

Personalized bleeding risk assessment for atrial fibrillation patients on direct oral anticoagulants: the DOAC score

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Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia that significantly increases the risk of stroke and systemic embolism. To mitigate these risks, individuals with AF are often prescribed anticoagulant medications, such as warfarin or direct-acting oral anticoagulants (DOACs). However, the use of anticoagulants comes with its own set of concerns, particularly the risk of bleeding. Current clinical tools for assessing bleeding risk in AF patients have been primarily developed for those treated with warfarin and have shown limited performance when applied to individuals on DOAC therapy.¹ In response to this gap, a recent study has introduced the *DOAC Score*, a novel clinical risk as-

essment tool designed to personalize bleeding risk estimates for AF patients on DOACs.²

Developing the *DOAC Score*

The study, conducted across 44 countries and involving 951 centers, drew upon a diverse cohort of AF patients taking dabigatran 150 mg twice daily.³ The researchers developed a risk score by analyzing various patient-specific factors using a Cox proportional hazards model. The resultant risk prediction model underwent rigorous internal validation through bootstrapping techniques. The *DOAC Score* was then further refined in the GARFIELD-AF registry, which included patients taking a range of DOACs, including dabigatran, edoxaban, rivaroxaban, and apixaban.⁴ Finally, to determine generalizability in external cohorts and among individuals on different DOACs, the risk prediction model was validated in the COMBINE-AF pooled clinical trial cohort,⁵ and in the Quebec Régie de l'Assurance Maladie du Québec and Med-Echo Administrative Databases (RAMQ) administrative database.⁶

Key findings

One of the primary outcomes assessed in this study was the incidence of major bleeding events among AF patients, defined according to the classification of the International Society on Thrombosis and Haemostasis.⁷ Of the 5684 patients in the RE-LY trial, 6.8% experienced a major bleeding event over a median follow-up period of 1.74 years. The *DOAC Score* proved to be a reliable predictor of bleeding risk, with an optimism-corrected C statistic of 0.73 after internal validation. Calibration plots demonstrated excellent goodness-of-fit ($p=0.57$), indicating that the model accurately estimated bleeding risk.

The *DOAC Score* assigns points based on various patient characteristics, including age, creatinine clearance/glomerular filtration rate, underweight status, history of stroke/transient ischemic attack/embolism, diabetes, hypertension, antiplatelet use, nonsteroidal anti-inflammatory use, liver disease, and bleeding history (Table 1). Importantly, each additional point on the *DOAC Score* was associated with a substantial 48.7% increase in the risk of major bleeding. This underscores the tool's effectiveness in stratifying patients based on their expected bleeding risk. The risk of bleeding is defined as being very low in case of a score ranging from 0 to 3, low 4 or 5, moderate 6 or 7, high 8 or 9, very high if the score is ≥ 10 . The assessment refers to the first year of antithrombotic therapy, so it does not apply to subsequent periods; conceptually, the score should be recalculated at the end of each year of treatment.

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Comparison with existing tools

One of the notable aspects of the study was the comparison of the DOAC Score with the widely used HAS-BLED score.^{8,9} The DOAC Score consistently outperformed HAS-BLED in all phases of the study. In the RE-LY trial, the DOAC Score had a higher C statistic (0.73 *versus* 0.60) and demonstrated superior predictive performance. Similar results were observed in the GARFIELD-AF registry (C statistic, 0.71 *versus* 0.66), COMBINE-AF cohort (C statistic, 0.67 *versus* 0.63), and the RAMQ administrative database (C statistic, 0.65 *versus* 0.58). These findings suggest that the DOAC Score is not only more accurate but also more robust across different cohorts and DOAC types.

Implications and future directions

The introduction of the DOAC Score represents a significant advancement in personalized medicine for AF patients. By providing a more accurate and tailored assessment of bleeding risk, this tool enables healthcare providers to make more informed decisions when prescribing anticoagulant therapy. This, in turn, can help optimize treatment strategies, minimize the risk of bleeding complications, and improve patient outcomes. In addition, the DOAC score has the potential to help physicians choose the most appropriate dosages of DOACs, and identify candidates for left atrial appendage occlusion, which increasingly qualifies as a suitable tool for subjects at high hemorrhagic risk.¹⁰

The study's broad international scope and validation across diverse patient populations lend credibility to the DOAC Score's generalizability. However, as with any clinical risk assessment

tool, ongoing evaluation and refinement will be necessary to ensure its continued accuracy and relevance. Future research should also explore the implementation of the DOAC Score in real-world clinical practice to assess its impact on patient care and outcomes.

Conclusions

In conclusion, the development and validation of the DOAC Score represent a significant step forward in the management of AF. This innovative tool offers a personalized approach to assessing bleeding risk in AF patients on DOAC therapy, outperforming existing scoring systems and providing clinicians with a valuable resource for making treatment decisions.

As we move toward an era of precision medicine, the DOAC Score exemplifies the potential of data-driven healthcare to improve patient safety and the quality of care provided to individuals with AF.

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Table 1. DOAC score.

Clinical risk prediction tools	Points
Age, years	
65-69	2
70-74	3
75-79	4
≥80	5
Creatinine clearance, mL/min	
30-60	1
<30	2
Underweight (body mass index <18.5 kg/m ²)	1
Stroke/transient ischemic attack/embolism history	1
Blood hypertension	1
Diabetes mellitus	1
Antiplatelet use	
Aspirin	2
Dual-antiplatelet	3
Nonsteroidal anti-inflammatory use	1
Bleeding history	3
Liver disease*	2

*Defined as: aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase ≥3X upper limit of normal, alkaline phosphatase ≥2X upper limit of normal, or liver cirrhosis.