LETTERS TO THE EDITOR

International Normalized Ratio Control in Patients With Atrial Fibrillation and CKD

To the Editor:

The analyses by Jun et al[1] and Shen et al[2] add to the growing list of observational studies suggesting a net clinical benefit for warfarin in patients with chronic kidney disease (CKD) with atrial fibrillation. The debate about warfarin safety in CKD is ongoing, with as many proponents as opponents. We want to emphasize the possible confounding effect of the quality and intensity of anticoagulation control using international normalized ratios (INRs) and time in therapeutic range (TTR). This information is usually lacking in administrative records, but it is of fundamental importance when assessing warfarin safety and effectiveness in clinical practice. In the general atrial fibrillation population, it is well established that maintenance of INR in the therapeutic range ensures anticoagulant efficacy with reduced risk for ischemic stroke and bleeding. It is becoming apparent that patients with moderate to severe CKD, including those with CKD requiring dialysis, have reduced TTR despite comparable INR monitoring intensity.[3] It is possible that worse INR control explains the observed increased risk for adverse events in warfarin-treated patients with CKD in previous studies. We have observed that in both patients with CKD not on dialysis[4] and those on dialysis,[5] an optimal TTR while receiving warfarin was associated with better outcomes. Although the industry is pushing hard for the introduction of novel oral anticoagulants, we should not disregard a likely valid therapy on the basis of observational studies. We believe that more effort should be made to identify the reasons behind the poorer INR control in this population and to design more intensive warfarin management strategies.

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In Reply to 'International Normalized Ratio Control in Patients With Atrial Fibrillation and CKD'

Genovesi and Carrero[1] raise the important issue of achieving and maintaining optimal international normalized ratio (INR) control in patients with atrial fibrillation, a task that may be more challenging among those with chronic kidney disease (CKD). Given the importance of time in therapeutic range in determining the safety and effectiveness of warfarin,[2] we agree that better understanding of the predictors of poor INR control and the implementation of risk-based management strategies based on this assessment could contribute to a favorable risk-benefit profile with warfarin therapy in patients with CKD with atrial fibrillation. However, we also note that there remain issues regarding the safety of warfarin in patients with CKD that are independent of INR control and that underscore the need for randomized trials in this area. Although accumulating observational data provide promising evidence on the safety profile of warfarin in this patient group, there is also evidence to suggest that besides the hemorrhagic mechanism for stroke, warfarin may accelerate vascular calcification in patients with CKD, potentially leading to further increased risk for ischemic stroke.[3,4] Such conflicting data highlight the need for: (1) large multicenter trials to elucidate the efficacy and safety of warfarin therapy (and anticoagulation more broadly) across the spectrum of CKD, and (2) the careful consideration of baseline stroke and bleeding risks in eligible participants to ensure that ethical concerns associated with such trials are appropriately addressed.

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