Renal Dysfunction
The Wake-Up Alarm for Chronic Vascular Disease*

Manesh R. Patel, MD

Atherosclerotic vascular disease is a chronic progressive disorder affecting the arterial vessels leading to plaque formation, rupture, healing, narrowing, and occasionally thrombotic occlusion with downstream clinical consequences. Most of our current care is aimed at acutely treating the clinical sequela of thrombosis and encouraging healthy behaviors and prescribing therapies that are aimed at preventing this process. Inherent in this patient-centered care is the determination of individual risk, risk that warrants both aggressive preventive and clinical therapeutic interventions. Until we are able to rapidly incorporate all of the possible individual data streams in health care, clinicians use primary prevention, secondary prevention, and risk markers to help define thresholds for care. Unfortunately, aside from lipid levels and blood pressure, there are limited markers or triggers used to escalate care for patients with chronic vascular disease.

Renal dysfunction, or chronic kidney disease (CKD), may be the ideal alarm for practicing clinicians to escalate care for patients with vascular disease. Renal dysfunction has been associated with increased atherothrombotic events in patients with congestive heart failure (1), acute coronary syndromes (2), and atrial fibrillation (3,4). In addition to increasing cardiovascular events, renal dysfunction is associated with increased bleeding risk. For all of these observations, 2 central questions exist around the risk associated with CKD: 1) is the risk with renal dysfunction physiologically causal and modifiable; and 2) what is the benefit to risk of newer therapies in patients with renal dysfunction specifically?

With this background, Fox et al. (5) present the findings of the COMPASS (Cardiovascular Outcomes for People using Anticoagulation Strategies) trial in patients with renal dysfunction in the Journal (5). They perform a secondary analysis from the trial involving 27,395 patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD).

Notably, 6,276 (23%) patients had renal dysfunction defined as estimated glomerular filtration rate (GFR) <60 ml/min. The patients with renal dysfunction were older and were more likely to be female, have peripheral artery disease, and have diabetes. The rate of major adverse cardiovascular events (MACE) (including cardiovascular death, myocardial infarction, and stroke) was almost double in patients with renal dysfunction (8.4% in the aspirin-alone arm) compared with patients without renal dysfunction (4.5% in the aspirin-alone arm). Rates of major bleeding were also increased in patients with renal dysfunction (2.7% in the aspirin-alone arm) compared with patients without renal dysfunction (1.6% in the aspirin-alone group). These data confirm that indeed, renal dysfunction even at the moderate rate noted in the trial was associated again with increased cardiovascular events and bleeding rates.

The unique findings are the consistent effects of 2.5 mg rivaroxaban twice daily plus aspirin in both patients with and without renal dysfunction. The reduction in MACE in patients with chronic CAD and PAD without renal dysfunction was hazard ratio (HR): 0.75 (95% confidence interval [CI]: 0.64 to 0.90) compared with HR: 0.75 (95% CI: 0.60 to 0.94) in patients with renal dysfunction. With regard to major bleeding, there was an increase with the dual therapy antithrombotic regimen of 2.5 mg twice daily of
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Aspirin. Although prior robust and encouraging regarding the clinical effect “dysfunction could be considered a marker of with the rate of MACE events nearly doubling in patients with chronic CAD and PAD. In essence, renal dysfunction could be considered a marker of “polyvascular” disease carrying a similar risk to patients with evidence of atherosclerosis in more than 1 clinical vascular bed (6). This recognition is important, as measures of CKD and health system data on populations of patients at risk for atherothrombotic events could be identified using this single marker. Second, renal dysfunction is also a marker of bleeding risk, with many of the underlying comorbidities associated with renal dysfunction leading to higher rates of bleeding in patients with vascular disease.

Finally, the data presented by Fox et al. (5) are robust and encouraging regarding the clinical effect of the antithrombotic regimen of rivaroxaban and aspirin. Although prior findings with the non-vitamin K antagonists in patients with renal dysfunction and atrial fibrillation have been supportive (7,8), the exact benefit to risk trade off compared to the overall trial population and dosage in clinical practice varies. In the COMPASS trial, the patients with renal dysfunction had higher rates of MACE and major bleeding, and seem to have marked benefit to risk profiles with dual antithrombotic therapy with 2.5 mg BD rivaroxaban plus aspirin when compared to aspirin alone. Hence, in this specific chronic vascular disease population, the risk with renal dysfunction seems to be modifiable and beneficial to most patients with this therapy. Although there are limited patients with severe CKD and the majority of patients have moderate renal dysfunction in this study, this likely represents the vast majority of chronic vascular patients in practice. Therefore, the finding of renal dysfunction should serve as a wake-up alarm for both clinicians and patients with chronic vascular disease; it alerts of an increased risk for adverse cardiovascular events, and this risk is modifiable.

REFERENCES


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