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Resumption of anticoagulation after major bleeding decreases the risk of stroke in patients with atrial fibrillation

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Context
Anticoagulation decreases the risk of stroke and other thromboembolic complications in patients with atrial fibrillation (AF) at the cost of an increased risk of major bleeding. If patients experience an anticoagulation-related major bleeding complication, the clinician faces the dilemma of whether to resume anticoagulation treatment or not. Evidence-based recommendations are lacking, and there is a wide variation in treatment of these patients, with anticoagulants, antiplatelets or no anticoagulation at all, while there is even less experience with non-vitamin K oral anticoagulants (NOACs), such as dabigatran. This study aimed to (1) evaluate anticoagulation use after a major bleeding event on dabigatran or warfarin and (2) compare outcomes between patients discontinuing anticoagulation and those restarting dabigatran or warfarin.

Methods
This was a retrospective study using data from a Medicare database between 2010 and 2012, early after the introduction of the NOACs. Patients were included if they were known with AF and had experienced a major bleeding event requiring hospitalisation while using dabigatran (n=404) or warfarin (n=1135) and were discharged alive. Patients who received a prescription for dabigatran or warfarin and patients who never filled a prescription for an oral anticoagulant after the index bleeding event were followed until the end of 2012 or until the occurrence of stroke, recurrent bleeding or death. Covariates and outcome variables were assessed using International Classification of Diseases, Ninth Revision (ICD-9) codes.

Findings
After the bleeding event, 49% of dabigatran and 47% of warfarin users reintitated anticoagulation. Discontinuation of oral anticoagulation occurred significantly more often in older patients. Risk of ischaemic stroke and all-cause mortality was lower in patients who reintitated anticoagulation than in those who discontinued anticoagulation: HR 0.66, 95% CI 0.44 to 0.99 for dabigatran; HR 0.76, 95% CI 0.59 to 0.97 for warfarin. Recurrent major bleeding occurred more often in warfarin than in dabigatran users (HR 2.31, 95% CI 1.19 to 4.76) or in those who discontinued anticoagulation (HR 1.56, 95% CI 1.10 to 2.22), while there was no difference in recurrent bleeding between dabigatran users versus those who discontinued anticoagulation (HR 0.65, 95% CI 0.32 to 1.33).

Commentary
Other studies have shown a decreased risk of stroke and mortality when reinitiating oral anticoagulation after a major bleeding event, compared with discontinuing anticoagulation. However, resumption of anticoagulation can lead to an increased risk of recurrent bleeding as was observed with warfarin in the current study, while a number of studies have shown comparable bleeding risk with or without anticoagulation during follow-up.

Strengths of this study include the presentation of real-life data, while an important limitation is the retrospective nature; baseline characteristics and follow-up variables were deducted from ICD-9 codes. Not all variables of interest were available, for example, international normalised ratio levels, dabigatran dosages or comorbidities such as cancer, which could influence decision-making and outcome. Furthermore, only oral anticoagulants were taken into account; patients classified as discontinuing anticoagulation could have been using, for example, low molecular weight heparins. Data regarding antiplatelet use during follow-up, which could be used as alternate anticoagulant, are also lacking. If prescribed in combination with (non-vitamin K) oral anticoagulants, antiplatelets could add to bleeding risk. Most importantly, a selection bias was probably present in this observational study, both concerning the decision to discontinue anticoagulation (more likely in older patients and patients with significant comorbidities) and the decision to prescribe dabigatran (more likely in low-risk patients in these early days of dabigatran and/or lower dabigatran dosage), which could importantly influence outcome. We are therefore in need of randomised clinical trials to avoid this selection bias. The question as to whether anticoagulation should or should not be prescribed after a major bleeding event is currently under investigation in the APACHE-AF trial.

Implications for practice
The major implication of this study is that after an anticoagulation-related bleeding event in patients with AF, resumption of oral anticoagulation should strongly be considered to decrease the risk of stroke and mortality. However, randomised clinical trials are much awaited for to be able to provide robust recommendations.

Competing interests None declared.
Provenance and peer review  Commissioned; internally peer reviewed.
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References