

## Comments on “A simple and easily implemented risk model to predict 1-year ischemic stroke and systemic embolism in Chinese patients with atrial fibrillation”

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Risk stratification for ischemic stroke is essential for patients with atrial fibrillation (AF) before the consideration of anticoagulation therapy. According to current AF management guidelines, about 90% of AF patients should receive anticoagulation therapy, and risk of stroke death in AF patients was around 68%. It is thus of importance to precisely define the patients who are in urgent need of anticoagulation therapy. In this context, study results from Ma *et al*<sup>[1]</sup> published in this issue could be helpful to precisely define the AF patients who are at real risk of stroke. The study aims to develop an accurate and easy-to-use predictive model for the 1-year risk of thromboembolic events (TEs), including ischemic stroke and systemic embolic events, in Chinese patients with AF.

Based on a large prospective cohort study including Chinese AF patients without anticoagulation therapy, the study designed a simplified risk model for predicting TEs in patients with AF – the CAS (Congestive heart failure or left ventricular dysfunction, Age, and prior Stroke) model. The CAS risk model can be easily achieved in clinical practice and contains only three variables.

The study included 6601 AF patients who did not receive anticoagulation or ablation treatment from the prospective China AF Registry cohort study,<sup>[2]</sup> and the simplified CAS model was used to predict the 1-year TEs, and compared the predicting efficacy with the CHA<sub>2</sub>DS<sub>2</sub>-VASc score. During the 1-year follow-up, a total of 163 TEs occurred. The model classified 30.9% of patients as low-risk for TEs (CAS score = 0), and the corresponding 1-year TE risk was only 0.81%. The study confirmed that among Chinese AF patients, a novel and simple CAS risk model predicted 1-year TEs better than the widely-used CHA<sub>2</sub>DS<sub>2</sub>-VASc score by identifying a large proportion of patients with low TE risk, anticoagulation therapy could, therefore, be avoided in these patients. This finding has important

guiding significance and practical value for the anti-coagulation decision of AF patients.

In this risk model, prior stroke, elder age, and cardiac dysfunction were used as the main predictors. Previous studies have shown that even in young patients with AF, heart failure or left ventricular dysfunction served as a powerful driver of stroke risk. Heart failure is related to a hypercoagulable state, which might promote thrombosis and stroke. In previous report, female sex was not an independent risk factor for TEs, while hypertension, diabetes, vascular disease, or a combination thereof did not add significant incremental information to the risk of stroke. In the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, all these factors are assigned 1 score point despite their limited contribution to the risk of stroke. It is undeniable that controlling these risk factors can improve the clinical outcome of patients with AF.

### Simple Risk Model and CHA<sub>2</sub>DS<sub>2</sub>-VASc Model: Which is Better?

When it comes to the simple TEs risk model of AF, we have to mention the predecessor of the CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring system – the CHADS<sub>2</sub> scoring system. In essence, there are only two changes between the two systems: one is to increase the weight of age (elder than 75 years old) to 2 points, and the other is to add several new risk factors: age 65 to 75 years old, female sex and vascular diseases, both of which are scored with 1 point. However, there are obvious differences in background and concepts behind these seemingly minor changes.

The CHADS<sub>2</sub> scoring system was based on several clinical trials in the 1990s, to evaluate the efficacy of warfarin and aspirin. At that time, it was not clear whether and how to anticoagulate non-valvular AF patients internationally,

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DOI:

10.1097/CM9.0000000000001608

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Chinese Medical Journal 2021;134(19)

Received: 06-05-2021 Edited by: Ning-Ning Wang

and anticoagulants were not given to these patients in clinical practice. Therefore, clinical trials evaluating warfarin and aspirin were placebo-controlled. According to the analysis of the control group (AF patients who did not receive anticoagulation) at that time, some risk factors of stroke in patients with non-valvular AF were obtained, and CHADS<sub>2</sub> scoring system was first introduced by Gage in 2001, which was considered to be a good predictor of stroke risk in these patients. CHADS<sub>2</sub> score was formally recommended in ESC/AHA/ACC guidelines in 2006, and was widely used in clinical risk stratification for AF patients.

The CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring system was first published in the 2010 ESC guidelines for AF, anticoagulation is widely applied to AF patients in Europe at that time. Although the anticoagulation rate was not ideal in several countries, the overall anticoagulation rate of AF in Europe was very high, especially in Nordic countries such as Sweden. Not only the anticoagulation treatment rate reached as high as 70% to 80%, but also the international normalized ratio (INR) compliance rate was very high (up to 70%–80%). It can be seen that the CHADS<sub>2</sub> system was generated at the initial stage of anticoagulation therapy, while the CHA<sub>2</sub>DS<sub>2</sub>-VASc system was born when the anticoagulation therapy had reached a significant high level. Therefore, many researchers think that CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring model is more advanced than simple risk models (such as CHADS<sub>2</sub> and CAS). But is that really the case?

Simple risk scoring model, taking CAS model as an example, is based on the concept of risk stratification according to the level of the score, by dividing 0 into low risk, 1 to 2 into high risk, and anticoagulant treatment strategy is determined according to this stratification. Patients with a score of 0 could be treated with aspirin instead of anticoagulation, and those with a score of 1 or 2 should start anticoagulation therapy. Therefore, an important feature of the CAS scoring system is the ability to screen out AF patients with true high risk of TEs, who should be recommended with anticoagulation therapy immediately. However, in the 2010 ESC guidelines for AF, the idea of diminishing the importance of risk stratification among AF patients was put forward. The reason was that, a considerable number of patients with AF without risk factors also received anticoagulation therapy in Europe at that time, resulting in over treatment. The risk-benefit ratio of this approach was unequal. Therefore, ESC proposed a scoring system that could identify low-risk patients appropriately, which was also the original intention of the CHA<sub>2</sub>DS<sub>2</sub>-VASc model. In the subsequent guideline updated in 2012, it was clearly stated that the main purpose of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was to screen out truly low-TEs-risk patients with AF, who did not require anticoagulation therapy. Thus, it can be seen that the applicable backgrounds of the two scoring models were different.

Study by Ma *et al*<sup>[1]</sup> confirmed that the risk of thromboembolism was even lower in patients with a CAS score of 0 than in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 0. In high-risk patients, the value of the two scoring systems is similar. It is to note, CHA<sub>2</sub>DS<sub>2</sub>-VASc

score can be used again to stratify risk of high TEs among patients with a CAS score of 0. After distinguishing these patients, the remaining patients are truly at low-risk of TEs and do not need anticoagulation therapy.

### China's Current AF Anticoagulation Situation is Still Not Optimal

What is the current anticoagulation situation in China? According to several previous registration studies, although the situation has somehow improved in recent years, the overall anticoagulation treatment rate in China is still very low. At present, among Chinese AF patients with high CHA<sub>2</sub>DS<sub>2</sub>-VASc score, only a low proportion of patients received anticoagulation therapy. Therefore, at this stage in China, the more urgent task is to initiate anticoagulation therapy in high-risk patients immediately. In addition, there are a considerable number of patients with valvular AF in China, especially among elderly patients. The RE-LY AF registration study<sup>[2]</sup> showed that the anticoagulant treatment rate for AF patients with rheumatic heart valve disease in China was only 40%, while a considerable part of the anticoagulant treatment was initiated after mechanical valve replacement. If AF patients with valvular diseases also adopt the CAS scoring system, it will be able to identify a large group of high-risk patients, and anticoagulation treatment is thus urgent for these patients. Therefore, the CAS model is applicable in China at this stage.

### Research Limitations and Future Directions

Several limitations of the study by Ma *et al*<sup>[1]</sup> should be noted. First, the study only verified the CAS model in a Chinese AF patient cohort, and it should be validated by international registry cohorts. Second, this study did not incorporate biomarkers, left atrial morphology and function, or AF load into the risk prediction model, future studies are warranted to investigate the incremental predicting efficacy for TEs risk of these factors. In addition, the study did not compare the CAS scoring model with the traditional CHADS<sub>2</sub> model. As pointed out by the authors, blood pressure and glycemic control seemed to be more important than the history of hypertension or diabetes. Future studies are warranted to validate above hypothesis.

### CAS Model Can Be Recommended as First Line Risk Stratification Model for TEs of AF Patients in China at This Stage

In summary, when choosing stroke risk assessment models for AF patients, it is necessary to focus on its scientificity and rationality, as well as its feasibility and practicability. We believe that, as an overall strategy, the CAS scoring model can be recommended as the first line scoring system at this stage in China, so that most clinicians can quickly grasp and apply it, screen out the TEs high-risk AF patients, and immediately initiate anticoagulation therapy. In particular, it is necessary to strengthen the awareness of risk scoring and anticoagulation treatment for patients at high risk of TEs among primary-level

doctors. In institutions where anticoagulation treatment rate has reached a considerable level, it is possible to conditionally use the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, but it is necessary to know the basis and concept of this model. It is the responsibility of clinicians to correctly understand the anticoagulation status of AF in China and improve the anticoagulation treatment rate of AF patients, especially those with high risk of TEs.

#### **Conflicts of interest**

None.

#### **References**

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**How to cite this article:** Li YG, Gong CQ. Comments on “A simple and easily implemented risk model to predict 1-year ischemic stroke and systemic embolism in Chinese patients with atrial fibrillation”. *Chin Med J* 2021;134:2290–2292. doi: 10.1097/CM9.0000000000001608