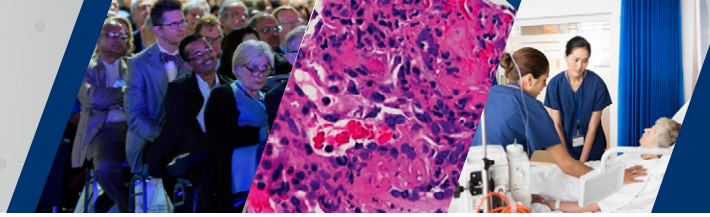

Screening Transplant Waitlist Candidates for Coronary Artery Disease

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Introduction

To avoid loss to patients and society (*i.e.*, scarcely available deceased donor kidneys), the transplant community adopted a uniquely vigilant screening program for coronary artery disease (CAD) as the standard of care (1). The standard of care involves screening on the basis of the presence of clinical risk factors for CAD both at the time of activation to the waiting list and periodically during waitlisting using noninvasive screening tests, with the objective of identifying patients with occult disease who are candidates for revascularization or medical therapy (1). The standard of care is now out of step with current general cardiology practice, which does not include screening asymptomatic surgical candidates for CAD (2). Whether the current screening paradigm improves patient survival or transplant outcomes is uncertain, and it is possible that screening may cause harm by unnecessarily subjecting patients to invasive procedures and delaying or excluding patients from transplantation (3). The Canadian Australasian Randomized Trial of Screening Kidney Transplant Candidates for Coronary Artery Disease will test the hypothesis that eliminating the regular use of noninvasive screening tests for CAD after waitlist activation is not inferior to regular screening for CAD during waitlisting for the prevention of major adverse cardiac events (www.clinicaltrials.gov). Until new evidence is available, who, how, and when to screen asymptomatic waitlist candidates require assessment of the risks and benefits of screening in individual patients. This version of "how I treat" illustrates our patient-centered team approach to managing asymptomatic waitlist candidates.

Patient

A 66-year-old man with ESKD secondary to presumed diabetic nephropathy treated with hemodialysis for 14 months is referred for consideration of transplantation. His diabetic kidney disease–related complications include retinopathy and peripheral neuropathy. He had a possible transient ischemic attack 3 years prior, but there is no history of a major vascular disease event. He has hypertension, orthostasis, dyslipidemia, gout, and obesity (body mass index of 35 g/m^2). He is an ex-smoker with a 30–pack-year history. He is sedentary due to osteoarthritis in both knees but states he can walk four level blocks. He denies chest pain or shortness of breath on exertion. His focused cardiac examination reveals hypertension, orthostasis, euvolemia, cardiomegaly, and decreased peripheral pulses. His electrocardiogram shows normal sinus rhythm and left ventricular strain; his echocardiogram shows left ventricular hypertrophy, no wall motion abnormality, and a left ventricular ejection fraction of 50%. His medications include insulin, acetylsalicyclic acid, and losartan.

Does This Patient Require Additional Testing for CAD?

The fact that he is asymptomatic is not reassuring. Patients with CKD have limited exercise capacity due to fatigue, frailty, and other comorbid conditions, and they may not manifest classic symptoms of CAD due to uremic or diabetic neuropathy. Therefore, general cardiology guidelines, which rely on symptoms and functional status to determine whether to screen surgical patients for CAD, may not be applicable in transplant candidates (2).

Will a Noninvasive Test Change Management?

Before screening, I estimate the patient's pretest likelihood of CAD. The most commonly available noninvasive tests (dobutamine stress echocardiography and myocardial perfusion scintigraphy) have average sensitivity and specificity of only 70% for obstructive CAD (3). Accordingly, a negative noninvasive test will only have a sufficiently high negative predictive value for occlusive CAD when the pretest probability of disease is low (4). For example, the negative predictive value of a noninvasive test is good (90%) if my pretest probability of CAD is 20% but no better than a coin toss (50%) if the pretest probability of disease is 70%. In contrast, the positive predictive value of a noninvasive test is only useful (*i.e.*, >50%) when the pretest probability of disease is ≥40%. Therefore, we do not normally do noninvasive screening tests in patients when the pretest probability of CAD is ≤20%, despite the high negative predictive value of noninvasive tests; I ask our cardiologist to go straight to coronary angiography in patients with a high pretest probability of occlusive disease (≥80%) in whom I would not be reassured by a

negative noninvasive test (for example, a previously revascularized patient with high-risk coronary artery anatomy).

The pretest probability of CAD is imprecisely estimated by the presence of risk factors (*i.e.*, diabetic kidney disease, prior cardiovascular disease, duration of dialysis exposure >1 year, left ventricular hypertrophy, age >60 years old, smoking, hypertension, and dyslipidemia) (3). My estimated pretest probability of disease in this patient is 60%; therefore, if his noninvasive test is positive, it would be reasonable to investigate him further with coronary angiography (positive predictive value of 80%), but a negative test would not be completely reassuring (negative predictive value of 60%).

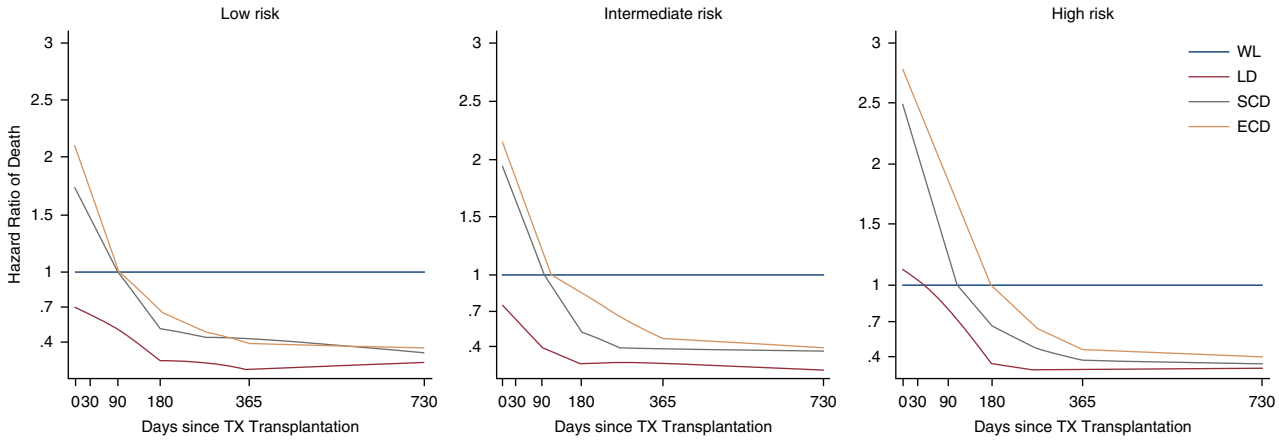
What Noninvasive Test Should Be Used?

Because of his osteoarthritis and left ventricular hypertrophy, an exercise stress test would be of limited use. A myocardial perfusion scintigraphy test was performed and revealed reversible ischemia.

Does the Patient Warrant a Coronary Angiogram, and If So, When?

Although the patient was asymptomatic, our transplant cardiologist agreed that an angiogram might be useful, with additional consideration given to his left ventricular ejection fraction of 50% (which raised the possibility of left main or multivessel disease).

The timing of angiography was informed by several factors: The patient was ABO blood group O and unsensitized. His estimated waiting times for transplantation from the date of dialysis initiation were 5 years for a low kidney donor profile index deceased donor kidney and 3 years for a high low kidney donor profile index deceased donor kidney. In the absence of a living donor, we would monitor the patient clinically and perform an angiogram approximately 18 months before his anticipated date of transplantation to allow for sufficient time for recovery from any required revascularization surgery that may be recommended. A discussion with the patient of the average perioperative risks in similar patients undergoing transplantation with a kidney from different donor sources was undertaken (Figure 1) (5). The discussion was useful in helping the patient accept the possibility of a living donor transplant. Preliminary testing of his spouse revealed that she was ABO blood group compatible, had normal eGFR, and had no obvious health concerns that would exclude her from donation. Given the possibility of a living donor, a diagnostic angiogram was



Patient risk	Transplant with living donor		Transplant with a standard criteria / low KDPI Donor		Transplant with an expanded criteria / high KDPI Donor	
	Days to equal risk	Day to equal survival	Days to equal risk	Day to equal survival	Days to equal risk	Day to equal survival
Low	immediate	immediate	90	203	95	264
Intermediate	immediate	immediate	96	285	110	470
High	43	130	110	368	180	521

Figure 1. | Living donor transplantation is associated with the lowest risk of peri-operative death. The figure shows the multivariable-adjusted relative risks of death in patients ≥65 years of age with low (left panel), intermediate (center panel), and high (right panel) cardiovascular risk. In each panel, the multivariable-adjusted risk of death in living donor (LD; shown in red), standard criteria deceased donor/low kidney donor profile index (SCD; shown in purple), or expanded criteria deceased donor/high kidney donor profile index (ECD; shown in green) transplant recipients is compared with that in waitlisted patients (WL) of similar cardiovascular risk (shown in blue) who had been on dialysis for equal lengths of time but who had not yet received a kidney transplant. The accompanying table shows the time to equalize the risk of death and survival in transplant recipients compared with patients who remained waitlisted. The times to equal risk and equal survival were far lower for patients who received an LD transplant. KDPI, kidney donor profile index; TX, transplantation. Modified from reference 5, with permission.

performed, and it revealed 50%–60% stenosis in his dominant left circumflex artery and a 20%–30% stenosis in his right coronary artery.

Should the Patient Be Revascularized?

The patient did not have occlusive disease (*i.e.*, stenosis ≥70%) that would normally warrant revascularization (6). The relevant considerations regarding revascularization include the fact that the degree of coronary stenosis does not predict future plaque rupture and that 30% of perioperative myocardial infarctions occur in areas supplied by arteries with nonocclusive plaque (7,8). In this patient, a large territory of myocardium would be at risk in the event of a myocardial infarction. Furthermore, the patient's orthostasis would limit medical therapy (*i.e.*, use of β-adrenergic blocking agents). Although revascularization would delay living donor transplantation by 12 months and the risks of revascularization are higher in patients with CKD, the patient and his spouse both accepted revascularization before transplantation, despite the limited direct evidence that this would improve patient or allograft survival (9).

The patient underwent percutaneous coronary artery revascularization of the circumflex artery with a drug-eluting stent followed by 12 months of dual antiplatelet therapy, and he subsequently underwent an uneventful living donor kidney transplant from his spouse.

Disclosures

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