Resuming warfarin after gastrointestinal tract bleeding linked with lower risk for thrombosis, death

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A study of patients treated with the anticoagulant medication warfarin suggests that resuming warfarin therapy after an episode of gastrointestinal tract bleeding was associated with lower risk for thrombosis (blood clot) and death, according to a report published Online First by *Archives of Internal Medicine*.

Gastrointestinal tract bleeding (GIB) affects about 4.5 percent of patients treated annually with warfarin. A history of major bleeding can be a predictor for future serious bleeding, but interrupting or stopping warfarin therapy can increase the risk for complications. Therefore, patients with warfarin-associated GIB present two clinical dilemmas: should warfarin therapy be stopped and, if so, when should it be resumed, according to the study background.

Daniel M. Witt, Pharm.D., F.C.C.P., B.C.P.S., of Kaiser Permanente of Colorado, and colleagues sought to determine the incidence of thrombosis (stroke, systemic embolism and venous thromboembolism), recurrent GIB and death, as well as the time until warfarin therapy was resumed during the 90 days following a GIB event. Researchers used administrative and clinical databases from Kaiser Permanente Colorado in their retrospective cohort study, which included 442 patients (average age 74 years) with a warfarin-associated index GIB.

"The results highlight the clinical dilemma of managing warfarin therapy

following a hospitalization or ED [emergency department] visit for GIB. Although we observed a numerical increase in recurrent GIB associated with not interrupting or resuming warfarin therapy in the 90 days after the index GIB, this increase was not statistically significant," the authors note. "However, a decision not to resume warfarin therapy was associated with a significantly increased risk of both thrombosis and death from any cause."

Following the index GIB, 260 patients (58.8 percent) resumed warfarin therapy, including 41 patients whose therapy was never stopped. The median time to resume therapy was four days (2-9 days). Resuming warfarin therapy was associated with a lower risk for thrombosis (hazard ratio [HR], 0.05) and with a lower risk of death (HR, 0.31), according to the study results.

Among the 260 patients who resumed warfarin, there was one thrombotic event, 26 episodes of recurrent GIB, and 15 deaths in the 90 days following the initial GIB event, whereas among the 182 patients who did not resume warfarin, there were 10 thrombotic events, 10 episodes of recurrent GIB, and 37 deaths.

"Our analysis suggests that, for many patients who have experienced GIB, the benefits of resuming warfarin therapy will outweigh the risks. Further research will be needed to identify the optimal duration of warfarin interruption after a GIB event and the patients for whom a more prolonged interruption can be justified," researchers conclude.

In a commentary, Daniel J. Brotman, M.D., of Johns Hopkins Hospital, Baltimore, and Amir K. Jaffer, M.D., of the University of Miami, write: "First, this study demonstrates that physicians and patients are willing, in most instances, to resume anticoagulation after GI [gastrointestinal tract] bleeding."

"On the basis of these observations and in the absence of other studies providing competing data, we believe that most patients with warfarin-associated GI bleeding and indications for continued long-term antithrombotic therapy should resume anticoagulation within the first week following the hemorrhage, approximately 4 days afterward, if we use the median anticoagulation reinitiation time in this study as a benchmark," they continue.

"Although not specifically addressed in this study, we would hesitate to continue concurrent antiplatelet therapy in these patients without a compelling indication to do so (such as a recent coronary stent) and also would caution against extrapolating these findings to newer anticoagulants, such as dabigatran and rivaroxaban, that may be associated with more GI bleeding than warfarin when used long-term and whose effects are not easily reversed," the authors conclude.

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