JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.
VOL. 64, NO. 16, 2014
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2014.06.1203

Using the CHA_2DS_2-VASc Score for Refining Stroke Risk Stratification in 'Low-Risk' Asian Patients With Atrial Fibrillation

Tze-Fan Chao, MD,*† Chia-Jen Liu, MD,‡§ Kang-Ling Wang, MD,*† Yenn-Jiang Lin, MD,*† Shih-Lin Chang, MD,*† Li-Wei Lo, MD,*† Yu-Feng Hu, MD,*† Ta-Chuan Tuan, MD,*† Tzeng-Ji Chen, MD,‖ Gregory Y.H. Lip, MD,¶ Shih-Ann Chen, MD*†

ABSTRACT

BACKGROUND A new scoring system, the anticoagulation and risk factors in atrial fibrillation (ATRIA) score, was proposed for risk stratification in patients with atrial fibrillation (AF). Whether the ATRIA scheme can adequately identify patients who are at low risk of ischemic stroke remains unknown.

OBJECTIVES The goal of the present study was to compare the performance of ATRIA to that of CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65 to 74, female) scores for stroke prediction.

METHODS This study used the National Health Insurance research database in Taiwan. A total of 186,570 AF patients without antithrombotic therapy were selected as the study cohort. The clinical endpoint was the occurrence of ischemic stroke.

RESULTS During the follow-up of 3.4 ± 3.7 years, 23,723 patients (12.7%) experienced ischemic stroke. The CHA_2DS_2-VASc score performed better than ATRIA score in predicting ischemic stroke as assessed by c-indexes (0.698 vs. 0.627, respectively; $p < 0.0001$). The CHA_2DS_2-VASc score also improved the net reclassification index by 11.7% compared with ATRIA score ($p < 0.0001$). Among 73,242 patients categorized as low-risk on the basis of an ATRIA score of 0 to 5, the CHA_2DS_2-VASc scores ranged from 0 to 7, and annual stroke rates ranged from 1.06% to 13.33% at 1-year follow-up and from 1.15% to 8.00% at 15-year follow-up. The c-index of CHA_2DS_2-VASc score (0.629) was significantly higher than that of the ATRIA score (0.593) in this "low-risk" category ($p < 0.0001$).

CONCLUSIONS Patients categorized as low-risk by use of the ATRIA score were not necessarily low-risk, and the annual stroke rates can be as high as 2.95% at 1-year follow-up and 2.84% at 15-year follow-up. In contrast, patients with a CHA_2DS_2-VASc score of 0 had a truly low risk of ischemic stroke, with an annual stroke rate of approximately 1%. (J Am Coll Cardiol 2014;64:1658–65) © 2014 by the American College of Cardiology Foundation.

From the *Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; †Institute of Clinical Medicine, and Cardiovascular Research Center, National Yang-Ming University, Taipei, Taiwan; ‡Division of Hematology and Oncology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; §Institute of Public Health and School of Medicine, National Yang-Ming University, Taipei, Taiwan; ‖Department of Family Medicine, Taipei Veterans General Hospital, Taipei, Taiwan; and the ¶University of Birmingham Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom. The authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Tze-Fan Chao and Chia-Jen Liu contributed equally to this study. Drs. Gregory Y.H. Lip and Shih-Ann Chen are joint senior authors.

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Manuscript received May 13, 2014; revised manuscript received June 27, 2014, accepted June 30, 2014.

Atrial fibrillation (AF) is an important risk factor for ischemic stroke, and AF-related stroke has a worse prognosis and higher recurrence rate than non-AF-related stroke (1). Stroke prevention is the cornerstone for AF management, and effective stroke risk stratification is a key step. The current focus is the initial identification of "low risk" AF patients who do not need antithrombotic therapy, and, subsequent to this decision step, patients with stroke risk factor ≥1 can be offered effective stroke prevention, which is oral anticoagulation (OAC) (2).

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The congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke or transient ischemic attack (TIA) ($CHADS_2$) score has been commonly used to guide antithrombotic therapies for AF patients since it was proposed and validated in 2001 (3). However, the annual stroke rate is still nearly 2% for patients with a $CHADS_2$ score of 0, and a considerable proportion of patients may be misclassified as "low risk" without taking OACs for stroke prevention, accordingly (4,5). In 2010, the congestive heart failure, hypertension, age ≥75, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65 to 74, female (CHA_2DS_2-VASc) score (6) was developed and was suggested to be better than the $CHADS_2$ score for identifying truly low-risk patients in several independent cohorts (4,7–10).

More recently, another new scoring system, the anticoagulation and risk factors in atrial fibrillation (ATRIA) score was proposed (11). This score includes renal dysfunction (estimated glomerular filtration rate [eGFR] <45 ml/min or end-stage renal disease [ESRD]) and proteinuria in the model and requires different score weighting for primary and secondary prevention. Developers of the ATRIA scheme reported that the ATRIA score performed statistically better than the $CHADS_2$ and CHA_2DS_2-VASc scoring systems, although the differences in c-indexes were marginal with some overlap of the 95% confidence intervals (CI) (11). Also, the percentage of patients categorized as low-risk by ATRIA score was 46.7%, comparable to the percentage of low-risk patients stratified by $CHADS_2$ score (49.7%). The concern is raised as to whether the ATRIA score is able to identify patients with a truly low risk of ischemic stroke.

The goal of the present study was to compare the predictive accuracies of the CHA_2DS_2-VASc and ATRIA scores in predicting ischemic stroke in a contemporary unselected "real-world" cohort of nonanticoagulated AF patients from a nationwide cohort study. We also determined stroke rates in patients classified as low-risk by the ATRIA scheme (score 0 to 5) and ascertained event rates in these patients in relation to the CHA_2DS_2-VASc score. We tested the hypothesis that the CHA_2DS_2-VASc score would be better in identifying truly low-risk patients than the ATRIA score.

METHODS

This study used the National Health Insurance (NHI) research database released by the Taiwan National Health Research Institutes. The NHI system is a mandatory universal health insurance program that offers comprehensive medical care coverage to all Taiwanese residents. The NHI research database consists of detailed health care data from >23 million enrollees, representing >99% of Taiwan's population. In this cohort dataset, the patients' original identification numbers were encrypted to protect their privacy, using a consistent encrypting procedure so that it was feasible to link and continuously follow all of the claims belonging to the same patient within the NHI database. The large sample size of this database

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

ATRIA = anticoagulation and risk factors in atrial fibrillation

CI = confidence interval

CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65 to 74, female

eGFR = estimated glomerular filtration rate

ESRD = end-stage renal disease

NHI = National Health Insurance

NRI = net reclassification index

OAC = oral anticoagulation

ROC = receiver operating characteristic curve

TIA = transient ischemic attack

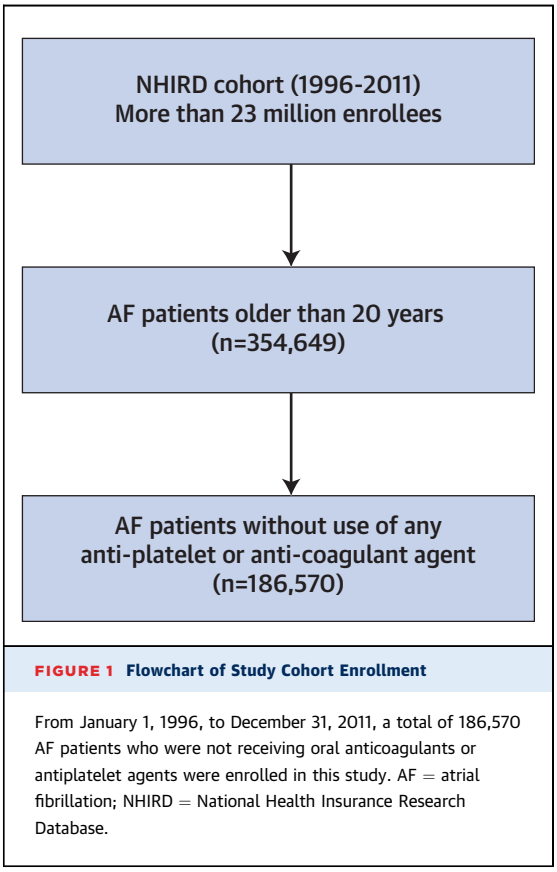

FIGURE 1 Flowchart of Study Cohort Enrollment

From January 1, 1996, to December 31, 2011, a total of 186,570 AF patients who were not receiving oral anticoagulants or antiplatelet agents were enrolled in this study. AF = atrial fibrillation; NHIRD = National Health Insurance Research Database.