The Case:
This is a 62-year-old man who presents with an intracerebral hemorrhage (ICH) while taking warfarin for atrial fibrillation. His INR is 2.5. His CHADS score is 3.

The Questions:
(1) Should warfarin be restarted to decrease the risk of future thromboembolism?
(2) Does the location of the ICH or the indication for anticoagulation influence the decision?
(3) If warfarin is to be restarted, when?

The Controversy:

Resumption of Oral Anticoagulation Following Warfarin-Associated ICH.

Yes

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The decision on restarting warfarin means to balance between 2 risks: ischemic stroke and rebleeding.

Without any secondary prophylaxis, this patient has an annual stroke risk rate of 5.9% according to his CHADS$_2$ score of 3 and anticoagulation is recommended as thromboprophylaxis in patients with atrial fibrillation and a CHADS$_2$ score of $\geq$2. These recommendations, however, cannot be directly applied to patients with bleeding complications. No prospective data are available that particularly looked at patients with atrial fibrillation, a CHADS$_2$ score $\geq$2 (or need for anticoagulation), and an intracranial bleeding that occurred in association with warfarin treatment. Smaller retrospective studies report low risk of ischemic events during the first 3 weeks before warfarin was restarted. The largest retrospective analysis reported rebleedings both in patients who resumed warfarin and those who did not; however, arterial thromboembolic events occurred more frequently.

In a follow-up study in 13 high-risk patients (mitral or aortic valve replacement) who had an intracerebral hemorrhage (ICH) at the time of being on warfarin, ICH recurrence was predominant during the acute phase, whereas the risk of ischemic stroke became a prominent issue during 2-year follow-up. There is no way of accurately estimate the bleeding risk of an individual patient after ICH occurring during warfarin treatment and bleeding risk scales such as the Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile International Normalized Ratio, Elderly, Drugs/alcohol concomitantly (HAS-BLED) does not include prior ICH in the basis of risk estimation.

It is assumed that patients with lobar location of ICH have a higher probability of rebleeding, compared with deep hemispheric bleeding, and only patients with deep hemispheric location should receive warfarin again. Factors indicating a high stroke risk in atrial fibrillation such as age, prior stroke, or hypertension also convey a higher risk of bleeding complications including ICH; however, a high risk of thromboembolic events accentuates the need for reliable thromboprophylaxis.

If warfarin is to be restarted, when? Currently available data are contradictory. A review of 6 observational studies on oral anticoagulation in patients with mechanical valves concluded that restarting oral anticoagulation after 7 to 14 days appeared safe; however, a delay of reintroduction of warfarin until between 10 and 30 weeks has also been suggested. Nevertheless, all studies, however, present a similar pattern: the probability of ICH recurrence is highest during the early phase after the index bleeding and decreases over time, whereas risk of ischemic events increases over time and will cross at some point in time.

In this patient, I suggest the following concerning secondary prophylaxis. If imaging shows lobar bleeding and clear signs of microangiopathy, he should receive antiplatelet therapy. If the patient has a deep hemispheric bleeding, he...
should be given warfarin provided that blood pressure, blood glucose, and lipid metabolism can be sufficiently controlled. Oral anticoagulation can be restarted 7 to 14 days after the incident if the patient is otherwise stable. The risk of intracranial hemorrhage might not inevitably be increased in warfarin-treated patients when compared with new (eg, dabigatran) oral anticoagulants. In fact, intracranial bleeding risks seem to align when the quality of warfarin therapy is optimized.7

Disclosures
T.S. joined the Advisory Board for Boehringer Ingelheim after the article was written.

References

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