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Evaluation of the Cardiovascular System Prior to Transplantation; an Endless Debate

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Abstract

Cardiovascular disease continues to be the most important cause of death after transplantation. Although there is a dramatic improvement in the diagnosis and management of cardiovascular disease, the rate of cardiovascular death after kidney transplantation still higher compared to general population. Chronic kidney disease is associated with many risk factors that lead to increased incidence and prevalence of cardiovascular diseases. In this mini-review, we will discuss recent advances in cardiovascular work up prior to kidney transplantation.

Keywords: Cardiovascular disease; Work-up; Assessment and renal transplantation

Abbreviations: ESRD: End Stage Renal Disease; CKD: Chronic Kidney Disease; KDOQI: Kidney Disease Outcomes Quality Initiative; ACR: American College of Cardiology; AHA: American Heart Association; CAD: Coronary Artery Disease; ICA: Invasive Coronary Angiography; MPI: Myocardial Perfusion Imaging; SPECT: Single Photon Emission Computed Tomography; DSE: Dobutamine stress echocardiography; ABI: Ankle-Brachial Index; CTA: Computed Tomography Angiography; MRA: Magnetic Resonance Angiography; DS-CMR: Dobutamine stress Cardiac Magnetic Resonance; ABI: Ankle-Brachial Index

Cardiovascular Assessment

Although renal transplantation reduces cardiovascular morbidity and mortality compared to end stage renal disease (ESRD), it is associated with an early increase of cardiovascular morbidity and mortality [1-9]. Renal transplantation recipients should undergo rigorous screening processes considering not only peri-operative risk, but also must be designed to provide information regarding CV risk in the early years post-transplantation [10,11].

There is no universally accepted screening process especially in asymptomatic chronic kidney disease (CKD) patients given their high cardiac risk even if asymptomatic [8,12-27]. All recipients must be tested by non-invasive methods as recommended by Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines and the only determinant for testing by American College of Cardiology/American Heart Association (ACR/AHA) guidelines were functional status tempered by risk factor profile [18,19].

Intermediate levels of testing result from application of guidelines developed by more kidney-specific stakeholder groups (Figure1) (Table 1) [20,21].

Table 1: Non-invasive cardiovascular assessment of potential kidney transplant recipient.

Resting electrocardiography
Conventional echocardiography
Stress electrocardiography
Stress echocardiography either exercise or pharmacologic
Myocardial perfusion scan
Carotid intimal medial thickness
Cardiopulmonary exercise test
Computed tomography coronary angiography
Magnetic resonance angiography
Cardiac magnetic resonance imaging
Electron beam computed tomography
Digital subtraction fluorography

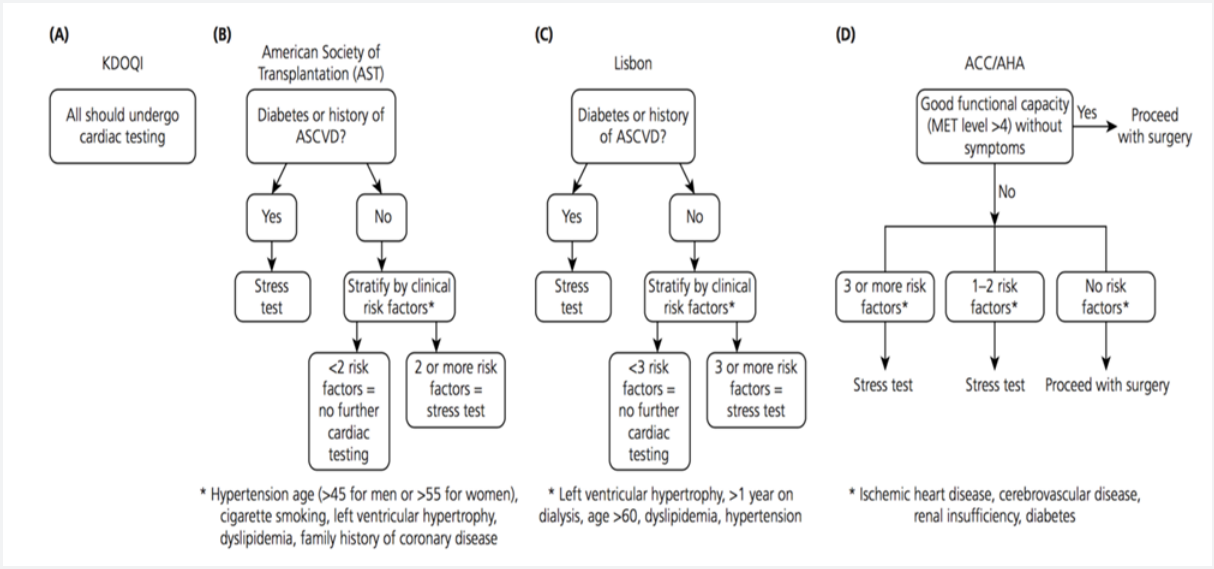

Figure 1: Cardiac risk assessment of four guidelines.

As conventional CV risk factors are highly prevalent in this population, exclusion of coronary artery disease (CAD) comprises a substantial component of CV screening in higher risk transplant candidates [17]. There is no consensus on which technique will be optimal when deciding that cardiovascular screening is mandatory [22-25]. The presence or absence of chest pain provides little clinical certainty in distinguishing between the presence and absence of significant CAD in potential renal transplant recipients [23,26-30]. There is substantial debate regarding the necessity to perform invasive coronary angiography (ICA) to exclude significant CAD prior to transplantation. Numerous studies have been published demonstrating the advantages and limitations of non-invasive investigations in the ESRD context [27,31-33].

Exercise-based stress testing is widely accepted as the preferred, and most accurate, methodology for the non-invasive exclusion of coronary ischemia. Uraemia, however, is commonly associated with reduced exertional capacity, frequently preventing ESRD patients from achieving the necessary level of tachycardia required to minimize the occurrence of a false negative result. Previous studies have demonstrated a higher risk of future cardiovascular events amongst patients unable to complete exercise stress tests, regardless of the presence of a negative result. Thus combinations of exercise and vasodilatory agents, or dobutamine infusion have been utilized to optimize non-invasive imaging results [34-36].

Conventionally, exercise (+/- dipyridamole or adenosine) or dobutamine single photon emission computed tomography (SPECT) and myocardial perfusion imaging (MPI) have been the most commonly utilized investigation in the non-invasive exclusion of ischemia prior to RTx. Dobutamine stress echocardiography (DSE) is a commonly utilized alternative, with some results indicating a higher specificity attributable to this investigation, but similar overall accuracy in non- renal failure patients [37,38]. The presence of a negative study does not entirely exclude the presence of haemo dynamically significant coronary artery disease, hence the preference within some RTx centers to rely solely upon ICA for the evaluation of coronary risk in this context, however are associated with procedural risk [32]. Myocardial perfusion studies and dobutamine stress echocardiography (DSE) show equally well results in diagnosing patients with stenosis ≥ 50% of a major coronary artery, which supported by Cochrane meta-analysis [39]. Data from large studies on general populations shows similar or superior outcomes of medical treatment over revascularization, except in triple vessel disease [15,40-42].

Alternatively, recent data from CKD studies compared to the general population confirm compromised therapeutic responses to medical treatment [43].

As diabetics have high risk of cardiac events and poor negative predictive value of non-invasive test, some advice use of cardiac catheterization as sole for prediction of adverse cardiac events in diabetics waiting transplantation [44,45]. Dobutamine stress Cardiac Magnetic Resonance Imaging (DS-CMR) has recently been demonstrated to provide a very high level of accuracy in the non-invasive detection of significant CAD, with low procedural risk [46-49].

Which results at cardiovascular assessment prevent transplantation? This is difficult to judge. Most centers currently will consider ischemia not responsive to revascularization as contraindication to transplantation. Similarly, after revascularization of advanced coronary disease, severe left ventricular dysfunction considered contraindication to transplantation as it associated with high mortality [50]. On the other hand, absence of coronary disease in the presence of severe left ventricular systolic dysfunction considered as

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indication for transplantation as many reports confirm cardiac function improvement after restoration of kidney function in adult and pediatric.

Many dialysis patients have pulmonary hypertension which worse with duration on dialysis. Data from recent studies shows increased risk of graft and/or patient loss in advanced elevation of right ventricular systolic pressure ≥50 mmHg [50].

Some data suggest that high right ventricular systolic pressure considered as contraindication to transplantation till treated. Finally, it is mandatory to manage advanced vascular heart disease before transplantation [51].

Assessment of Peripheral Vascular Disease

There is an absolute indication for vascular assessment including general assessment of prognosis as well as specific assessment of the vascular supply needed for the transplant operation. Atheromatous iliac arteries that have been ossified through years of CKD management must thus be carefully assessed by the surgeon planning to perform the transplant [52-54].

The presence of peripheral arterial disease (PAD) and its degree could be assessed by noninvasive tests. These tests include ultrasound, segmental limb pressures, the ankle-brachial index (ABI), segmental volume plethysmography, and exercise treadmill test. Furthermore, recent data suggest that computed tomography angiography (CTA) and magnetic resonance angiography (MRA) have become important noninvasive methods for the PAD assessment [55-60]. Arteriography still considered as gold standard for diagnostic evaluation of PAD. Nowadays, to establish the diagnosis of PAD and to plan the most adapted intervention, most vascular specialists use three-dimensional reconstructed angiography (CTA or MRA) or bidimensional images obtained with Duplex-ultrasound modalities [59-61]. However, diagnostic standard angiography may still remain necessary, in selected cases [62,63].

Conclusion

Cardiovascular screening and intervention for transplant recipient especially asymptomatic patients are common practice but the clear benefits of these interventions still questionable. Large Randomized controlled trial is needed to clearly define the risk/benefit of the current practice.

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