ORIGINAL RESEARCH

Cardiorespiratory Fitness (Peak Oxygen Uptake): Safe and Effective Measure for Cardiovascular Screening Before Kidney Transplant

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***Background*—**Significant heterogeneity exists in practice patterns and algorithms used for cardiac screening before kidney transplant. Cardiorespiratory fitness, as measured by peak oxygen uptake (VO_{2peak}), is an established validated predictor of future cardiovascular morbidity and mortality in both healthy and diseased populations. The literature supports its use among asymptomatic patients in abrogating the need for further cardiac testing.

***Methods and Results*—**We outlined a pre–renal transplant screening algorithm to incorporate VO_{2peak} testing among a population of asymptomatic high-risk patients (with diabetes mellitus and/or >50 years of age). Only those with VO_{2peak} <17 mL/kg per minute (equivalent to <5 metabolic equivalents) underwent further noninvasive cardiac screening tests. We conducted a retrospective study of the *a priori* dichotomization of the VO_{2peak} <17 versus ≥17 mL/kg per minute to determine negative and positive predictive value of future cardiac events and all-cause mortality. We report a high (>90%) negative predictive value, indicating that VO_{2peak} ≥17 mL/kg per minute is effective to rule out future cardiac events and all-cause mortality. However, lower VO_{2peak} had low positive predictive value and should not be used as a reliable metric to predict future cardiac events and/or mortality. In addition, a simple mathematical calculation documented a cost savings of ≈$272 600 in the cardiac screening among our study cohort of 637 patients undergoing evaluation for kidney and/or pancreas transplant.

***Conclusions*—**We conclude that incorporating an objective measure of cardiorespiratory fitness with VO_{2peak} is safe and allows for a cost savings in the cardiovascular screening protocol among higher-risk phenotype (with diabetes mellitus and >50 years of age) being evaluated for kidney transplant. **(*J Am Heart Assoc*. 2018;7:e008662. DOI: 10.1161/JAHA.118.008662.**

Key Words: function • ischemic heart disease • kidney • risk assessment • risk stratification

Cardiovascular disease (CVD) is the leading cause of mortality in patients with end-stage renal disease and in those individuals receiving a kidney transplant. Despite several consensus statements, there is wide variability among centers relating to the cardiac evaluation of a patient before kidney transplant (Tables S1 and S2).[1] The variability in practice patterns would indicate that no algorithm is uniformly considered ideal. In addition, none of these algorithms, to our knowledge, include an objective measure of cardiorespiratory fitness.

Peak oxygen uptake (VO_{2peak}) is an established objective measure of cardiorespiratory fitness and functional capacity and is a validated predictor of future cardiovascular morbidity and mortality in both healthy and diseased populations. VO_{2peak} <15 and <12 mL/kg per minute for men and women with diagnosed coronary heart disease, respectively, has been associated with the highest risk of death.[2] In addition, the measurement of VO_{2peak} is low cost and noninvasive. It outperforms more expensive and invasive tests, such as right-sided heart catheterization and echocardiogram, as an independent predictor of major adverse cardiovascular events and all-cause mortality.[2,3] VO_{2peak} is the product of maximal cardiac output and maximal arterial-venous oxygen difference.

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Accompanying Tables S1 through S3 are available at http://jaha.ahajournals.org/content/7/11/e008662/DC1/embed/inline-supplementary-material-1.pdf

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Clinical Perspective

What Is New?

- There is significant heterogeneity in the cardiac screening process for patients with end-stage renal disease being evaluated for kidney and/or kidney/pancreas transplant.
- There is little evidence to suggest that current conservative strategies are effective in mitigating future cardiovascular disease events.

What Are the Clinical Implications?

- We demonstrate that use of an objective metric of cardiorespiratory fitness, such as peak oxygen uptake in the pretransplant cardiovascular screening algorithm, had a high negative predictive value and resulted in minimizing additional cardiac testing.
- We advocate for the incorporation of cardiorespiratory fitness assessment (peak oxygen uptake) into the pretransplant cardiac screening algorithm.

It represents the ability of the cardiopulmonary system to deliver oxygen to exercising tissue and the ability of peripheral tissues to extract and use oxygen.[4] Individuals experiencing CVD have decreased tissue perfusion, thus necessitating higher tissue oxygen extraction and resulting in decreased VO_{2peak}. The typical resting metabolism of a human (resting VO_2) is 3.5 mL oxygen/kg per minute or by definition 1 metabolic equivalent (MET). Therefore, a 3 MET activity, such as walking at 2.5 mph, expends 3 times the energy used at rest. The MET values of typical activities of daily living have been extensively reported.[5] The measured VO_{2peak} of an individual can be translated to their MET capacity by dividing their VO_{2peak} by 3.5.

The American College of Cardiology/American Heart Association (ACC/AHA) recommends no cardiac testing before intermediate risk surgery, such as a kidney transplant, in an asymptomatic patient with functional status ≥4 METs (ie, VO_{2peak}=14 mL/kg per minute), even among those with known cardiac risk factors. However, most US transplant centers do not adhere to the ACC/AHA recommendations and perform, at minimum, a noninvasive cardiac stress test among asymptomatic patients who fit the cardiac high-risk criteria. The cardiac high-risk criteria include any of the following: older patients (>50 years of age), presence of diabetes mellitus, and/or presence of coronary artery disease (CAD). Some centers perform coronary angiography on all cardiac high-risk patients.

Despite this overcautious and conservative approach, there is little evidence to suggest that these strategies are effective in mitigating future CVD events, but they could potentially introduce more risk and cost with additional testing. None of the current pretransplant cardiac screening strategies objectively quantify and include cardiorespiratory fitness of the patient in the screening algorithm. We hypothesized that incorporating an objective measure of cardiorespiratory fitness, such as VO_{2peak}, allows for a safe and cost-effective pretransplant cardiovascular screening process.

Methods

Cardiovascular screening for patients undergoing kidney or kidney/pancreas transplant evaluation at Mayo Clinic (Phoenix, AZ) has evolved over time. In October 2011, after extensive discussion with all stake holders, including cardiologists, transplant nephrologists, transplant surgeons, and anesthesiologists, the decision was made to incorporate VO_{2peak}, obtained by performing cardiopulmonary exercise test (CPET), into the standard-of-care pretransplant cardiac screening algorithm (Figure). All patients ≥50 years of age and/or with diabetes mellitus underwent CPET. The VO_{2peak} provided an objective measure of cardiorespiratory fitness and was a branch point metric in the algorithm. Only those with VO_{2peak} <17 mL/kg per minute underwent further cardiac screening with pharmacologic sestamibi stress test. Among the cohort with known ischemic heart disease with or without prior cardiac intervention, our protocol includes the CPET being performed along with pharmacologic sestamibi stress test, irrespective of the result of VO_{2peak}.

Because the ACC/AHA guidelines were not written specifically for patients with end-stage renal disease with respect to the recommendations of no further cardiac testing among patients with functional capacity of >4 METs (VO_{2peak}=14 mL/kg per minute), we chose to adopt a more conservative measure of VO_{2peak}, <17 mL/kg per minute, to determine if noninvasive stress test should be performed. This is equivalent to an exertion of >5 METs. This more conservative cutoff for VO_{2peak} at <17 mL/kg per minute was chosen with the goal of optimizing the negative predictive value (NPV) of the test (ie, to identify those who did not require further testing). Thus, the threshold for VO_{2peak} at <17 mL/kg per minute was established a priori as a branch point metric in the screening algorithm to rule out the need for further cardiac testing.

Subjects underwent CPET testing on a treadmill/bicycle ergometer using a ramp protocol with the goal of achieving 6 to 9 minutes until voluntary exhaustion occurred. Gas exchange parameters were measured using a computerized breath-by-breath analyzer (Medgraphics Corp, St Paul, MN), which was calibrated before each test. A 12-lead ECG and oxygen saturations were monitored throughout the study, along with periodic blood pressure measurements. The test was conducted by a respiratory technician/exercise

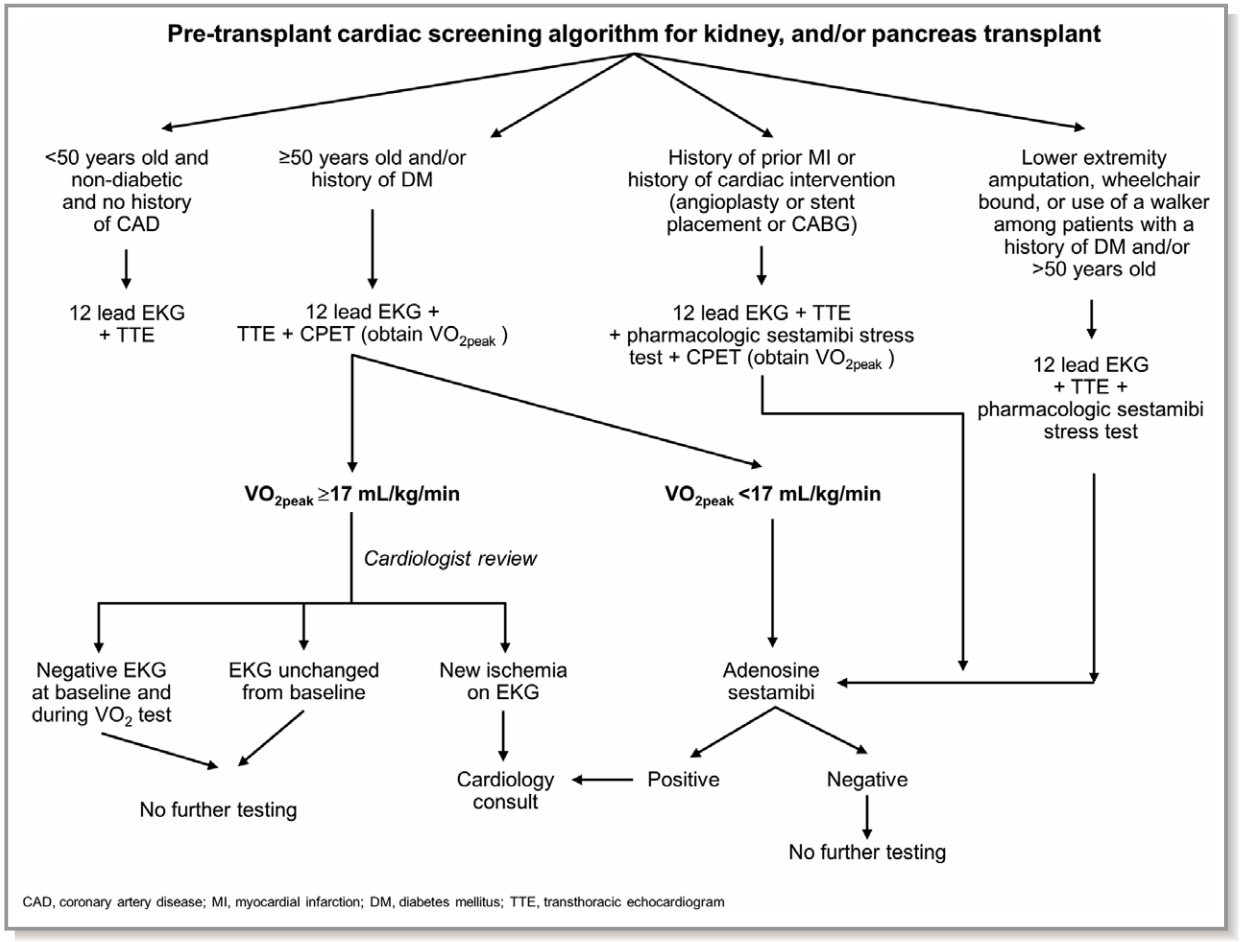

Figure. Pretransplant cardiac screening algorithm for kidney and/or pancreas transplant. CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; CPET, cardiopulmonary exercise test; DM, diabetes mellitus; MI, myocardial infarction; TTE, transthoracic echocardiogram; VO_{2peak}, peak oxygen uptake.

specialist, along with a cardiology registered nurse, and interpreted by a cardiologist with specific training in exercise testing.

Study Cohort

We conducted a retrospective study of all patients with documented VO_{2peak} who were evaluated for kidney/pancreas transplant between November 2011 and September 2014. The study was reviewed and approved by the Institutional Review Board at Mayo Clinic. The informed consent requirement was waived. Patients had an average follow-up of 4.04±1.11 years after baseline VO_{2peak} testing. During the follow-up, study outcome events, including CVD event, all-cause mortality, and a composite outcome of CVD event and all-cause mortality, were documented. CVD event was defined as cardiac ischemic event, myocardial infarction, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, or cerebrovascular accident.

Statistical Analyses

The data, analytic methods, and study materials will not be made available to other researchers because the methods are purely simple statistical methods and transparent and raw data are protected information.

Patient demographic characteristics are displayed comparing those with VO_{2peak} <17 mL/kg per minute versus those with VO_{2peak} ≥17 mL/kg per minute using Pearson χ^2 test for categorical variables or 2-sample *t* test for continuous variables. Log-rank test was used to compare the outcomes among the 2 groups. The positive predictive value (PPV), NPV, sensitivity, and specificity of VO_{2peak} at end of study period were calculated. Patients with known CAD with VO_{2peak} ≥17 mL/kg per minute were excluded from the analyses calculating PPV and NPV because the algorithm requires a pharmacologic sestamibi stress test in all patients with history of CAD, irrespective of the value of VO_{2peak}. $P<0.05$ was considered statistically significant. All statistical analyses were performed

using SAS software, version 9.4 (SAS Institute Inc, Cary, NC).

Results

Descriptive Analyses of Study Cohort

The study cohort included 637 recipients undergoing cardiac evaluation for kidney and/or pancreas transplant. Mean age of study cohort was 56.6 years, 74% were >50 years of age, 61% were men, 52% were diabetic, and 21% had a history of CAD (9% had cerebrovascular disease and 12% had known peripheral artery disease). During the average follow-up of 1476.0±408.5 days, 292 individuals received transplant, in which 288 received a kidney transplant. Of the 288 who received a kidney transplant, 71 received living donor transplants and 217 received deceased donor transplants.

Mean VO_{2peak} of study cohort was 15.1±4.4 mL/kg per minute. Among the study cohort of 637 patients receiving CPET, 183 (29%) had a VO_{2peak} ≥17 mL/kg per minute, and 23 of the 183 had history of known CAD. As outlined in the screening algorithm, all patients with CAD had pharmacologic sestamibi stress test performed, irrespective of VO_{2peak}; as such, these 23 patients with VO_{2peak} ≥17 mL/kg per minute were excluded from the analyses. Interestingly, among these 23 patients, 16 (70%) had normal pharmacologic sestamibi stress test.

Thus, our study cohort for statistical analyses included a total of 160 patients with VO_{2peak} ≥17 mL/kg per minute who did not undergo further CVD testing, and 454 patients had VO_{2peak} <17 mL/kg per minute and underwent noninvasive stress test with pharmacologic sestamibi stress test.

Table 1 compares the demographics and baseline characteristics of the patients with VO_{2peak} <17 versus ≥17 mL/kg per minute. Those with VO_{2peak} <17 mL/kg per minute were older; were more likely to be women, have history of diabetes mellitus, have history of CVD, and have history of peripheral vascular disease; and were more likely to be past or present smoker and to be taking aspirin.

Table 1. Comparison of Demographics and Comorbidities for VO_{2peak} <17 vs ≥17 mL/kg per Minute

Variables	VO_{2peak} <17 mL/kg per min (N=454)	VO_{2peak} ≥17 mL/kg per min (N=160)	*P* Value
Age, mean (SD), y	58.3 (11.9)	51.7 (14.1)	<0.0001
Aged ≥50 y, N (%)	354 (78)	98 (61)	<0.0001
Male sex, N (%)	260 (57)	110 (69)	0.011
Race, N (%)			0.58
Black	52 (11)	17 (11)	
White	301 (66)	113 (71)	
Others	101 (22)	33 (18)	
History of comorbidities, N (%)			
Hypertension	430 (95)	141 (88)	0.005
Diabetes mellitus	276 (61)	42 (26)	<0.001
Cerebrovascular disease	45 (10)	6 (4)	0.02
Peripheral vascular disease	72 (16)	3 (2)	<0.001
Hyperlipidemia	269 (59)	72 (45)	0.002
History of smoking, N (%)			0.002
Never	218 (48)	103 (64)	
Past	177 (39)	42 (26)	
Current	59 (13)	15 (9)	
Pretransplant ASA, N (%)	186 (41)	49 (27)	<0.001
Type of transplant			0.003
Kidney alone	182 (40)	84 (53)	
Simultaneous kidney and pancreas	9 (2)	3 (2)	
Pancreas alone	0 (0.0)	2 (1)	

ASA indicates acetylsalicylic acid; VO_{2peak}, peak oxygen uptake.

Outcomes: Comparison of Patients With VO_{2peak} <17 mL/kg per Minute Versus Those With VO_{2peak} ≥17 mL/kg per Minute

Cardiovascular events during study period

A total of 454 patients had VO_{2peak} <17 mL/kg per minute and underwent pharmacologic sestamibi stress test. As previously described, 160 patients with VO_{2peak} ≥17 mL/kg per minute did not undergo further CVD testing. The PPV and NPV of VO_{2peak} ≥17 mL/kg per minute and future CVD were calculated. We observed a high NPV. We observed this among the entire cohort and subgroups of those who underwent transplant during the follow-up and those who remained on the wait list (Table 2).

Among these 454 patients, with VO_{2peak} <17 mL/kg per minute, 28 had abnormal pharmacologic sestamibi stress test (presence of ischemia, infarction, and/or ejection fraction <40) requiring a referral to cardiologist for further recommendations. Cardiac (myocardial infarction, ischemia, percutaneous transluminal coronary angioplasty, coronary artery bypass grafting, and/or cerebrovascular accident) events among those patient with VO_{2peak} <17 versus ≥17 mL/kg per minute were 45 (10%) versus 13 (8%) events (log-rank *P*=0.23). The detailed description of the 13 events among the patients with VO_{2peak} ≥17 mL/kg per minute is included in Table S3. None of these 13 patients had any significant

Table 2. Outcomes: Comparing VO_{2peak} <17 vs ≥17 mL/kg per Minute

Variable	VO_{2peak} <17 mL/kg per min (N=Total Number), Event Number	VO_{2peak} ≥17 mL/kg per min (N=Total Number), Event Number	Log-Rank *P* Value	Sensitivity, %	Specificity, %	Positive Predictive Value, %	Negative Predictive Value, %
Cardiovascular event (ischemia/CABG/MI/CVA)							
Entire cohort	(N=454) 45	(N=160) 8	0.0481	84.9	27.1	9.9	95.0
Wait-listed cohort	(N=261) 30	(N=71) 5	0.2341	85.7	22.2	11.5	93.0
Transplanted cohort	(N=193) 9	(N=89) 2	0.323	81.8	32.1	4.7	97.8
All-cause mortality							
Entire cohort	(N=454) 79	(N=160) 17	0.0496	79.0	30.2	17.4	88.5
Wait-listed cohort	(N=261) 63	(N=71) 16	0.7334	79.7	21.7	24.1	77.5
Transplanted cohort	(N=193) 16	(N=89) 1	0.0194	94.1	33.2	8.3	98.9
Composite outcome (includes all-cause mortality and cardiovascular event)							
Entire cohort	(N=454) 110	(N=160) 30	0.0043	84.0	28.8	24.2	86.9
Wait-listed cohort	(N=261) 81	(N=71) 17	0.2204	82.7	23.1	31.0	76.1
Transplanted cohort	(N=193) 24	(N=89) 3	0.0184	88.9	33.7	12.4	96.6

CABG indicates coronary artery bypass grafting; CVA, cerebrovascular accident; MI, myocardial infarction; VO_{2peak}, peak oxygen uptake.

electrocardiographic changes noted during the CPET test. There was no specific pattern with respect to timing, description of event, and patient characteristics among those with positive event versus those without cardiac event among patients with VO_{2peak} ≥17 mL/kg per minute.

Mortality during study period

The PPV and NPV of VO_{2peak} ≥17 mL/kg per minute and all-cause mortality were calculated. We observed a high NPV. We observed this among the entire cohort and subgroup who underwent transplant during the follow-up and those who remained on the wait list (Table 2). Total number of deaths during study period was 100 (15.7%). The death rate among those patients with VO_{2peak} <17 versus ≥17 mL/kg per minute at the end of study period was 17.4% versus 11.5% (log-rank *P*=0.074).

Discussion

Cardiac testing before kidney transplant is highly debated, with no universally adopted pretransplant cardiac screening algorithm. Our proposed algorithm suggests that use of an objective metric of cardiorespiratory fitness, such as VO_{2peak}, in the pretransplant cardiovascular screening algorithm had a high NPV and resulted in minimizing additional cardiac testing. In our cohort, ≈25% (160 of 454) of high-risk patients safely averted further cardiac testing, which resulted in substantial cost savings (≈$272 600) during the pretransplant cardiac screening.

The literature, including a recent ACC/AHA suggests there is wide variation and heterogeneity in the cardiac screening pretransplant (Tables S1 and S2).[1] None of these recommendations use objective measure of cardiorespiratory fitness in the algorithm. The Kidney Disease Outcome Quality Initiative guidelines advocate a more liberal approach in the use of noninvasive stress tests for all high-risk patients, which is at odds with the ACC/AHA.[1] This could potentially raise concern from insurance companies and payers, questioning adoption of best practices that are not cost-effective and not congruent with the major cardiac societies' recommendations with respect to cardiac screening of patients before kidney and/or pancreas transplant. We demonstrated that even in "higher-risk" patient cohort, the high NPV of VO_{2peak} ≥17 mL/kg per minute supports ACC/AHA guidelines in this group and, thus, prevents unnecessary cardiac testing and results in significant cost savings.

The reimbursement charge of performing the CPET to obtain VO_{2peak} is ≈$200, and that of pharmacologic sestamibi stress test is >$2500. So, in this example, during study time period, 637 "high-risk" cohorts were evaluated. High risk was defined as anyone with one of the following criteria: ≥50 years of age, presence of diabetes mellitus, and/or history of CAD. All the 637 individuals had the CPET, incurring cost of $127 400 ($200×637=$127 400). A total of 183 (29%) of the study cohort had a VO_{2peak} ≥17 mL/kg per minute; of these individuals, 23 had history of CAD and, thus, had pharmacologic sestamibi stress test, per the protocol. However, 160 patients who otherwise would have had the pharmacologic sestamibi stress test did not have it done [savings of $400 000 (160×$2500)]. Thus, total cost saving of cardiac screening tests in this example was $272 600 ($400 000–$127 400). Our simple arithmetic calculation alludes to significant cost savings in using this approach; however, a robust formal economic model with cost-effectiveness analyses will need to be performed to validate the true cost-effectiveness of this approach.

Cardiorespiratory fitness, as measured by VO_{2peak} as a marker of cardiorespiratory fitness, is a strong predictor of future cardiac events and all-cause mortality[6] in otherwise healthy individuals and in those with advanced CVD, such as congestive heart failure.[7] The results of this present study are in keeping with the literature that supports the growing body of evidence that cardiorespiratory fitness, as measured by VO_{2peak}, can be safely used to rule out future cardiac events and mortality. Thus, VO_{2peak} testing could abrogate the need for more invasive cardiac testing in a cohort of patients with end-stage renal disease being evaluated for kidney transplant. In addition, event rates in our study were consistent with reported national rates, which enhance the external validity of this study. External validation using our protocol by other transplant programs on their high-risk phenotype will further consolidate the generalizability of our conclusions.

The goal of cardiac screening and testing before kidney transplant is to identify, intervene, and reduce future cardiovascular morbidity and mortality. The optimal screening test ideally will be cost-effective, with a high true positive rate and high true negative rate or proportion. However, given the relatively low event rate, a high true PPV may be difficult to achieve. However, one can strive to have high confidence in a negative test. We report a high NPV >90%, indicating that the high VO_{2peak} (as defined by VO_{2peak} ≥17 mL/kg per minute in this study) among those patients who were able to perform the CPET is sufficient to rule out future cardiac events and all-cause mortality. However, a low value cannot be used as a reliable predictive measure to determine development of future cardiac events or mortality. We conclude that the current cardiac screening algorithm before kidney and/or pancreas transplant needs to be refined. Incorporation of an objective measure of functional capacity using VO_{2peak} into the pretransplant cardiac screening algorithm is a safe "rule out" test for the requirement of further cardiac testing.

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Table S1. Published Recommendations for Testing for CAD in Asymptomatic Kidney Transplantation Candidates [1]

Reference	Recommendations
2012 AHA Scientific Statement	Noninvasive stress testing may be considered in kidney transplantation candidates with no active cardiac conditions on the basis of the presence of multiple CAD risk factors regardless of functional status (Class IIb, Level of Evidence C) Relevant risk factors among transplantation candidates include diabetes mellitus, prior cardiovascular disease, >1 y on dialysis, LV hypertrophy, age >60 y, smoking, hypertension, and dyslipidemia; the specific number of risk factors that should be used to prompt testing remains to be determined, but the committee considers ≥3 to be reasonable
2007 ACC/AHA Perioperative Guidelines for Noncardiac Surgery [2]	No testing recommended if functional status ≥4 METS If functional status <4 METS or unknown, then consideration of noninvasive stress testing is recommended based on the following clinical risk factors: • Ischemic heart disease • Compensated or prior heart failure • Diabetes mellitus • Renal insufficiency • Cerebrovascular disease Recommendations for testing are stronger if ≥3 clinical risk factors are present but may be considered in those with 1–2 risk factors
2007 Lisbon Conference [3]	Acknowledges that there are no data establishing that screening of asymptomatic patients in itself prevents cardiac events; noninvasive and/or invasive testing should be considered in highest-risk patients with the following conditions: • Diabetes mellitus • Prior cardiovascular disease • Multiple cardiac risk factors such as >1 year on dialysis, LV hypertrophy, age >60 years, smoking, hypertension, and dyslipidemia Does not specify the number of risk factors to justify testing
2005 NKF/KDOQI Guidelines [4]	Noninvasive stress testing recommended for All patients with diabetes; repeat every 12 months All patients with prior CAD If not revascularized, repeat every 12 months If prior PCI, repeat every 12 months If prior CABG, repeat after first 3 year and then every 12 months Repeat every 24 months in "high-risk" nondiabetic patients defined as ≥2 traditional risk factors Known history of CAD LVEF ≤40%

	Peripheral vascular disease
2001 AST Guidelines [5]	Noninvasive stress testing recommended for patients at "high-risk," defined as renal disease from diabetes, prior history of ischemic heart disease, or ≥2 risk factors Coronary angiography for possible revascularization before transplantation recommended for patients with a positive stress test Revascularization before transplantation recommended for patients with critical coronary lesions
2000 European Best Practice Guidelines [6]	Thallium scanning recommended for patients with history of myocardial infarction or "high-risk" clinical features Coronary angiography recommended if thallium scanning is positive Revascularization advised if lesions are suitable

ACC indicates American College of Cardiology; AHA, American Heart Association; AST, American Society of Transplantation; CABG, coronary artery bypass grafting; CAD, coronary artery disease; KDOQI, Kidney Disease Outcomes Quality Initiative; LV, left ventricular; LVEF, left ventricular ejection fraction; METS, metabolic equivalent tasks; and PCI, percutaneous coronary intervention

Table S2. Summary of Survey and Registry Data Demonstrating Variation in Cardiac Evaluation Practices Across US Transplantation Centers [1]

Authors, Year	Summary
Ramos et al, 1994 [7]	1993 survey of directors of UNOS-participating centers regarding practices for initial candidate evaluations; 81% response rate (147 of 182) Noninvasive stress testing was reported as the most common first approach to cardiac evaluation of asymptomatic patients, prompted by diabetes mellitus at 86% of responding centers, age (mean threshold 52 y) at 67%, and multiple risk factors at 68% A notable minority of centers espoused first-line angiography for patients with diabetes mellitus (15%), older age (7%; mean threshold, 57 y), or multiple risk factors (8%)
Danovitch et al, 2002 [8]	2001 survey of UNOS-participating centers regarding management practices for patients on the deceased donor waiting list 67% final response rate (192 of 287) 8% of programs reported cardiac testing for all listed candidates, whereas 18% did not order routine cardiac testing for any asymptomatic patient group
Zarifian et al, 2006 [9]	2005 survey of US kidney transplantation centers regarding reevaluation practices for patients on the deceased donor waiting list 26% final response rate (68 of 257) 51% of respondents indicated reliance on the initial cardiac evaluation and cardiac history; 7% of program representatives stated that AHA criteria were used to guide cardiac revaluation; and 32% espoused a combination of AHA criteria, the initial cardiac evaluation, and cardiac history

Lentine et al, 2008 [10]	Retrospective study of pretransplantation cardiac evaluation practices among 27 786 Medicare beneficiaries transplanted in 1991–2004 Pretransplantation cardiac evaluation testing was identified by billing claims for noninvasive stress tests and angiography Clinical traits defining "high" expected IHD risk were defined by AST guidelines[16] as diabetes mellitus, prior IHD, or ≥2 other CAD risk factors 46.3% (65.4% of high-risk and 20.4% of lower-risk patients) underwent cardiac evaluation testing before transplantation; the adjusted odds of transplantation without cardiac evaluation testing increased sharply with younger age and shorter dialysis duration, and also correlated with black race, female sex, and certain geographic regions Overall, 9.5% who received cardiac evaluation testing also received pretransplantation revascularization, but only 0.3% of lower-risk patients undergoing cardiac evaluation testing were revascularized before transplantation

AHA indicates American Heart Association; CAD, coronary artery disease; IHD, ischemic heart disease; and UNOS, United Network for Organ Sharing

Table S3. Characteristics of patients with cardiovascular event within study period among cohort with $VO_{2peak} \geq 17$ ml/kg/min (N= 183)

ID	Sex	Age	Transplant performed	History of DM	History of Prior CAD	History of Hyperlipidemia	Description of cardiac event	Days to Cardiac event post VO_{2peak} testing
1	M	52	✓	✗	✗	✗	3	148
2	M	42	✓	✗	✓	✗	3	336
3	M	40	✓	✗	✗	✗	5	63
4	M	64	✓	✗	✗	✓	7	448
5	M	48	✗	✓	✗	✓	3	715
6	F	66	✗	✓	✓	✓	4	477
7	M	66	✗	✓	✗	✗	4	41
8	M	60	✗	✗	✓	✓	5	17
9	M	66	✗	✓	✓	✓	5	1147
10	M	61	✗	✓	✗	✗	5	793
11	F	23	✗	✗	✗	✗	7	331
12	M	36	✗	✓	✗	✓	7	489
13	M	72	✗	✗	✓	✓	7	297

3: Ischemia with stent; 4: CABG; 5: MI; 7: CVA

Supplemental References:

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