

CARDIOVASCULAR DISEASE

Warfarin might be beneficial in nondialysis-dependent patients with CKD and atrial fibrillation

Regardless of renal function, warfarin therapy was associated with a reduced 1-year risk of death, myocardial infarction (MI) and ischaemic stroke, without a significantly increased risk of bleeding events, in a large cohort of nondialysis-dependent survivors of MI with atrial fibrillation. This new finding from an observational, prospective study by Juan Jesús Carrero and colleagues suggests that patients with atrial fibrillation and chronic kidney disease (CKD) who do not require dialysis might benefit from warfarin therapy.

“An important knowledge gap exists regarding the safety and effectiveness of common drugs in individuals with CKD,” says Carrero. He explains that because kidney dysfunction interferes with drug metabolism and elimination, these patients have traditionally been excluded from randomized clinical trials. Thus, clinical practice guidelines are often extrapolated to patients with CKD in the absence of formal evaluation. The use of warfarin and other oral anticoagulants in patients with CKD and atrial fibrillation is controversial and caution is advised regarding warfarin therapy in those who have stage 5 CKD or are on dialysis.

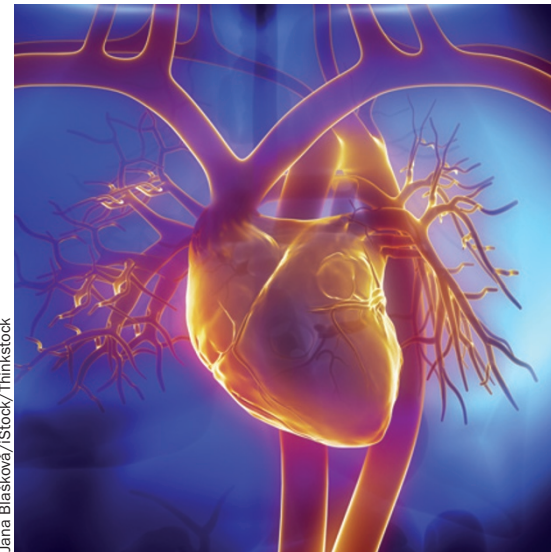
“Although patients with atrial fibrillation and kidney disease have a clear indication for anticoagulant therapy because of their increased risks of ischaemic stroke and thromboembolism, recent observational studies in patients undergoing dialysis have provided conflicting results, with some data suggesting that warfarin use may confer harm,” says Carrero. Indeed, one such study—which reported an increased risk of bleeding but no reduction in risk of stroke in warfarin-treated patients with atrial fibrillation and end-stage renal disease on dialysis—is discussed by Wolfgang C. Winkelmayer in this issue of *Nature Reviews Nephrology*.

“Whether CKD imposes a risk in warfarin therapy is a question of great

clinical relevance, particularly for disciplines in which kidney function is seldom considered,” says Carrero. “We, therefore, studied outcomes associated with warfarin use in patients with atrial fibrillation and various degrees of kidney dysfunction prior to dialysis initiation.”

Using the SWEDEHEART registry, the researchers identified 24,317 patients with atrial fibrillation who were admitted to Swedish hospitals with—and survived—an acute MI between 2003 and 2010. Carrero explains the advantages of this registry approach: “because of the availability of standardized creatinine assessments as per the established protocol, we were able to estimate the severity of underlying CKD using the Chronic Kidney Disease Epidemiology Collaboration formula. In addition, we could control for, and propensity-match, important patient characteristics at admission (including MI severity, bleeding risk and comorbidities), in-hospital procedures and discharge information.”

The researchers report that 5,292 (21.8%) study participants were prescribed warfarin at hospital discharge and 12,583 (51.7%) had stage 3 or greater CKD. Among patients with kidney disease, those with stage 5 CKD were least likely to be prescribed warfarin. The cumulative incidence of death and hospital readmission due to MI, ischaemic stroke or bleeding events (including haemorrhagic stroke, gastrointestinal bleeding and bleeding resulting in anaemia) within 1 year of hospital discharge increased with severity of CKD. However, in participants with normal renal function and in those with moderate or severe CKD, warfarin treatment versus no warfarin use was associated with a reduced incidence of the composite outcome of death, MI and stroke within 1 year of hospital discharge. Moreover, warfarin therapy was not associated with a significant increase in risk of bleeding events in any category of kidney function.



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“Our study supports the continued use of warfarin—with good international normalized ratio control—in patients with CKD. However, the generalizability of these findings to populations other than survivors of MI with atrial fibrillation cannot be assumed,” concludes Carrero. “As clinical trials to definitively assess the safety of warfarin therapy in patients with kidney disease would be unethical, clinical evidence must be derived from observational studies. Because of the design and representativeness of our study, we believe that we provide a robust scenario from which to continue discussing and evaluating anticoagulant treatment options for this vulnerable population.”

Ellen F. Carney

Original article Carrero, J. J. *et al.* Warfarin, kidney dysfunction, and outcomes following acute myocardial infarction in patients with atrial fibrillation. *J. Am. Soc. Nephrol.* 311, 919–928 (2014)

Further reading Shah, M. *et al.* Warfarin use and the risk for stroke and bleeding in patients with atrial fibrillation undergoing dialysis. *Circulation* doi:10.1161/CIRCULATIONAHA.113.004777 | Winkelmayer, W. Still unresolved: warfarin in ESRD with atrial fibrillation. *Nat. Rev. Nephrol.* doi:10.1038/nrneph.2014.48