

EDITORIAL COMMENT

Unveiling the Potential of COOL-AF Scores in Diverse Populations

Insights From External Validation*



Mingfang Li, MD, PhD

Atrial fibrillation (AF) is associated with an increased risk of mortality and ischemic stroke/systemic embolism (SSE). The Atrial fibrillation Better Care (ABC) holistic pathway has been recommended as an integrated care approach to the management of AF patients.^{1,2} According to the A criterion of the ABC pathway, stroke prevention with oral anticoagulant agents (OACs) is central to the modern management of AF.³

OACs are effective in preventing approximately 64% of strokes and 26% of all-cause deaths.⁴ However, they also come with a bleeding risk.⁴ In addition, the risk of SSE is not consistent across all individuals with AF. It varies depending on the presence of risk factors and risk modifiers.² Therefore, anticoagulation management should balance the benefit of preventing SSE against the risk of bleeding in patients with AF. We should first evaluate the individual risk of stroke and determine whether the patient needs stroke prevention therapy. This should be followed by an assessment of the specific risk of experiencing major bleeding while on OAC. Several risk stratification schemes have been developed to help guide clinical decisions and improve outcomes. The CHA₂DS₂-VASC score and the HAS-BLED score have been proven to have a good predictive value for assessing stroke risk and bleeding risk, respectively.^{5,6} They have been incorporated into

contemporary guidelines and represent the most commonly used stratification schemes.^{1,2}

Although primarily developed using data from Western populations, both the CHA₂DS₂-VASC score and the HAS-BLED score have been validated in Asian populations.⁷⁻¹¹ However, it is still crucial to note the disparities between Asians and non-Asians regarding the population-specific nature of AF. Asian patients with AF have a distinct thromboembolic risk profile marked by a higher incidence of heart failure and diabetes, as well as a lower occurrence of vascular disease. In randomized trials of the non-vitamin K (direct) OACs, Asians had a numerically higher incidence of ischemic stroke than non-Asians. Furthermore, bleeding is always of particular concern in Asia, as bleeding rates in Asians taking OACs are notably higher when compared with non-Asians.¹² Therefore, the predictive models derived from Asian cohorts may facilitate the estimation of the risk of experiencing adverse clinical outcomes in this unique population. The COOL-AF (Cohort of Antithrombotic Use and Optimal INR Level in Patients With Non-Valvular Atrial Fibrillation) scores, derived from a Thailand study, were formulated with a broader set of risk factors in comparison to the CHA₂DS₂-VASC score and the HAS-BLED score. The COOL-AF scores were proposed as potential Asian-specific risk scores with good predictive capacities for identifying AF patients at risk of all-cause death, major bleeding, and thromboembolic events.¹³ Nevertheless, external validation of these scores is required to determine their broader applicability.

In the new study in this issue of *JACC: Asia*, Bucci et al¹⁴ conducted a comprehensive assessment of the COOL-AF scores in 2 distinct populations, one representing an Asian demographic (APHRS [Asia-Pacific Heart Rhythm Society] registry) and the other predominantly European (EORP-AF registry [EURObservational Research Programme in AF General Long-Term Registry]). Meanwhile, the predictive

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From the Division of Cardiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China.

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ability of the COOL-AF scores was compared to the CHA₂DS₂-VASC score and the HAS-BLED score. In APHRS, the COOL-AF scores exhibited a moderate-to-good predictive value for all-cause mortality (area under the curve [AUC]: 0.77; 95% CI: 0.71-0.83), major bleeding (AUC: 0.68; 95% CI: 0.60-0.76), and thromboembolic events (AUC: 0.61; 95% CI: 0.51-0.71). The predictive value of the COOL-AF scores was found similar to the well-established CHA₂DS₂-VASC and HAS-BLED scores in APHRS. However, in EORP-AF, the performance of the COOL-AF scores was notably different. Although they still displayed a modest predictive value for all-cause mortality (AUC: 0.68; 95% CI: 0.65-0.70) and major bleeding (AUC: 0.61; 95% CI: 0.60-0.62), the results were less robust compared with their performance in the Asian cohort. Moreover, the COOL-AF score for thromboembolic events was found to be inferior to the CHA₂DS₂-VASC score in EORP-AF.

The study by Bucci et al¹⁴ adds to our existing knowledge on the performance of the COOL-AF scores. One of the study's major strengths is the external validation of risk prediction tools using 2 remarkably large datasets. Score systems are often proposed but seldom subjected to external validation, resulting in limited data available to guide clinicians in determining the most effective risk assessment method. In this study, the good performance of the COOL-AF scores, particularly in an Asian context, suggests that these scores might be of great value in conjunction with other established risk scores to enhance the precision of risk assessment in Asian populations. One practical limitation, though, is that in the COOL-AF scores, no points have been assigned to each risk factor yet, which may diminish their user-friendliness at the bedside. Although it is outside the scope of this study, the lower predictive value of the COOL-AF scores in EORP-AF emphasizes the need for assessing the effect of ethnic and

geographical factors on the performance of these scores.

The findings of Bucci et al¹⁴ underscore the importance of further efforts that aim at providing a detailed evaluation of the calibration of the COOL-AF scores. The basic premise of a risk stratification scheme is to find someone who needs anti-coagulation. However, patients with truly low risk do exist. If these patients are subjected to lifelong anti-coagulation, they may not have sufficient net clinical benefit considering the potential bleeding risk of OACs. If the COOL-AF scores have some value in identifying patients at very low risk of stroke, they could be utilized to refine risk assessment in selected patients.

There is room for the development of population-specific scoring systems or direct OAC-specific scoring systems. However, clinicians and researchers should keep in mind that the risk of stroke and bleeding is dynamic, and it changes as comorbidities accumulate. Hence, regular re-evaluation of the risk is essential to ensure appropriate management of AF and to minimize the likelihood of adverse outcomes.

Taken together, the performance of the COOL-AF scores in external validation suggests that they represent a promising tool for risk assessment in Asian AF patients. However, potential use of these scores needs further research.

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ADDRESS FOR CORRESPONDENCE: Dr Mingfang Li, Division of Cardiology, The First Affiliated Hospital of Nanjing Medical University, 300 Guangzhou Road, Nanjing, China. E-mail: mingfangli@njmu.edu.cn.

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