Multimodality Imaging for CAD Detection Before Renal Transplantation*

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The latest data from the United States Renal Data System indicate that 17,305 renal transplants were performed in the United States in 2012, the majority from deceased donors (1). At the end of 2012, there were 81,981 candidates listed on the transplant list. Although a proportion of these had an inactive status on the waiting list, the imbalance between the availability of organs and the number of candidates clearly poses a challenge for allocating organs; the result is a median wait time to transplantation of 3.6 years. While the kidney transplant list has been growing over the years, the number of kidney transplants performed in the United States has been relatively stable since 2005, indicating that the relative paucity of organs is expected to intensify going forward. Cardiovascular disease is the leading cause of morbidity and mortality in patients with end-stage renal disease pre-transplantation, the leading cause of death in the peri-transplant period, and a major cause of loss of functioning allografts at 10 years after transplantation (2–4). Thus, there is a general consensus on the need for pre-transplant cardiovascular evaluation and risk stratification, although the best strategy to achieve this goal has been controversial.

The 2012 scientific statement from the American Heart Association and the American College of Cardiology Foundation on Cardiac Disease Evaluation and Management Among Kidney and Liver Transplantation Candidates was endorsed by the American Society of Transplant Surgeons, the American Society of Transplantation, and the National Kidney Foundation. The statement recommends that noninvasive stress testing may be considered in kidney transplantation candidates with no active cardiac conditions based on the presence of multiple coronary artery disease (CAD) risk factors regardless of functional status (Class Iib, Level of Evidence: C) (5). Routine invasive coronary angiography in all patients being considered for transplantation is unlikely to be justified due to the associated risk of the procedure and the inconsistency of the prognostic data derived from angiography (6). In the absence of solid data for or against screening for myocardial ischemia, transplant centers have varied in their implementation of screening protocols but have generally relied on noninvasive stress testing in a variable proportion of patients listed for possible transplantation (based on age and number of risk factors) to assist in risk stratification (7).

In this issue of iJACC, Winther et al. (8) report on a prospective study of 138 patients referred for pre-renal transplant cardiac evaluation who underwent routine imaging with computed tomography for Agatston coronary artery calcium scoring (CACS) and coronary computed tomography angiography (CTA), stress myocardial perfusion imaging (MPI) with gated single-photon emission computed tomography, and invasive coronary angiography (ICA). The aim of the study was to identify the accuracy of these noninvasive tests for the diagnosis of obstructive CAD by using ICA. With ICA, 22% had obstructive CAD (>70% luminal area reduction or 50% diameter reduction), the majority of which were 1-vessel disease (73%); 17% had 2-vessel disease, and 10% had 3-vessel or left main disease.

The sensitivity and specificity for obstructive CAD were 67% and 77% for CACS (>400), 93% and 63% for coronary CTA (nonevaluable segments were defined...
as having obstructive CAD), and 53% and 82% for MPI (summed difference score ≥4, a reduction of left ventricular ejection fraction >10% during stress, transient ischemic dilation, and left ventricular ejection fraction <45% in patients without prior coronary revascularization) (8). The authors concluded that coronary CTA had a higher sensitivity but a lower specificity for diagnosing obstructive CAD than CACS or MPI. When the data for coronary CTA and MPI were combined, the sensitivity decreased (67%) and the specificity increased (86%) compared with coronary CTA alone. However, these numbers were not statistically different from those obtained by MPI alone.

These results (8) are interesting and provide important data regarding the diagnostic capabilities of the different noninvasive imaging modalities in this patient population. The study design was appropriate to avoid referral bias, the readers were blinded to the results of the other imaging modalities (including ICA), and it is notable that only 29 patients were excluded because they did not undergo imaging with all modalities. Some factors that may have altered the performance of MPI include the use of a nonconventional cutoff for the summed difference score and the inclusion of nonperfusion abnormalities, which are not universally accepted as predictors of CAD in the presence of normal perfusion on imaging. Furthermore, imaging in patients with chronic kidney disease poses special challenges related to artifacts that are particular to this population (2). For coronary CTA, considering nonevaluable segments to have obstructive CAD may have artificially inflated the sensitivity and deflated the specificity of this modality because it affected 25 patients (18%). The influence of nonevaluable segments is of clinical concern because it may lead to downstream testing with a different modality in 1 of every 5 patients. The authors tried to account for the nonevaluable segments by combining the data from coronary CTA and MPI, but this approach resulted in unconventional definitions that are not applicable in practice (e.g., a patient with 2-vessel CAD by coronary CTA and normal perfusion by MPI was labeled as normal) and the obvious implication of the need for dual imaging in every patient.

An important consideration in the diagnostic performance of MPI is the lack of concordance between myocardial ischemia and obstructive CAD, a concept that has been rediscovered in light of fractional flow reserve data (9). One can argue that a 70% luminal area stenosis by ICA is not the proper gold standard for assessment of myocardial ischemia because many patients meeting this criterion do not have ischemia, and myocardial ischemia can be present with less severe obstruction. The real question yet to be addressed is not whether these patients have obstructive CAD on angiography but rather whether they are at high cardiovascular risk in the near-term and the long-term. As alluded to earlier, studies have shown that MPI may carry more prognostic information than ICA in this population (10,11) and has been associated with cardiac outcomes after transplantation (12,13). In this regard, it has been observed that the majority of deaths in patients with end-stage renal disease are related to sudden cardiac deaths rather than myocardial infarction. This finding suggests that assessment of left ventricular function and other novel predictors of sudden death may add prognostic data to the assessment of myocardial ischemia and CAD (2,14).

When implementing a screening protocol in an asymptomatic cohort, we must be cautious with respect to the risk–benefit ratio so that we do not inadvertently produce net harm to the patients. Contrast-induced nephropathy associated with coronary CTA and ICA is of particular concern if screening is to be performed before initiation of dialysis. In the described cohort, 15% of patients were started on dialysis after coronary CTA and within 30 days of ICA. Finally, it may be prudent to use imaging in a subset of patients at clinically high risk of events rather than in the entire population if the purpose is to identify patients with 3-vessel CAD (only 2% in this cohort). The scientific statement from the American Heart Association (5) provides a starting point. Further research is needed, however, to determine who will benefit from imaging during evaluation before renal transplantation and how to intervene to decrease risk in response to imaging findings (7).

**REFERENCES**


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