Which Score Should Be Used for Risk Stratification of Ischemic Stroke in Patients With Atrial Fibrillation

– A Simple or Detailed Approach? –

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Atrial fibrillation (AF) is a common cardiac arrhythmia, the incidence of which increases with age. Approximately 1.5% of the general population in Japan has at least 1 type of AF.^{1,2} AF is known to be associated with an increased risk of ischemic stroke and all-cause mortality. When patients develop ischemic stroke (cerebral infarction) because of AF, it is generally attributed to left atrial thromboembolism. The risk of ischemic stroke in patients with AF depends on associated stroke risk factors. The management of patients with AF involves 4 objectives: (1) prevention of thromboembolism, (2) rhythm control, (3) rate control, and (4) upstream therapy. Of these, prevention of thromboembolism (antithrombotic therapy)

is the most important for managing AF. The ACCF/AHA guidelines in the USA,³ the CCS guidelines in Canada,⁴ and the JCS guidelines in Japan⁵ recommend using the conventional stroke risk stratification scheme, the CHADS₂ (congestive heart failure, hypertension, age >75 years, diabetes mellitus, and stroke [double]) score, for antithrombotic therapy in patients with non-valvular AF.⁶ On the other hand, guidelines in Europe⁷ recommend the use of a more complicated scheme, namely, the CHA₂DS₂-VASc (congestive heart failure, hypertension, age >75 years [double], diabetes mellitus, stroke [double], vascular disease, age: 65–75 years, and sex category) score for an increased risk of ischemic stroke with HAS-BLED (hypertension,

Figure. Comparison of 3 proposed scores for stratifying patients with non-valvular atrial fibrillation at risk for thromboembolism.

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abnormal renal/liver function, stroke, bleeding history or pre-disposition, labile INR, elderly >65 years, and drugs/alcohol concomitantly) in order to avoid major bleeding complications. Recently, an alternative R₂CHADS₂ (renal failure [double], congestive heart failure, hypertension, age >75 years, diabetes mellitus, and stroke [double]) score was proposed to improve the precision of risk stratification by incorporating renal failure into the CHADS₂ score.⁸ These novel scores may outperform the CHADS₂ scoring system in estimating the risk of ischemic stroke in AF patients.

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In this issue of the Journal, Hoshino et al⁹ assess the predictive value of the CHADS₂, CHA₂DS₂-VASc, and R₂CHADS₂ scores for poor outcome in stroke patients with a prior history of coronary artery disease. Multivariate analysis showed that CHADS₂ >2 (odds ratio =1.65), CHA₂DS₂-VAsC >4 (odds ratio =1.60), and R₂CHADS₂ >3 (odds ratio =1.57) significantly predicted a poor outcome. Therefore, all 3 can be used as prognostic models in a high-risk patient population. Furthermore, the authors compared the predictive value for poor outcome among the 3 scores and found they were not significantly different. The CHADS₂ score does not include many common stroke risk factors, whereas the CHA₂DS₂-VAsC and R₂CHADS₂ scores include some (Figure). Herein lies the question: Which score allows better risk stratification for ischemic stroke in high-risk patients with AF? Of the 3 scores, CHADS₂ is the simplest, and conversely, CHA₂DS₂-VAsC is the most detailed. According to the study by Hoshino et al,⁹ there was no difference in risk stratification for a poor prognosis between the simple and detailed strategies. Simpler risk stratification may be better because AF is a common disease, and in many cases is managed by general physicians.

Until 2010, warfarin (vitamin K antagonist) was the only class of oral anticoagulant available in Japan. Although the drug is highly effective in preventing thromboembolism, its use is limited because of its narrow therapeutic index, necessitating frequent monitoring and dose adjustments, and thus resulting in substantial risk and inconvenience. In addition, because the Japanese frequently consume foods such as natto (fermented soybeans) that contain vitamin K, the effect of warfarin may not be as substantial. These limitations have translated into poor patient adherence and an insufficient blood concentration of warfarin to prevent ischemic stroke, particularly in the Japanese. Several new oral anticoagulants (NOACs) dose-dependently inhibit thrombin (eg, dabigatran) or factor Xa (eg, rivaroxaban, apixaban, and edoxaban) and have more advantages than warfarin, such as rapid onset and off set of action, effect on dietary vitamin K intake, and fewer drug interactions. The predictable anticoagulant effects of the NOACs enable the administration of fixed doses without the need for routine coagulation monitoring, thereby simplifying treatment. Clinical trials in which outcomes with NOACs have been compared with those of warfarin (RE-LY¹⁰ with dabigatran, ROCKET AF¹¹ with rivaroxaban, ARISTOTLE¹² with apixaban, and ENGAGE AF-TIMI 48¹³ with edoxaban) have shown that each NOAC is at least as safe and effective as warfarin for preventing stroke and systemic embolism in patients with non-valvular AF. Meta-analyses have demonstrated that these 4 NOACs are effective and safe.¹⁴

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