CHRONIC KIDNEY DISEASE

Reduced benefit of coronary interventions in chronic kidney disease

Although cardiovascular disease is the major cause of death in patients with chronic kidney disease (CKD), these individuals are typically excluded from trials of cardiovascular interventions. As a result, evidence to guide the management of acute coronary syndromes in CKD is lacking. Registries provide a unique opportunity to draw conclusions on the basis of data from large numbers of patients treated in the 'real world'. According to two studies published in the same issue of the *Journal of the American College of Cardiology Cardiovascular Interventions* that assessed data from registries, CKD is associated with poor outcomes after reperfusion therapy.

Caroline Medi *et al.* used the international GRACE (Global Registry of Acute Coronary Events) database to identify patients with ST-segment elevation myocardial infarction or left bundle branch block, who had or had not undergone primary percutaneous coronary intervention (PCI) or fibrinolysis. In the second study, Faisal Latif *et al.* analyzed data from the EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) registry, which prospectively records data from patients who undergo PCI at any of 42 US centers. Both sets of investigators stratified patients into groups according to their level of renal function.

The GRACE study included 12,532 patients, of whom 3,450 (28%) had impaired

renal function (that is, a glomerular filtration rate <60 ml/min/1.73 m², as estimated by the Modification of Diet in Renal Disease equation). Analysis showed that the likelihood of reperfusion therapy decreased with declining renal function. Neither fibrinolysis nor primary PCI seemed to significantly reduce in-hospital mortality among patients with renal dysfunction; in fact, the mortality risk in patients with moderate CKD increased by 35% in those who had received fibrinolysis. Among patients with moderate renal dysfunction who survived long enough to leave hospital, primary PCI—but not fibrinolysis—was associated with a 59% reduced risk of death within 6 months, although this apparent benefit of PCI was accompanied by an increased incidence of major bleeding during hospitalization.

In the EVENT study, the researchers divided the cohort into four groups on the basis of Cockcroft–Gault-estimated creatinine clearance (>75 ml/min, 50–75 ml/min, 30–49 ml/min and <30 ml/min). Among the 4,791 patients who underwent PCI (generally with drug-eluting stents), outcomes worsened progressively as renal dysfunction declined. The likelihood of death or myocardial infarction during hospitalization increased from 5.8% in the group with the highest rate of creatinine clearance ($n = 2,827$) to 10.0% in the group with the lowest rate of creatinine clearance ($n = 140$); the corresponding percentages after 1 year were 8.5% and 22.1%, respectively. Similarly, the risk of bleeding during hospitalization more than tripled from 3.3% in the patients with the highest level of renal function to 14.3% in the patients with the lowest level of renal function.

"The suggestion (admittedly based on small numbers) that primary PCI might be superior to fibrinolysis in patients with CKD is a potentially important message," comments Charles Herzog, Director of the Cardiovascular Special Studies Center of the US Renal Data System, "as the fear of

contrast nephropathy might be a barrier to performing PCI". Before this superiority can be confirmed, Medi and colleagues note that efforts need to be directed toward lessening the risk of major bleeding. They describe the lack of appreciable benefit of fibrinolysis in patients with renal impairment as "unsettling" in view of the widespread use of this reperfusion strategy.

The authors of the EVENT study argue that the only proven way of improving cardiovascular outcomes in patients with CKD is "good medical therapy". Paradoxically, however, these researchers found that patients were less likely to receive cardioprotective therapy after PCI if they had impaired renal function. In view of the increased bleeding risk associated with reduced renal function, Latif suggests that clinicians should also "be more careful with dosing, choice and monitoring of anticoagulation medications used during the stenting procedure" in patients with CKD. "We all know about altered clearance of these agents [in patients with CKD]," adds Herzog, "but maybe our real-world practice needs to be refined to deal with a special group of patients who may be unforgiving of dosing errors."

To confirm the observations made in these registry studies and determine the optimum management of acute coronary syndromes in patients with CKD, the authors of both studies underscore the urgent need for such patients to be included in randomized interventional trials. The overarching question of why poor renal function is associated with increased mortality remains unanswered.

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Original articles Medi, C. *et al.* Reperfusion in patients with renal dysfunction after presentation with ST-segment elevation or left bundle branch block: GRACE (global registry of acute coronary events). *JACC Cardiovasc. Interv.* 2, 26–33 (2009). Latif, F. *et al.* In-hospital and 1-year outcomes among percutaneous coronary intervention patients with chronic kidney disease in the era of drug-eluting stents: a report from the EVENT (evaluation of drug-eluting stents and ischemic events) registry. *JACC Cardiovasc. Interv.* 2, 37–45 (2009).