AJKD
Editorial

Drug-Eluting Coronary Stents in Patients With Kidney Disease

Related Article, p. 202

The presence of kidney failure in patients with cardiovascular disease implies an increased risk of acute myocardial infarction, congestive heart failure, and sudden cardiac death within 3 years and as early as 6 months after starting renal replacement therapy.[1] Furthermore, the severity of chronic kidney disease (CKD) has been shown to correlate with increased mortality in those with coexisting coronary artery disease in a dose-dependent fashion, despite percutaneous coronary intervention (PCI) with balloon angioplasty, atherectomy, or placement of a bare-metal stent (BMS).[2] Since the creation of the US Renal Data System in 1989, there has been a steady rise in the diagnosis of kidney failure treated by dialysis or transplant (end-stage renal disease) with nearly 30,000 new patients each quarter; as of 2009, the prevalence approached 573,000 patients. Additionally, among patients with self-reported cardiovascular disease in the United States, the percentage with stage 3 CKD (estimated glomerular filtration rate of 30 to 59 mL/min/1.73 m^2) increased from 13.6% in 1994 to 26.9% in 2006.[3] Drug-eluting stents (DES) for the treatment of coronary artery disease first emerged in 2003 when the sirolimus-based DES was shown to be more effective than BMS in clinical restenosis.[4] Currently, there are 4 approved DES for use in the United States for the treatment of native coronary artery disease (sirolimus [Cypher, Cordis Corp], paclitaxel [Taxus, Boston Scientific], zotarolimus [Endeavour, Medtronic], and everolimus [Xience V, Abbott]), all of which have a strong evidence base for a marked reduction in target lesion restenosis and need for repeat intervention.[5-8] Due to the exclusion of patients with CKD in prior randomized trials of DES compared to BMS, it is unclear whether the benefits of PCI with DES extend to patients with CKD.[9]

In this issue of the *American Journal of Kidney Diseases*, Charytan and colleagues performed a retrospective cohort study including 1,749 patients treated by dialysis or with advanced CKD (serum creatinine $>$ 2 mg/dL) who underwent PCI in Massachusetts between April 2003 and September 2005 and received either DES (1,256 patients) or BMS (493 patients).[10] Patients treated with both DES and BMS were excluded from the study. The primary endpoint consisted of all-cause mortality at 2 years, while post-PCI myocardial infarction and target vessel revascularization were included as secondary outcomes. This study failed to demonstrate a difference in all-cause mortality between the 2 groups. However, a higher rate of mortality and myocardial infarction was observed compared with those without CKD and is consistent with prior studies demonstrating increased overall cardiovascular mortality in this group.[2,11,12]

There are several factors that may be responsible for the observed increase in mortality in patients with CKD. First, decreased kidney function along with the background use of antithrombotic therapy and antiplatelet therapy (aspirin, thienopyridines, glycoprotein IIb/IIIa inhibitors) place patients with CKD undergoing PCI at a high risk for procedure-related bleeding and need for blood transfusion post PCI.[8] Second, the incidence of stent thrombosis, particularly after implantation of DES, mandates uninterrupted treatment with dual antiplatelet therapy for at least 1 year in all patients receiving DES or those receiving BMS implantation in the setting of acute coronary syndrome.[13] The full course of dual antiplatelet therapy along with the complex medical regimen often encountered in patients with CKD make nonadherence to or abrupt discontinuation of antiplatelet therapy more likely. Interestingly, irrespective of dual antiplatelet therapy, the presence of kidney failure has been shown to be an independent predictor of thrombotic events following successful implantation of DES.[14]

Although the nature of this study did not allow for a universal assessment of target vessel revascularization, ie angiographic versus clinically-driven target vessel revascularization, the incidence of target vessel revascularization at 2 years in the DES compared with the BMS group was 13.0% versus 17.6% ($P = 0.06$). Historically, patients with CKD have demonstrated an increase in target vessel revascularization compared with those without decreased kidney function.[15] This finding may be a result of increased surveillance both angiographically and clinically. Patients with CKD, particularly those with kidney failure, may be more likely to undergo repeat cardiac catheterization due to diffuse complex coronary artery disease and a greater number of medical encounters for chest discomfort.[16] This could facilitate evaluation of a previously implanted stent while performing the procedure to assess the severity of a different lesion.

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Charytan et al recognize the limitations of this retrospective study, particularly the designation of kidney disease based on a single recorded creatinine value without knowledge of the chronicity (acute versus chronic). Nevertheless, the study attempts to assess the effectiveness of DES compared to BMS in a complex population of patients with severe CKD. The data presented suggest that for patients with CKD, DES do not represent an advance over BMS, and although not reported, rates of bleeding with the more regimented use of aspirin and clopidogrel in patients with DES was undoubtedly higher.[17] Future research is needed in the area of vascular pathobiology in stented patients with reduced kidney function. The combination of greater degrees of vascular calcification, more circulating thrombin-antithrombin complexes, and circulating cytokines associated with atherosclerosis appears to work against the benefits of slowed endothelialization of DES in this patient population.[18-19] For now, the clinical treatment of CKD patients undergoing PCI should be focused on adequate stent deployment with judicious use of antiplatelet and antithrombotic management. There is no clinical mandate for the use of DES in this complicated patient group at this time; however, the potential reduction in target vessel revascularization with DES remains clinically attractive as we move forward.

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