

## CHRONIC KIDNEY DISEASE

## Warfarin bleeding risk increased in CKD

Patients with chronic kidney disease (CKD) might require lower starting doses of the anticoagulant warfarin and more careful monitoring during treatment with this agent than the general population, say researchers at the University of Alabama at Birmingham.

“The adjusted risk of major hemorrhage was more than twofold greater among patients with severe CKD”

Currently, anticoagulation with warfarin is generally prescribed and managed in patients with CKD in the same way as in those without CKD. Although it is recognized that reduced doses of warfarin may be required in patients on dialysis, data on the advantages and risks of long-term warfarin treatment in the CKD population have been limited.

The current study was a secondary analysis of data from 565 participants in the Pharmacogenetic Optimization of Anticoagulation Therapy (POAT)

study, 59.5% of whom had no or mild CKD (defined as an estimated glomerular filtration rate [eGFR]  $\geq 60$  ml/min/1.73 m<sup>2</sup>), 31.2% of whom had moderate CKD (eGFR 30–59 ml/min/1.73 m<sup>2</sup>) and 9.4% of whom had severe CKD (eGFR  $< 30$  ml/min/1.73 m<sup>2</sup>).

The researchers found that individuals with severe CKD required significantly lower warfarin doses than those with no, mild or moderate CKD, even after adjustment for clinical factors (for example, age, sex, warfarin dose and vitamin K intake) and genetic factors (*CYP2C9* and *VKORC1* genotype). In addition, patients with severe CKD had much poorer anticoagulation control (that is, spent less time in the international normalized ratio [INR] target range) and a much higher risk of excessive anticoagulation (INR  $> 4$ ) than patients with no, mild or moderate CKD. The adjusted risk of major hemorrhage was more than twofold greater among patients with severe CKD than among those with no or mild CKD. The adjusted risk of minor hemorrhage was also increased

among individuals with severe CKD, but this increased risk was mainly a result of access-related minor bleeding after dialysis.

The findings indicate that reduced renal function could have implications for a greater proportion of warfarin users than previously believed. However, the investigators caution that the decision to use or withhold warfarin should not be made solely on the basis of renal function. “We need to balance the risk of hemorrhage on treatment with the thromboembolic risk associated with withholding warfarin therapy in patients with severe CKD,” concludes lead investigator Nita Limdi. “Perhaps ongoing and future research efforts evaluating both thromboembolic and hemorrhagic events will facilitate a more-robust assessment of risk estimates and balanced clinical decisions”.

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