Use of Recommended Medications after Myocardial Infarction—Is Kidney Function Really the Problem?

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Editorial

Patients with chronic kidney disease (CKD) suffer the paradox of high risk for heart disease and yet reduced use of standard therapies for treatment and prevention of heart disease. The classic example in the literature is the reduced use of standard of care medications after acute myocardial infarction (AMI), now shown in a variety of settings even where the cost of prescription drugs should be a minimal factor (1,2). Only since 2002 has the Joint Commission on Accreditation of Hospitals (JCAHO) stipulated ORYX core indicators, which recommend the use of aspirin and β blockers in a setting of AMI unless explicitly contraindicated, a timeframe only one study yet published has included (2,3).

Are primary care physicians really basing therapy after AMI on kidney function (and in most studies this means serum creatinine)? This seems difficult to believe, especially as many studies indicate that a large proportion of patients admitted for AMI never have serum creatinine levels drawn. If true, this would seem a potentially “easy” fix in this era of electronic medical records and automated reminders. However, perhaps poor kidney function is strongly associated with other factors that lead to reduced use of standard of care medications. The identification of these other potential factors has been only partially addressed by previous studies, and is the primary focus of the study by Winkelmayer et al. in the current issue of CJASN 4. As the authors suggest, given the observational nature of all literature in this area, these are murky waters.

Nephrologists are well aware that conditions such as hypertension, diabetes, heart failure, and many others are more common among patients with CKD than among those with normal kidney function. CKD also is more common with increasing age. However, previous studies did not adjust the association of kidney function with medication use after AMI for these other factors. Winkelmayer and colleagues report in their study of 431 patients of the US Department of Defense (DOD) health system from 2001 to 2004 that of all measured factors, the site of admission had the strongest association with medication use (either upon admission or upon discharge), and therefore stratified analysis by admission to the Coronary Care Unit (CCU) in the Mayo Clinic from 1988 to 2000 5. While that study reported significant disparities in medication use based on Cockcroft-Gault creatinine clearance, analysis was not adjusted for multiple factors and trends over time were not assessed. A recent, relatively small study (3000 patients admitted to the CCU versus other wards (2)). In this study, patients admitted to the CCU for AMI in a DOD health system had no evidence of reduced use of medications according to kidney function, while those who suffered AMI in other settings had marked disparity in use of medications by kidney function, although these differences were attenuated to nonsignificance in adjusted analysis. Age was not an independent predictor of medication use. Of note, kidney function was significantly higher among patients admitted to the CCU than for other wards, and CCU patients were distinct from non-CCU patients in many other important respects. Site of care for AMI, which may be difficult to identify from large registries, is also noteworthy as there may be substantial biases in the decision of where to admit a patient for AMI, including the degree of subspecialist oversight, and patients who suffer after AMI in non-CCU settings, particular after surgery, may not tolerate or otherwise be candidates for standard intervention. Although some previous studies have tried to identify “ideal” candidates for therapy, the rationale for admission to one unit versus another may be poorly documented. In addition, patients presenting with advanced directives declining heroic measures may also be difficult to identify in registry databases.

Perhaps the most substantial difference in study design be-
between the Winkelmayer study and that of other studies is that medication use was assessed at 90 d after AMI, by which time 26% of the original cohort had died. Because we know from other studies that reduced use of medications after AMI (as well as reduced kidney function after AMI) may be associated with increased risk of death, the findings of this study may represent survival bias. In other words, the patients who did not receive standard of care medications, as well as those with reduced kidney function, may have died prematurely, leading to spuriously negative findings. Because the authors have information on medication use before hospitalization, this would be relatively straightforward to prove or disprove on reanalysis.

Another possibility is that physician prescribing practices truly are improving over time. So far at least three studies, including the one by Winkelmayer et al., have assessed populations after the 1997 ORYX indicators were promulgated. A study of the Veterans Health Administration system reported statistically significant differences in use of β blockers, aspirin, and angiotensin-converting enzyme inhibitors after AMI between the highest (≥90 cc/min per 1.73 m²) and the lowest (<30 cc/min per 1.73 m²) levels of eGFR, but these disparities were substantially smaller than previously reported (<10% difference in β blocker use and exactly 10% difference in aspirin use). The previously cited DOD study reported even smaller differences, and attenuation of all statistical significance after adjustment, findings not previously reported.

Given differences in populations and study design, as well as the observational and unstandardized nature of this literature, it will be difficult to assess progress in this area. Kidney function itself may not be the true culprit for reduced use of medications after AMI, but it may help point the way.

References


Please see the related article, “Kidney Function and Use of Recommended Medications after Myocardial Infarction in Elderly Patients,” on pages 796–801.