recommended (IIIC). However, the situation of potential kidney transplant recipient is much more challenging because we do perform all the diagnostic tests to assess eligibility for kidney transplantation and the patients on the waiting list. Because this is not the evaluation for an immediate surgery, great caution should be exercised and the cardiological status should be assessed very carefully before transplantation. Therefore, we do need to repeat some diagnostic tests in predefined time intervals. In a section on renal diseases, the authors focused predominantly on contrast-induced acute kidney injury and preventive measures. Therefore, this section is not relevant to the evaluation of potential kidney transplant recipients, unless in the case of preemptive transplantation, when elective or urgent PCI is considered. The most recent ESC guidelines on revascularization address the issue of renal dysfunction (in nephrology, the term "CKD" would be more appropriate).[56] A table presenting dose adjustment for antithrombotic drugs in patients with CKD is particularly valuable but the major breakthrough is the section on surgery in patients on dual antiplatelet therapy. According to these guidelines, most surgical procedures can be performed on dual antiplatelet therapy or at least on acetylsalicylic acid alone with acceptable rates of bleeding. However, it is recommended that elective noncardiac surgery be delayed until completion of the full course of recommended dual antiplatelet therapy (ideally 6 months in stable CAD and 1 year in patients with acute coronary syndrome [ACS]). From the clinical perspective, in urgent cases (such as lack of vascular access), patients do not need to be kept inactive on the waiting list due to dual antiplatelet therapy. The guidelines stated that in surgical procedures with low-to-moderate bleeding risk, including kidney transplantation, surgeons should be encouraged to operate while maintaining dual antiplatelet therapy.[56] In this particular situation, a multidisciplinary approach is required (involving a cardiologist, anesthesiologist, hematologist, nephrologist, and surgeon) to

determine the patient's risk (bleeding and thrombosis) and to choose the best strategy.

In 2013, the ACS NSQIP surgical risk calculator was introduced as a decision-support tool based on reliable multi-institutional clinical data, which can be used to estimate the risks of most operations. The ACS NSQIP surgical risk calculator would allow clinicians and patients to make decisions using empirically derived, patient-specific postoperative risks.[57] However, the calculator does not include a procedure of kidney transplantation.

Patients with known coronary heart disease are eligible for transplantation but require careful evaluation. On the other hand, some patients have been shown to undergo renal transplantation safely despite clinical markers of high cardiovascular risk. In a study by Jeloka et al.,[58] 5-year survival in the high-risk group was 82.8% compared with 93.1% in the low-risk group (P <0.004). Among the subgroup who underwent coronary revascularization before transplantation (PCI or CABG), 43% subsequently experienced a cardiac event. The authors concluded that, in selected high-risk patients, overall 5-year survival after renal transplantation was actually quite good and superior to the expected 5-year survival with continued dialysis.

Cardioprotective therapy in potential kidney allograft recipients

Conservative treatment Clearly, the underutilization of pharmacological therapies in CAD/ACS patients with CKD is now well established. How can we explain this phenomenon? At first, there were no trials involving patients with CKD or those on renal replacement therapy, including kidney transplant recipients, designed specifically to investigate the treatment for CAD/ACS. In the published studies, patients with CKD were either excluded or underrepresented. Since CAD/ACS therapies have not been well studied in patients with CKD, they were not accepted as standard of care by numerous physicians. Many physicians do not prescribe cardioprotective drugs for fear of their side effects, which could be aggravated by the hematologic, metabolic, and endocrine abnormalities present in CKD. A classic example is the uncertainty about antiplatelet therapy—aspirin and thienopyridines—in CKD patients who tend to have anemia and platelet dysfunction. Many drugs require dose modification according to kidney function. Another practical issue should be taken into account, namely, that patients with CAD and CKD are often simultaneously managed by cardiologists and nephrologists with different practice styles and according to different guidelines. In addition, the current population of patients with CAD and CKD is getting older and is prescribed increasingly more drugs for numerous other comorbidities; therefore, drug interactions, patients' compliance, and financial issues should be taken into account. Drugs prescribed do not necessarily mean drugs taken. Finally, in the recent years, there have been a lot of nonpositive trials in the field of nephrology, and the landmark trilogy of statin trials in CKD (AURORA, 4D, and SHARP) did not prove a reduction in mortality in this population, making nephrologists somehow reluctant to extrapolate all the data from cardiology into their everyday practice. A recent study investigating the extent to which pharmacological treatment for cardiovascular causes in dialysis patients complied with the European guidelines showed that acetylsalicylic acid was taken by 89% of the patients with CAD, clopidogrel by 25%, β-blockers by 70%, angiotensin-converting enzyme inhibitors (ACEIs) by 50%, angiotensin receptor blockers (ARBs) by 8%, and statins by 41%.[59] Diabetes was associated with a significantly higher probability of ACEI/ARB use (by 21%), but chronic heart failure was associated with no increase in the probability of β-blocker use and no increase in ACEI/ARB use.[59] The study clearly showed that patients with CVDs were given less cardioprotective drugs such as acetylsalicylic acid, β-blockers, ACEIs, ARBs, and statins than they should be given according to the guidelines. As Berger and Herzog[60] wrote: "the relationship between worsening renal function and lack of adherence to guidelines cannot be adequately explained by individual hospital performance. Only when physicians 'Connect the Cs' – recognizing the risk of premature CAD in patients in CKD and Crusading for Compliance with the ACS guidelines – will patient outcomes be improved." This is also, or particularly, true for kidney transplant recipients.

Invasive therapy There is a significant gap in the literature in terms of the outcomes of prophylactic coronary revascularization in the renal transplantation candidate population. To our knowledge, there is only 1 randomized controlled trial that seemed to show an improvement in outcomes after revascularization versus medical management in diabetic patients before renal transplantation.[61] However, this trial is difficult to interpret because it was small and had suboptimal use of aspirin. Several observational studies have reported outcomes after coronary revascularization in selected cohorts of potential kidney transplantation candidates from nonsignificant, through survival benefit only in patients with 3-vessel CAD, to excellent survival in transplant recipients who received preemptive revascularization.[53,62,63] On the other hand, Patel et al.[64] challenged the hypothesis that cardiovascular testing before renal transplantation improves cardiovascular mortality outcomes after transplantation and suggested that cardiac testing may only serve as a barrier to being placed on the wait list. In the previous study on dialyzed patients, the diagnosis of CAD, especially that confirmed by coronary angiography, resulted in the withdrawal from the wait list for renal transplantation. Even after successful revascularization, patients were never put on the list again.[49] The choice of

the best method for coronary revascularization in patients with ESRD is also controversial. According to Szczech et al.,[65] among patients with ESRD from the New York State Health Department studied in the years 1993–1995, CABG was associated with a relative reduction in mortality by 61% compared with PCI after adjustment for severity of CAD, left ventricular dysfunction, and other comorbid conditions. Herzog et al.[66] analyzed the USRDS data from 2003 to 2005 and reported superior 12-month unadjusted survival after revascularization in dialyzed patients who received drug-eluting stents (DES; 69.7%) compared with CABG (66.6%) or PCI with bare metal stents (BMS; 3.6%). However, unadjusted 36-month survival favored CABG over DES (42.0% vs. 38.1%), especially among patients who underwent CABG with an internal thoracic artery. At the conference of the American Society of Nephrology in San Diego in November 2012, during the session of the high-impact clinical trials, Herzog presented the most recent data from the USRDS on revascularization therapy in patients on renal replacement therapy. CABG was associated with higher perioperative mortality but with better long-term survival compared with PCI (PCI with DES was better than with BMS) (personal communication to JM and JMR).

In the world of evidence-based medicine, Wang et al.[67] provided a systematic review of test accuracy for CAD in potential kidney transplant recipients. Their objective was to investigate the accuracy of noninvasive cardiac screening tests compared with coronary angiography to detect CAD in potential kidney transplant recipients. They compared dobutamine stress echocardiography, myocardial perfusion scintigraphy, echocardiography, exercise stress electrocardiography, resting electrocardiography, electron beam computed tomography, exercise ventriculography, carotid intima–media thickness, and digital subtraction fluorography, and found that dobutamine stress echocardiography had superior accuracy compared with myocardial perfusion scintigraphy (P = 0.02) when all studies were included in the analysis, but this was not significant after we excluded studies that did not avoid partial verification or use a reference standard threshold of stenosis equal to or higher than 70% (P = 0.09). Finally, they concluded that additional studies directly comparing these cardiac screening tests are needed and the absence of significant CAD may not necessarily correlate with cardiac event-free survival after transplantation.

What is important is that, while on the waiting list, patients do not become healthier but continue to be sick and reevaluation before transplantation may be needed.

Conclusions In summary, organ transplantation is often the only effective treatment for patients with ESRD. Kidney transplant requirements vary from program to program and country to country. Many programs have requirements regarding age (eg, a candidate must be under a certain age to be listed) and health status (eg, a candidate should be in good general condition, apart from kidney disease). Patients with significant CVD, incurable terminal infectious diseases, and cancer are often excluded. Owing to scarcity of the organs available for transplantation, the careful evaluation of potential transplant recipients is extremely important. CVD is the most significant burden in the aging population of patients on dialysis and remains a leading cause of mortality in patients on renal replacement therapy including transplantation. Therefore, careful cardiac evaluation is vital to ensure the best possible outcomes.

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ARTYKUŁ POGLĄDOWY

Choroby układu sercowo-naczyniowego u pacjentów kwalifikowanych do zabiegu przeszczepienia nerki

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STRESZCZENIE

Kwalifikacja kardiologiczna potencjalnego biorcy nerki jest wciąż przedmiotem licznych kontrowersji. Problemem jest także brak jednoznacznych zaleceń oraz to, że przy małym prawdopodobieństwie choroby badania przesiewowe są przeprowadzane niepotrzebnie oraz częste są wyniki fałszywie dodatnie. Ogólnie rzecz biorąc, zaleca się następujące postępowanie: zebranie wywiadu i badanie przedmiotowe, elektrokardiografia, zdjęcie rentgenowskie klatki piersiowej, ocena profilu lipidowego, glikemia na czczo, badanie echokardiograficzne i na końcu koronarograficzne. Test wysiłkowy nie jest zalecany z powodu niskiej czułości i problemów w wykonaniu. Badanie echokardiograficzne powinno zostać wykonane po hemodializie, gdy pacjent nie jest przewodniony lub jest znacznie mniej przewodniony. Wszystkie nieinwazyjne badania obrazowe, podobnie jak izotopowe, są zwykle niedoskonałe, w dużym stopniu zależne od ośrodka i osoby je wykonującej. Badanie koronarograficzne należy rozważyć u pacjentów z dodatnim testem wysiłkowym po przebytym ostrym zespole wieńcowym, z niestabilną chorobą niedokrwienną serca oraz wysokim ryzykiem sercowo-naczyniowym. Natomiast decyzję co do formy leczenia, tj. przezskórnej interwencji wieńcowej (*percutaneous coronary intervention* – PCI), stentu (rodzaj stentu) czy pomostowania aortalno-wieńcowego (*coronary artery bypass graft* – CABG) powinno się podjąć na posiedzeniu kardiogrupy. Wytyczne poruszają też problem przeciwwskazań kardiologicznych do zabiegu transplantacji nerki. Zawsze należy również pamiętać, że pacjent zgłoszony do zabiegu transplantacji cały czas jest chory i będąc na liście oczekujących po kilku latach oczekiwania nie jest w tym samym stanie klinicznym, w jakim był w chwili kwalifikacji. Dlatego też konieczna może być ponowna ocena kardiologiczna. Przeszczepienie wyprzedzające (*preemptive transplantation*) lub krótki okres dializoterapii przed przeszczepem (poniżej 6 miesięcy) są związane z lepszym przeżyciem i pacjenta i graftu, co w efekcie przyczynia się do zmniejszenia częstości powikłań sercowo-naczyniowych i poprawy jakości życia. W pracy omówiono dostępne wytyczne dotyczące kwalifikacji potencjalnego biorcy przeszczepu nerki.

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