DISCLOSURE
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chronic kidney disease

Coronary artery disease in chronic kidney disease: highlights from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

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The risk of coronary artery disease (CAD) increases as chronic kidney disease (CKD) advances, despite adjustment for traditional cardiovascular risk factors.[1] Conventional therapies have failed to improve these outcomes, especially in patients with end-stage kidney disease (ESKD).[2] The abrupt decline in CAD risk after kidney transplant, despite years of exposure to traditional CAD risk factors, suggests a role for reversible factors associated with ESKD and dialysis. Here, we briefly highlight select topics from the recent Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference on CAD in CKD.[2]

Screening and diagnosis

Traditional CAD risk prediction models perform poorly in patients with CKD. Performance improves when CKD status is considered, but standard risk equations do not include granular estimates of glomerular filtration rate and albuminuria.[3] Despite the high prevalence of CAD in patients with CKD, routine screening of even high-risk asymptomatic patients is not currently recommended.[2] CKD also presents unique limitations to non-invasive diagnostic studies. Baseline electrocardiographic abnormalities due to left ventricular hypertrophy and the frequent inability to achieve sufficient workloads may limit the diagnostic utility of stress testing in patients with advanced CKD, and the coronary artery calcium score has a poor sensitivity (67%) and specificity (77%) for detection of clinically relevant coronary artery stenosis in this population.[2] Computed tomography angiography circumvents these limitations at the expense of contrast exposure, which may have implications even for patients with ESKD and residual kidney function. Conference attendees did not reach a consensus on the

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optimal approach to CAD screening and diagnosis in patients with CKD, recommending an individualized approach pending much-needed research in this area.

Patients with CKD often present with acute myocardial infarction (AMI), rather than presenting with exertional angina earlier in the course of disease.[4] In addition, CKD complicates the diagnosis of AMI. Chronic troponin elevations are common in patients with ESKD; this baseline elevation curtails the specificity of AMI diagnosis.[5] Newer troponin assays have improved the AMI diagnostic specificity in CKD; for example, although they are elevated, high-sensitivity troponin T levels remain relatively constant in patients with ESKD. Conference attendees suggested that nephrologists may be able to improve the specificity of AMI diagnosis by establishing a baseline troponin level during routine laboratory monitoring. However, studies are needed to evaluate the prognostic and diagnostic significance of outpatient changes in troponin in this population.

Treatment

Several unique factors complicate the choice of appropriate medical and/or revascularization therapies for CAD in patients with CKD. First, the underlying pathology of coronary lesions in CKD patients differs compared to that of non-CKD patients, with a smaller contribution of traditional atherosclerosis to CAD events.[2] This alternate pathophysiology may explain why clinical trials of statins, the mainstay of therapy in the general population, have yielded lesser benefits among patients with CKD and no cardiovascular benefit among patients with ESKD. A second complicating factor is that patients with advanced CKD and ESKD have been poorly represented in clinical trials; thus, the evidence base to support recommendations is lacking. This lack of strong evidence has hampered progress in understanding the role of revascularization among CKD patients. Absent clinical trial data, observational studies support the role of revascularization for ST-elevation MI; however, limited clinical trial data suggest no benefit of revascularization over optimal medical management for stable symptomatic CAD in patients with CKD.[2] Although limited clinical trial data were available at the time of the KDIGO conference, the recently reported results of ISCHEMIA-CKD (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches–Chronic Kidney Disease; NCT01985360) demonstrate no benefit of revascularization over optimal medical management in patients with Stage 4-5 CKD and moderate to severe ischemia on stress testing. In the trial, assignment to an invasive strategy including cardiac catheterization followed by revascularization did not improve the composite outcome of death or myocardial infarction compared to optimal medical management (Bangalore S, *et al.*, presented at the American Heart Association Annual Meeting, Philadelphia, PA, November 16, 2019). In cases where revascularization is indicated, a meta-analysis of trial data demonstrated superiority of coronary artery bypass grafting (CABG) over percutaneous coronary intervention (PCI) among patients with moderate CKD and multivessel CAD.[6] Observational data also suggest better long-term outcomes with CABG among patients with ESKD and multivessel disease, despite an increase in short-term risks compared to PCI.[2]

Transplant candidates and recipients

Pretransplant CAD screening aims to lower the risk of peri- and post-transplant cardiac events, but no study has definitively demonstrated improved patient and allograft outcomes with routine pretransplant CAD screening in asymptomatic patients.[7] In addition, the unpredictable timing of surgery for deceased donor transplantation complicates pretransplant CAD screening, and the optimal frequency of repeat CAD screening among waitlisted candidates is unclear. The current American Heart Association/American College of Cardiology joint guidelines do not recommend periodic CAD screening in asymptomatic patients waitlisted for kidney transplant.[8] Moreover, in absence of a clear benefit, this practice may create an unnecessary barrier or delay to kidney transplant. Revascularization prior to transplant should be considered for transplant candidates with known high-risk (left main, proximal left anterior descending, or multivessel) disease,[9] but no trials have evaluated revascularization strategies in transplant candidates with lower-risk coronary anatomy.

The decision to continue, start, or stop certain cardioprotective medications in the perioperative period is another crucial aspect of CAD management in kidney transplant recipients. Based on extrapolation from other populations, acetylsalicylic acid and beta blockers are often continued perioperatively

unless the risks of complications clearly outweigh the risk of perioperative ischemia.[2] While continued perioperatively, the dose and choice of statin may need to be adjusted after initiation of calcineurin inhibitors for immunosuppression.[2]

Conclusions

The accumulation of traditional and non-traditional CAD risk factors in patients with CKD creates a unique, high-risk population. The atypical presentation of CAD, the amplified risk of surgical and medical CAD therapies, and the general lack of randomized trial data specific to this population highlight the urgent need for quality research at the intersection of CAD and CKD. Among the research needs identified by the conference attendees, we would like to highlight the following research priorities with the potential to directly impact patient care: establishment of large CKD cohorts for the study of longitudinal CAD outcomes; development and validation of CKD- and ESKD-specific CAD risk equations with more granular assessment of kidney function (e.g., albuminuria); and rigorous prospective evaluation of the current pretransplant CAD screening paradigm. Although the recently reported ISCHEMIA-CKD trial results represent an important advance, additional studies are also needed to inform clinical guidelines for the management of CAD in patients with advanced CKD.

DISCLOSURE

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