JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER

VOL. 71, NO. 2, 2018
ISSN 0735-1097/$36.00
https://doi.org/10.1016/j.jacc.2017.11.038

EDITORIAL COMMENT

Stroke Prediction Rules in Atrial Fibrillation*

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Anticoagulant therapy for atrial fibrillation (AF) is a double-edged sword: on the one hand, it prevents approximately 64% of strokes, but on the other hand, it can cause hemorrhage (1,2). Thus, the decision to prescribe anticoagulant therapy to patients with AF depends on these risks.

Several approaches have been developed to guide anticoagulant therapy in AF. For example, decision aids allow patients to trade off risks of strokes and risk of hemorrhage to choose their antithrombotic therapy (3). These aids, along with decision analyses, have found that when the baseline rate of stroke increases, patients are more willing to take anticoagulant therapy. For example, at a baseline rate of 1 stroke per 100 patient-years of aspirin therapy, only one-half of patients are willing to take an anticoagulant, but at a baseline rate of 2 strokes per 100 patient-years, two-thirds of patients would prefer to take an anticoagulant (4). Because many studies of patient preferences were conducted before direct oral anticoagulants were available, the threshold for anticoagulant therapy may be evolving.

This evolution and the heterogeneity in patient preferences have contributed to variability in anticoagulant use. Many AF studies have found underuse of anticoagulants among patients at high risk of stroke and overuse of anticoagulants in patients at low risk of stroke (5,6). To help patients and clinicians choose antithrombotic therapy judiciously, several stroke prediction rules have been developed (7-11). For example, in 2001, my colleagues and I developed the $CHADS_2$ stroke rule, which assigned 1 point each for congestive heart failure, hypertension, age ≥75 years, and diabetes mellitus, and 2 points for a prior stroke or transient ischemic attack (7). One virtue of the $CHADS_2$ stroke rule was its simplicity: patients with 1 or more $CHADS_2$ points were offered anticoagulant therapy (unless contraindicated) (12). In 2010, Lip et al. (8) added additional points for vascular disease, age, and sex to form the CHA_2DS_2-VASc score. Although more complicated, the CHA_2DS_2-VASc score slightly improved the prediction of stroke and has been incorporated into recent AF guidelines.

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In the new study in this issue of the *Journal*, Chao et al. (13) examine 3 ways of using the CHA_2DS_2-VASc score to predict stroke in a Taiwanese AF population: 1) the baseline CHA_2DS_2-VASc score; 2) a time-dependent CHA_2DS_2-VASc score called the "follow-up CHA_2DS_2-VASc score"; or 3) the change in the score, called the "Delta CHA_2DS_2-VASc score." In this retrospective study of 31,039 low-risk AF patients who did not receive antithrombotic therapy, the baseline CHA_2DS_2-VASc score was not very predictive of long-term strokes. Its low C-index (0.578) was not surprising because patients with stroke predictors other than age and female sex were excluded, and patients were retrospectively followed for several years. By contrast, both the follow-up CHA_2DS_2-VASc and the Delta CHA_2DS_2-VASc scores were predictive of ischemic stroke, with C-indices of 0.729 and 0.742, respectively.

Because the baseline CHA_2DS_2-VASc score was not very predictive over the long term, the take-home message of Chao et al. (13) is that when the CHA_2DS_2-VASc score is used, it should be reassessed periodically, at least for low-risk patients who are not prescribed anticoagulant therapy. Clinicians who are accustomed to recalculating the atherosclerotic cardiovascular disease pooled equation (14) periodically for their patients who are not prescribed a statin will find this recommendation familiar. It may also sound familiar because some AF guidelines have stated that, "Individual risk

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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varies over time, so the need for anticoagulation must be re-evaluated periodically in all patients with AF" (15).

In contrast to this guidance, use of the Delta CHA_2DS_2-VASc score awaits validation. For example, Chao et al. (13) could validate that score among patients in their Taiwanese National Health Insurance Research Database who were excluded because they were taking aspirin. If the Delta score is validated, then some AF patients might have a temporary indication for anticoagulant therapy: of 31,039 low-risk AF patients, 8,901 patients developed 1 CHA_2DS_2-VASc point, and they experienced 2.04 strokes per 100 patient-years—a high enough rate that most patients would choose anticoagulant therapy, at least until their stroke rate declined to the baseline rate of 0.88 strokes per 100 patient-years among patients with 1 CHA_2DS_2-VASc point.

Not only should further research validate the Delta CHA_2DS_2-VASc score, but it also should explain why a rise in CHA_2DS_2-VASc score has an especially high stroke risk. One possible explanation is that when a new risk factor develops, it is often uncontrolled. For example, when hypertension is first diagnosed, the blood pressure is high. High blood pressure is a stronger predictor of stroke than is a history of hypertension with controlled blood pressure (11,16). Likewise, immediately after a transient ischemic attack, the stroke rate is very high, but gradually declines (17). However, there are limits to this logic: the risk of stroke does not rise abruptly on a patient's 75th birthday. An alternative explanation is confounding. For example, patients with AF who develop an infection are more likely to have a rise in their CHA_2DS_2-VASc score detected (when presenting for their infection), and also are more like to experience a stroke after the onset of an infection (18).

Before adopting any stroke prediction rule, clinicians should ask how it will affect outcomes. For example, would use of a Delta CHA_2DS_2-VASc score increase the appropriate use of anticoagulant therapy? Or would it obfuscate prescription of stroke prophylaxis? More importantly, how would use of a Delta CHA_2DS_2-VASc score affect clinical outcomes? Because answers to these questions are unknown, potential use of the proposed Delta CHA_2DS_2-VASc score awaits further research.

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KEY WORDS atrial fibrillation, clinical prediction rules, stroke prophylaxis