Cardiovascular Evaluation before Renal Transplantation: To Cath or Not to Cath?

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Patients with chronic kidney disease (CKD) are at increased risk for cardiovascular morbidity and mortality, related in large part to the particularly high burden of coronary artery disease (CAD) in this patient group (1). Furthermore, cardiovascular disease is the leading cause of death after renal transplantation, with the risk for myocardial infarction (MI) being highest in the perioperative period (2). As a result, it has become common practice to screen aggressively patients who are being evaluated for renal transplantation for the presence of obstructive CAD to identify preemptively vascular lesions amenable to revascularization. This approach, which is based on the belief that preemptive coronary intervention decreases adverse cardiovascular events during and after transplantation, is reflected in and informed by opinion-based consensus guidelines regarding the kidney transplant evaluation process (3-5).

However, a preemptive strategy of revascularization is incongruent with our understanding of the pathophysiology of MI in the nonoperative setting, where it is generally accepted that it is disruption of vulnerable, nonobstructive coronary artery plaque and not obstructive CAD that leads to acute coronary artery thrombosis (6). Furthermore, pathology studies have confirmed that this mechanism accounts for the majority of all fatal MIs after noncardiac surgery (7). It is therefore not surprising that data from randomized, controlled trials in the general population have failed to show that routine screening for and revascularization of stable CAD before major noncardiac surgery improves outcomes (8,9). These observations support the consensus opinion among cardiologists that routine screening with angiography of asymptomatic patients facing intermediate- to high-risk surgery is not recommended if they have normal functional capacity. Nonetheless, the question of how we apply our understanding of CAD in the perioperative setting and data from studies in the general population to the evaluation and treatment of CAD in patients being evaluated for renal transplantation, in whom the underlying burden of CAD is remarkably high, remains unanswered.

It is important to note that patients with CKD were poorly represented in past trials that investigated preoperative coronary revascularization, constituting less than 20% of enrolled patients (8,9). This significantly limits the generalizability of the results to patients who undergo renal transplant evaluation. Moreover, although past trials demonstrated that preemptive revascularization did not reduce the risk for serious patient-centered outcomes (death or MI), these studies were unable to assess the impact of early revascularization on renal allograft loss. This is an important issue because kidneys from living or deceased donors remain a precious and extremely limited resource. These observations underscore the importance of research seeking to elucidate the optimal and most cost-effective approach to preoperative cardiovascular screening in patients with CKD, including those being evaluated for renal transplantation.

In this issue of CJASN, Kumar et al. (10) report the results of an observational study seeking to shed light on our understanding of the effect of cardiovascular screening and revascularization in patients who undergo evaluation for renal transplantation. This single-center, observational study describes the outcomes of 657 patients who had CKD and underwent pretransplantation assessment with coronary angiography between 2006 and 2009. A systematic decision to proceed with coronary angiography was made when patients were older than 50 years, had diabetes, or had cardiac symptoms or evidence of cardiac disease or when their electrocardiogram showed evidence of ischemia or previous MI. Of 657 patients who underwent coronary angiography, 573 (87%) were subsequently deemed fit for transplantation, whereas 84 (13%) were not referred for transplantation because of noncardiac conditions (n = 44), cardiac reasons (n = 27), or patient choice/noncompliance (n = 13). Of the 573 patients deemed fit for transplantation, 247 (43%) received a kidney during the study period. The survival of these 247 patients, as well as of those who were placed on the waiting list but had not yet received a kidney, was higher than that of the 84 patients deemed unfit for transplantation. Overall, 184 (28%) of 657 patients were found to have angiographically significant CAD, 168 (91%) of whom agreed to and underwent revascularization. The majority of these 168 patients were free of symptoms. The authors note the markedly lower survival of the 16 patients who declined intervention as compared with patients who underwent revascularization. Collectively, these observations led to the conclu-
clusion that an aggressive strategy of preemptive coronary revascularization in patients who are being considered for renal transplantation and have significant CAD is associated with low cardiac morbidity and mortality.

Notwithstanding its important contribution to our understanding of outcomes associated with a standardized strategy of preemptive screening for CAD in this patient population, certain factors should be considered when interpreting this study’s findings and seeking to place the results in clinical context. First, it is evident that a robust, standardized, and comprehensive pretransplantation evaluation is critical in identifying patients who are unlikely to survive because of significant comorbidities. However, although preemptive coronary angiography was routinely performed as part of the pretransplantation evaluation, noncardiac conditions among study participants accounted for the majority of exclusions from the transplant list. Just three patients were excluded because of an inability to revascularize their coronary disease fully; therefore, coronary angiography may represent only one of multiple important components of the pretransplantation evaluation. Second, as acknowledged by the authors, this study does not support the superiority of an approach of preemptive angiography/revascularization compared with a less aggressive strategy because of the lack of a comparator group of patients who did not undergo angiography/revascularization but proceeded to transplantation. Third, interestingly, the authors report that “no major adverse events occurred as a result of the coronary angiograms carried out in this study.” However, no details are provided on potential cardiovascular complications that are known to occur with some frequency after these procedures, including access site bleeding, periprocedural MI and cerebrovascular accident, and stent thrombosis. A robust and comprehensive assessment for such complications is critical to weigh effectively the potential benefits of a preemptive strategy of screening and treatment with the inevitable risks that accompany such an approach. Fourth, it is widely recognized that the performance of coronary angiography is associated with risks for contrast-induced acute kidney injury and renal atheroembolic disease, both of which may accelerate the progression of underlying CKD and precipitate the need for dialysis. Although the authors highlight the important findings of their previous study that demonstrated a low risk for loss of kidney function in this population after coronary angiography, no such assessment was carried out in this study; therefore, the reader is left to wonder whether certain patients with non–dialysis-dependent CKD in this analysis experienced renal complications and a more rapid decline in kidney function than would had occurred had preemptive coronary angiography not been performed. In this regard, several studies suggest that clinicians’ fears of accelerated deterioration in renal function after coronary angiography/revascularization in patients with CKD contributes to underuse of indicated angiographic procedures (11,12). Growing awareness of such biases along with an absence of data from adequately powered clinical trials of patients with CKD, as alluded to by Kumar et al. (10), underscores the urgent need to investigate fully the safety and efficacy of coronary revascularization in patients with CKD in general, as well as in the context of operative risk assessment.

Individuals who have CKD and are being evaluated for renal transplantation represent a group of patients with highly prevalent CAD and heightened cardiovascular risk. As demonstrated by Kumar et al. (10), a strategy of systematically screening for and treating clinically significant CAD in such patients seems to be associated with high survival rates. However, in the context of an observational study that lacked a suitable comparator group, it remains unclear whether these favorable outcomes are attributable to coronary revascularization and/or they may be offset by the potential harm associated with the unrestricted performance of invasive coronary intervention. Nevertheless, the incremental knowledge gained by observational studies such as this should be used to inform the aims, hypotheses, and design of adequately powered, randomized, clinical trials rather than as proof of benefit. Such trials, which seem to be in the planning stages (13), would shed important light on the most effective approach to the preemptive evaluation of CAD in this highly comorbid patient population and would serve as a “breath of fresh air” in a clinical domain in which there is a striking dearth of well-conducted, adequately powered clinical trials.

Disclosures
None.

References


See related article, “Cardiac Survival following Pre-emptive Coronary Angiography in Transplant Patients and Those Awaiting Transplantation,” on pages 1912–1919.