Dynamic stroke risk scores of atrial fibrillation

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Atrial fibrillation (AF) is associated with a nearly five-fold increased risk of ischemic stroke, and that 1 in 5 cases of stroke can be attributed to this arrhythmia (1-3). Stroke prevention is a major priority in the clinical management of AF. When compared to control/placebo, oral anticoagulation (OAC) therapy reduces the risk of stroke by 64% and the risk of death by 26% (4), but it can cause hemorrhage (4,5). Thus, the decision to prescribe anticoagulant therapy to patients with AF depends on these risks. Current guidelines recommend OAC for stroke prevention of AF patients unless they are deemed to be at low risk of stroke (6-9). Given that OAC also increases bleeding risk (which can be fatal), OAC therapy should be decided on the basis of the expected net clinical benefit of OAC therapy. Therefore, stroke risk stratification is a critical step, and an annual stroke risk of 1–2% is considered as the threshold at which OAC therapy yields a net clinical benefit (10,11).

Based on various clinical, imaging or biomarker criteria, several risk stratification schemes have been developed to predict those at high risk of ischemic stroke and to aid decision-making on thromboprophylaxis. Based on baseline clinical factors identified in the non-OAC arms of the historical randomized trials, the CHADS$_2$ [congestive heart failure, hypertension, age ≥75, diabetes mellitus, prior stroke or transient ischemic attack (doubled)] score was proposed and validated in 2001 in a registry of hospitalized AF patients, to help identify 'high risk' patients (12). More recent focus of stroke prevention in non-valvular AF has shifted away from predicting 'high risk' patients towards initially identifying patients with a 'truly low risk' of ischemic stroke in whom OAC has no net clinical benefit (13-16). Hence, the CHA$_2$DS$_2$-VASc [congestive heart failure, hypertension, age ≥75 (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65 to 74, female] score (17) is now used in most guidelines for stroke prevention in AF, with OAC being generally recommended for those with ≥2 CHA$_2$DS$_2$-VASc stroke risk factors, or considered in those with one CHA$_2$DS$_2$-VASc stroke risk factor (6-8,18).

Usually when the baseline rate of stroke increases, patients are more willing to take OAC 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 (19). Because many studies of patient preferences were conducted before non-vitamin K oral anticoagulants were available, the threshold for anticoagulant therapy may be evolving.

Many clinical variables of stroke risk score have a "dynamic" variation through the follow-up. Age will increase annually in all patients, and incident hypertension, diabetes mellitus, vascular disease, congestive heart failure, and prior stroke or transient ischemic attack may become evident in some patients. These dynamic changes in risk factors may increase the CHA$_2$DS$_2$-VASc score, stroke risk category, and absolute ischemic stroke rate. However, baseline CHA$_2$DS$_2$-VASc stroke risk factors have been

used to assess follow up stroke rates, with events occurring remotely, for example, between 1–10 years later (20).

In the recent paper by Chao *et al.* (21), the authors proposed the new concept of "*follow-up CHA$_2$DS$_2$-VASc score*" and "*Delta CHA$_2$DS$_2$-VASc score*". Despite using only baseline CHA$_2$DS$_2$-VASc score in predicting risk of ischemic stroke in AF patients, they also used a time-dependent CHA$_2$DS$_2$-VASc score ("*follow-up CHA$_2$DS$_2$-VASc score*"), and "*Delta CHA$_2$DS$_2$-VASc score*" (follow-up CHA$_2$DS$_2$-VASc score minus baseline CHA$_2$DS$_2$-VASc score) in predicting ischemic stroke risk in Taiwan AF database.

The authors included a total of 31,039 low-risk AF patients who did not use any antithrombotic agents, and did not have any comorbidities of the CHA$_2$DS$_2$-VASc score, except for age and sex at baseline. During the follow-up, approximately 51.9% of AF patients would experience new comorbidities, the most common being hypertension. Also their data showed that most patients (approximately 90%) with AF who experienced ischemic stroke developed ≥1 stroke risk factor(s) over the follow-up period. This result can be extended to the concept that many clinical variables of stroke risk score have a dynamic variation through the follow-up and, stroke risk in AF patients does not remain static.

They also showed and compared the predictive power in ischemic stroke by using "baseline", "follow-up", and "Delta" CHA$_2$DS$_2$-VASc score. Their data showed the AUC was significantly higher for the Delta CHA$_2$DS$_2$-VASc score (0.742; 95% CI, 0.732–0.750) compared with baseline (0.578; 95% CI, 0.569–0.587) or follow-up (0.729; 95% CI, 0.721–0.737) scores. Although they showed Delta CHA$_2$DS$_2$-VASc score performed better in predicting ischemic stroke than the baseline CHA$_2$DS$_2$-VASc score and follow-up CHA$_2$DS$_2$-VASc score, they did not aim to propose a new scoring scheme to replace the CHA$_2$DS$_2$-VASc score. Their main purpose was to emphasize that the stroke risk of AF patients may continuously increase, and careful regular evaluation and/or detection of incident comorbidities with reassessment of the CHA$_2$DS$_2$-VASc score are important. It may sound familiar because some AF guidelines have stated that, "*Individual risk varies over time, so the need for anticoagulation must be re-evaluated periodically in all patients with AF*" (22).

They also demonstrated that the slope of the score change was important predictor for increased risk of ischemic stroke. For patients with the same Delta CHA$_2$DS$_2$-VASc score, more rapid score change lead to a higher risk of ischemic risk. AF patients who acquired more comorbidities over a short period represent a particularly high-risk population. It emphasized that clinician should keep alert for the development of new comorbidities among patients with AF.

The proposed Delta CHA$_2$DS$_2$-VASc score awaits further research. The research by Chao *et al.* (21) selected only limited patients who did not use any antithrombotic agents and did not have any comorbidities except for age and sex at baseline. Validation of Delta CHA$_2$DS$_2$-VASc to broad spectrum patients group may be needed because these effects of Delta CHA$_2$DS$_2$-VASc could be different from this study data. Also, further research would be needed to explain how rise in CHA$_2$DS$_2$-VASc score induce an especially high ischemic stroke risk.

The important message of this study is that the regular reassessment of CHA$_2$DS$_2$-VASc score in AF patients has not been previously emphasized in real world practice. Therefore, clinician should be aware that many clinical variables of stroke risk score can change, and the reassessment of CHA2DS2-VASc score is important. Further study may be needed to demonstrate how these applications of dynamic change of risk factor in AF and reassessment of CHA2DS2-VASc score could affect real world outcomes.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Wolf PA, Abbott RD, Kannel WB. Atrial-Fibrillation as an Independent Risk Factor for Stroke - the Framingham-Study. Stroke 1991;22:983-8.
2. January CT, Wann LS, Alpert JS, et al. AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. Available online: http://circ.ahajournals.org/content/circulationaha/early/2014/04/10/CIR.0000000000000041.full.pdf

3. Kim TH, Yang PS, Uhm JS, et al. CHA2DS2-VASc Score (Congestive Heart Failure, Hypertension, Age ≥75 [Doubled], Diabetes Mellitus, Prior Stroke or Transient Ischemic Attack [Doubled], Vascular Disease, Age 65-74, Female) for Stroke in Asian Patients With Atrial Fibrillation: A Korean Nationwide Sample Cohort Study. Stroke 2017;48:1524-30.

4. Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med 2007;146:857-67.

5. Connolly SJ, Eikelboom J, Joyner C, et al. Apixaban in patients with atrial fibrillation. N Engl J Med 2011;364:806-17.

6. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Europace 2016;18:1609-78.

7. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation 2014;130:e199-267.

8. National-Institute-for-Health-and-Care-Excellence. Atrial fibrillation: the management of atrial fibrillation. (Clinical guideline 180). Available online: http://guidance.nice.org.uk/CG180

9. Chiang CE, Wang TD, Li YH, et al. 2010 guidelines of the Taiwan Society of Cardiology for the management of hypertension. J Formos Med Assoc 2010;109:740-73.

10. Eckman MH, Singer DE, Rosand J, et al. Moving the tipping point: the decision to anticoagulate patients with atrial fibrillation. Circ Cardiovasc Qual Outcomes 2011;4:14-21.

11. Overvad TF, Nielsen PB, Lip GY. Treatment thresholds for stroke prevention in atrial fibrillation: observations on the CHA2DS2-VASc score. Eur Heart J Cardiovasc Pharmacother 2017;3:37-41.

12. Gage BF, Waterman AD, Shannon W, et al. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA 2001;285:2864-70.

13. Olesen JB, Torp-Pedersen C, Hansen ML, et al. The value of the CHA2DS2-VASc score for refining stroke risk stratification in patients with atrial fibrillation with a CHADS2 score 0-1: a nationwide cohort study. Thromb Haemost 2012;107:1172-9.

14. Coppens M, Eikelboom JW, Hart RG, et al. The CHA2DS2-VASc score identifies those patients with atrial fibrillation and a CHADS2 score of 1 who are unlikely to benefit from oral anticoagulant therapy. Eur Heart J 2013;34:170-6.

15. Chao TF, Liu CJ, Wang KL, et al. Using the CHA2DS2-VASc score for refining stroke risk stratification in 'low-risk' Asian patients with atrial fibrillation. J Am Coll Cardiol 2014;64:1658-65.

16. Kim TH, Yang PS, Kim D, et al. CHA2DS2-VASc Score for Identifying Truly Low-Risk Atrial Fibrillation for Stroke: A Korean Nationwide Cohort Study. Stroke 2017;48:2984-90.

17. Lip GY, Frison L, Halperin JL, et al. Identifying patients at high risk for stroke despite anticoagulation: a comparison of contemporary stroke risk stratification schemes in an anticoagulated atrial fibrillation cohort. Stroke 2010;41:2731-8.

18. Chiang CE, Wu TJ, Ueng KC, et al. 2016 Guidelines of the Taiwan Heart Rhythm Society and the Taiwan Society of Cardiology for the management of atrial fibrillation. J Formos Med Assoc 2016;115:893-952.

19. Man-Son-Hing M, Gage BF, Montgomery AA, et al. Preference-based antithrombotic therapy in atrial fibrillation: implications for clinical decision making. Med Decis Making 2005;25:548-59.

20. Olesen JB, Lip GY, Hansen ML, et al. Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study. BMJ 2011;342:d124.

21. Chao TF, Lip GY, Liu CJ, et al. Relationship of Aging and Incident Comorbidities to Stroke Risk in Patients With Atrial Fibrillation. J Am Coll Cardiol 2018;71:122-32.

22. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. Circulation 2006;114:e257-354.