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EDITORIAL COMMENT

PCI or CABG for LMCA Revascularization in Patients With CKD

The Jury Is Still Out*

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Although under-represented in clinical trials, patients with chronic kidney disease (CKD) are frequently encountered in cardiovascular (CV) practice and present unique challenges in decision making. It is well established that CKD is associated with higher CV event rates and reduced survival (1). Comorbid hypertension, diabetes mellitus, atherosclerotic vascular disease, and heart failure or their combination are routinely present and confer additional risk. CKD affects the pharmacokinetics of many CV drugs and is known to adversely influence the response to invasive diagnostic, interventional, and surgical procedures (2). Certainly, not all CKD patients are alike, although there is broad recognition of the direct relationship between progressive renal dysfunction and harm. Treatment of some CV disorders may therefore be avoided or withheld, even for patients in whom the anticipated benefit would be high.

Coronary artery disease (CAD) patients with impaired renal function for whom either elective or urgent revascularization is felt to be indicated constitute a subgroup in which many of these issues collide. Angiographic assessment may be delayed or deferred out of concern for the precipitation of acute kidney injury, the choice of revascularization strategy in patients with multivessel or left main coronary artery (LMCA) disease may be less clear than recommended by current guidelines, and there may be a relatively higher tolerance for accepting procedural results that under other circumstances would be considered less than complete. Worsening renal function may compromise post-procedural management. Bleeding rates are increased, and thrombotic risk remains elevated (2). The evidence base to help inform management of the complicated CAD patient with impaired renal function is limited but growing (3-5). Practice guidelines and reviews currently include such patients under "special populations," and management recommendations are sparse (6-8).

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In this issue of the *Journal*, Giustino et al. (9) provide a pre-specified subgroup analysis of the 30-day and 3-year outcomes of evaluable patients with (n = 361) versus without (n = 1,508) CKD who were enrolled in the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial (10). In their original report, which showed noninferiority of percutaneous coronary intervention (PCI) with everolimus-eluting stents compared with coronary artery bypass grafting (CABG) for the treatment of patients with LMCA and site-determined low or intermediate SYNTAX scores (11), the 3-year rates of the primary composite endpoint of death, stroke, and myocardial infarction (MI) did not favor one strategy over the other across multiple pre-specified patient subgroups, including those defined by the presence or absence of CKD or of diabetes mellitus (10). Ischemia-driven revascularization was not a component of the primary outcome, a design feature that distinguishes EXCEL from several other coronary revascularization trials (12-14). In EXCEL, 30-day adverse event rates, including those for the composite endpoint,

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arrhythmia, bleeding, periprocedural MI, and infection, were lower and quality of life scores were higher in the PCI arm (10,15).

The current subgroup analysis from EXCEL (9) confirms previous observations that short- and intermediate-term outcomes after revascularization of complex CAD are worse for patients with compared with patients without CKD, an outcome that relates to the more advanced endothelial dysfunction, heavier burden of CV and non-CV comorbidities, and higher prevalence of diffuse, small vessel disease that characterize this population. The rate of adverse events increases in relation to the degree of impairment of renal function, and the development of acute renal failure is associated with a higher risk of death, stroke, or MI at 3 years (9).

But, do the comparative differences in outcomes between PCI and CABG in the context of CKD enable the multidisciplinary heart team to make better decisions regarding the choice of revascularization strategy in individual patients with LMCA disease? How can such nuanced considerations be communicated effectively to enable shared decision-making? The authors provide a balanced interpretation of their findings in a population of patients with predominantly Stages 3A to 5 CKD (10). They acknowledge the principal study finding of the lack of a difference between revascularization strategies in the rate of the 3-year primary composite endpoint, but identify early and late secondary considerations that might influence treatment choice (9). PCI is associated with fewer early major adverse events (including the 30-day composite of death, stroke, or MI; acute renal failure; bleeding; and blood product transfusions) and fewer episodes of stent thrombosis versus symptomatic graft occlusion, but higher rates of ischemia-driven revascularization and noncardiac death over time. The significance of the latter observation is uncertain. Longer (5-year) follow-up is planned, and it will be of interest to see if other treatment-associated differences emerge.

These are complicated considerations that would be difficult for most patients to grasp, especially in urgent clinical situations. Attention to patient preferences and values is critical, but clinical experience would suggest that the majority would opt to avoid the early hazards associated with CABG and take their chances with the late sequelae related to PCI. It is not clear whether there are enough patients or events in this CKD subgroup to allow construction of multivariable risk models using patient-level data that incorporate quality of life and other functional outcomes to predict benefit and harm so that individual decision-making could be made more personal and more precise (16).

The detailed findings presented here add to the evidence base regarding outcomes in CKD patients undergoing revascularization with either PCI or CABG. In the absence of a clear winner, they also accentuate the need for longer-term follow-up in trials of coronary revascularization and argue strongly for the promotion of efforts to utilize validated risk models to help guide difficult decisions.

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