

A risk model predicted major bleeding in older patients with atrial fibrillation receiving warfarin therapy

Shireman TI, Mahnken JD, Howard PA, et al. Development of a contemporary bleeding risk model for elderly warfarin recipients. *Chest*. 2006;130:1390-6.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Geriatrics ★★★★★☆ Hematol/Thrombo ★★★★★☆

QUESTION

In older patients with atrial fibrillation (AF) who are receiving warfarin therapy at hospital discharge, does a contemporary bleeding risk model (BRM) predict major bleeding?

METHODS

Design: 2 cohort studies, 1 for derivation and 1 for validation from the National Registry of Atrial Fibrillation.

Setting: United States.

Patients: 26 345 patients ≥ 65 years of age (88% > 70 y, 43% > 80 y, 53% women; 19 875 for derivation, 6470 for validation) with AF who were receiving warfarin therapy at hospital discharge. Exclusion criteria included discharge against medical advice, transfer to another acute care hospital, enrollment in managed care, or death during hospitalization.

Description of prediction guide: The risk score (range 0 to 4.17) categorized patients into low- (score ≤ 1.07), moderate- (score > 1.07 to < 2.19), or high-risk (score ≥ 2.19) groups. The risk score was a summation of the log likelihood of 8 clinical variables: age (≥ 70 y = 0.49), sex (women = 0.32), remote bleeding = 0.58, recent bleeding = 0.62, alcohol or drug abuse = 0.71, diabetes = 0.27, anemia = 0.86, and antiplatelet drugs = 0.32.

Outcomes: Hospitalization for major acute bleeding within 90 days of index hospital discharge.

MAIN RESULTS

8 independent clinical predictors of major bleeding were identified in the derivation cohort (Table). In the validation cohort, major bleeding events developed in 35 (0.9%) low-risk patients [likelihood ratio [LR] 0.6]*, 48 (2.0%) moderate-risk patients {LR 1.4}* , and 12 (5.4%) high-risk patients {LR 3.8}* ($P < 0.001$). The area under the receiver-operating characteristic (AUROC) curve was 0.632. This model had similar predictive characteristics compared with 2 previous BRMs: Outpatient Bleeding Risk

Index (AUROC curve 0.613) and Kuijer and colleagues' model (AUROC curve 0.503).

CONCLUSION

In older patients with atrial fibrillation who were receiving warfarin therapy at hospital discharge, a bleeding risk model predicted major bleeding.

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*LR defined in Glossary and calculated from data in article.

Multivariate predictors of major bleeding from the derivation cohort of older patients with atrial fibrillation receiving warfarin therapy at hospital discharge†

Predictors	Hazard ratio (95% CI)
Age ≥ 70 y	1.6 (1.1 to 2.5)
Women	1.4 (1.1 to 1.7)
Remote bleeding	1.8 (1.4 to 2.4)
Recent bleeding	1.8 (1.4 to 2.4)
Alcohol or drug abuse	2.0 (1.1 to 3.8)
Diabetes	1.3 (1.0 to 1.7)
Anemia	2.4 (1.8 to 3.2)
Receipt of antiplatelet drugs	1.4 (1.1 to 1.8)

†CI defined in Glossary.

COMMENTARY

The risk for stroke in patients with AF can be greatly reduced with warfarin. However, many patients who would benefit from warfarin therapy are not receiving anticoagulation. A model that accurately predicts an individual patient's risk for major bleeding would allow for weighing the risks and benefits of warfarin therapy with greater confidence. Such a model would also identify reversible risk factors that providers can act on to minimize bleeding risk (e.g., avoidance of antiplatelet drugs).

Prevalence of AF and risk for warfarin-associated bleeding both increase with advancing age. Previously published BRMs included few patients > 80 years of age (1, 2). The BRM derived and validated by Shireman and colleagues adds to previous work in this area because $> 10\,000$ patients ≥ 80 years of age were included in the study.

The proposed BRM has drawbacks. First, the equation is complex, and clinicians will not find it easy to use without a calculator. Second, only 222 (3.4%) of the 6470 patients in the validation cohort were classified as high risk for bleeding by the present model. Even if the BRM was more user-friendly, it is unclear whether clinicians would find such a model, in which $> 96\%$ of patients are deemed to have $\leq 2\%$ 90-day risk for major bleeding, helpful in making everyday decisions. Third, 38 089 of 76 177 patients with AF were discharged without receiving warfarin. It is likely that the physicians caring for many of the patients chose not to prescribe anticoagulation because of a per-

ceived risk for bleeding. If a substantial number of patients at risk for bleeding was thus excluded from both derivation and validation cohorts, can we generalize these results to an unselected population of AF patients? Finally, international normalized ratio (INR) values were not considered in the model. This limitation, shared by previously published clinical prediction guides, is important because bleeding risk is independently associated both with supratherapeutic INR values and with INR variability (3).

The study by Shireman and colleagues provides a step forward in assessing the bleeding risk of warfarin-treated patients. However, the limitations of the study highlight the need for further work in this important area.

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