

Are newer anticoagulants safer than warfarin?



A new study compared outcomes among patients with atrial fibrillation hospitalised for bleeding after starting anticoagulation (warfarin, dabigatran, or rivaroxaban). Results show rivaroxaban and dabigatran were associated with shorter hospitalisations; however, there were no differences in 30- and 90-day mortality. These findings suggest bleeding associated with the newer agents is not more dangerous than bleeding associated with warfarin.

The development of Non-vitamin K Oral Anticoagulants (NOACs) has provided an alternative to warfarin for stroke prophylaxis in atrial fibrillation. Two widely used NOACs are dabigatran, a direct thrombin inhibitor, and rivaroxaban, a factor Xa inhibitor. Two other factor Xa inhibitors, apixaban and edoxaban, are also FDA-approved. The effectiveness and safety — including incidence of bleeding — of each NOAC compared to warfarin have been studied in randomised controlled non-inferiority trials.

There has been little investigation to determine if NOAC-associated bleeding is more severe or complicated than warfarin-associated bleeding. Most research has focused on intracranial haemorrhage. One meta-analysis of trial data found NOACs to be associated with reduced mortality and intracranial haemorrhage but that, after adjusting for site of bleeding, there was no difference in incidence of fatal bleeding for any given bleeding site.

This study aimed to investigate the complexity and severity of NOAC-associated bleeding. A U.S. commercial database of 38 million members from 1 November 2010 to 31 March 2014 was used to examine adults with atrial fibrillation hospitalised for bleeding after starting warfarin (2,446), dabigatran (442), or rivaroxaban (256). Outcomes included difference in mean total length of hospitalisation, proportion of ICU admissions, mean length of ICU stay, and all-cause 30- and 90-day mortality.

Multivariable regression modelling with propensity score weighting showed warfarin users were hospitalised 2.0 days longer (95% CI 1.8–2.3; $p < 0.001$) than dabigatran users and 2.6 days longer (95% CI 2.4–2.9; $p < 0.001$) than rivaroxaban users. Dabigatran users were hospitalised 0.6 days longer (95% CI 0.2–1.0; $p = 0.001$) than rivaroxaban users. There were no differences in the proportion of ICU admissions. Among ICU admissions, warfarin users stayed 3.0 days (95% CI 1.9–3.9; $p < 0.001$) longer than dabigatran users and 2.4 days longer (95% CI 0.9–3.7; $p = 0.003$) than rivaroxaban users. There was no difference in ICU stay between dabigatran and rivaroxaban users. There were no differences in 30- and 90-day all-cause mortality.

Even among patients who discontinued anticoagulation at discharge, researchers say, warfarin was associated with longer hospitalisation. Among patients restarting anticoagulation, warfarin's association with prolonged hospitalisation was stronger, suggesting that the need to titrate warfarin dose and devise appropriate follow up may contribute to the increased medical complexity of warfarin-associated bleeding in some patients, the researchers explain.

"The significant risk of mortality after admission for both warfarin- and NOAC-associated bleeding underscores the need for further research into the complexity, severity, and treatment of bleeding during oral anticoagulation. Particular attention should be paid to the newest oral anticoagulants and how associated bleeding is affected by transfusion of blood products and the use of reversal agents," the study concludes.

Source: [PLOS One](#)
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