

Care of Patients With Chronic Kidney Disease Presenting With Acute Coronary Syndrome: Improved, But Not Good Enough

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Chronic kidney disease (CKD) is widely prevalent, with >11 million people affected in the United States and rising.¹ Community studies have shown a rise in prevalence of concomitant cardiovascular disease with worsening renal function.² It is a debilitating illness with a mortality rate for patients undergoing hemodialysis of >20% per year, with approximately half attributable to a cardiovascular cause. Below 81 mL/min per 1.73 m², each reduction of the estimated glomerular filtration rate by 10 units has been shown to be associated with a hazard ratio for death and nonfatal cardiovascular outcomes of 1.10 (95% CI, 1.08–1.12).³

Among patients presenting with acute coronary syndromes (ACSs), ≈30% to 40% have CKD, with ≈1% to 2% undergoing dialysis.^{4,5} This percentage is much higher than the representation of these patients in clinical trials of several therapies and strategies involving patients with ACS, in which patients with severe renal dysfunction have been routinely excluded. A recent analysis showed that nearly half of contemporary cardiovascular disease trials have excluded patients with CKD.⁶ After ACS, the risk of subsequent adverse cardiovascular events is higher in patients with CKD, with a 2-year mortality rate of 50%, double that of patients with normal renal function.⁷ This is attributable to a combination of higher prevalence of comorbidities leading to elevated risk of adverse events as well as lower use of therapies and strategies to mitigate this risk compared with patients with normal renal function. This is despite several studies showing evidence of benefit in patients with all stages of CKD, of most short-term evidence-based treatments, including aspirin, β blockers, statins, and coronary revascularization

procedures.^{4,5,8–10} It is not known how use of evidence-based therapies in this patient population has changed over time and the effect on outcomes. In this issue of the *Journal of the American Heart Association (JAHA)*, Bagai et al present an analysis from the National Cardiovascular Disease Registry Chest Pain–Myocardial Infarction (MI) registry of temporal trends in care delivery and short-term outcomes in patients with CKD and end-stage renal disease undergoing dialysis compared with patients with normal renal function.¹¹

In this study, the authors once again confirm prior observations that patients with severe CKD and undergoing dialysis have a higher prevalence of comorbid conditions, including cardiogenic shock and cardiac arrest, along with a lower likelihood of receiving evidence-based therapies, including timely reperfusion in ST-segment–elevation MI, drug-eluting stents, and medications for secondary prevention. However, these rates are an overall improvement compared with a prior study linking the US Renal Data System database with the National Registry of Myocardial Infarction that showed only 45% of eligible patients undergoing dialysis received reperfusion therapy, only 67% of patients undergoing dialysis were prescribed aspirin, and 57% were prescribed β blockers at discharge.¹² In-hospital mortality of patients undergoing dialysis, however, is unchanged at ≈20% in patients with ST-segment–elevation MI despite the improvements in use of evidence-based therapies and similar ACTION (Acute Coronary Treatment and Intervention Outcomes Network) registry risk score for mortality. This is difficult to explain and may be related to the increase in cardiogenic shock seen in patients with CKD and end-stage renal disease over time.

Management of patients with CKD presenting with ACS is challenging because CKD is associated with an increase in the risk of both thrombotic and bleeding events. These patients frequently received excessive doses of antithrombotic therapy, such as enoxaparin and eptifibatid, which further contributes to bleeding and death.^{13,14} As shown in this study, there was a decrease in use of glycoprotein IIb/IIIa inhibitors over time in all patients. Along with use of other bleeding avoidance strategies not reported in the study, this likely contributed to the decrease in bleeding. Patients undergoing dialysis had the most pronounced decrease in bleeding, which may also have led to the decrease in

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in-hospital mortality noted in patients with non-ST-segment-elevation MI.

When considering the choice of P₂Y₁₂ inhibitors, the newer, more potent agents, like ticagrelor and prasugrel, are associated with a reduction in thrombotic events and an increase in bleeding events compared with clopidogrel. It remains unclear how the presence of CKD impacts the benefits and risks of using these novel P₂Y₁₂ inhibitors. For example, in the PLATO (Study of Platelet Inhibition and Patient Outcomes) trial, there was a greater absolute and relative risk reduction in the primary end point of vascular death, MI, and stroke as well as total mortality in patients with CKD compared with those with normal renal function with ticagrelor as opposed to clopidogrel. Interestingly, although there were more major bleeding events with ticagrelor in all patients, this was not impacted by worsening renal function.¹⁵ Despite these promising benefits of ticagrelor in patients with CKD, an analysis from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium showed that the use of potent P₂Y₁₂ inhibitors (prasugrel and ticagrelor) declined with increasing severity of renal dysfunction.¹⁶ This is similar to the results shown in this study. It is important to further evaluate this potential benefit of novel P₂Y₁₂ inhibitors in patients with CKD presenting with ACS and the effect on cardiovascular and bleeding outcomes.

Another factor to consider is completeness of revascularization. Most patients with extensive multivessel disease undergoing coronary artery bypass graft surgery receive complete or nearly complete revascularization, which is associated with improved long-term outcome. Although patients with CKD tend to have more extensive and severe multivessel coronary artery disease and benefit from coronary artery bypass grafting compared with percutaneous coronary intervention, they are also at increased early surgical risk for adverse in-hospital events.^{17–19} This leads to a higher proportion of patients with CKD receiving percutaneous coronary intervention and incomplete revascularization, which likely impacts their long-term outcomes. In this study, although extent of disease and number of diseased vessels was not reported, we would anticipate that the rates of coronary artery bypass grafting in patients with CKD and undergoing dialysis should have been higher than in patients with normal renal function. If percutaneous coronary intervention is pursued, it is recommended to use drug-eluting stents as opposed to bare metal stents to improve long-term outcomes.^{20,21} Although use of drug-eluting stents increased in all groups over time, it was lowest in patients with ST-segment-elevation MI undergoing dialysis.

An interesting observation from this study is the role played by race and sex in the prevalence of CKD and the association with adverse outcomes. The proportion of nonwhite patients receiving dialysis in this study was ≈50%,

as was the proportion of female patients, much higher than in patients with normal renal function. Race and sex have been independently associated with a lower likelihood of receiving evidence-based therapies and adverse in-hospital and long-term cardiovascular events. It is possible that if treatment bias with race and sex improves, care in patients with CKD may also improve, given its prevalence in nonwhite patients and women seen herein.

Conclusions drawn from this study are that although care of all patients with ACS improved between 2007 and 2015, more work needs to be done in providing evidence-based care to patients with CKD and more so in patients with end-stage renal disease undergoing dialysis. Although these patients are at increased risk for adverse in-hospital events, they are also perhaps more likely to benefit from interventions, such as coronary angiography and complete revascularization. Although long-term outcomes remain to be assessed and there is a need for weighing risks and benefits in each individual patient, it is critical to not overstate the risk of worsening renal function and adverse short-term events or understate the potential short- and long-term benefit of evidence-based therapies in these patients.

Disclosures

Hira is a consultant and proctor for Abbott Vascular Incorporated.

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