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Relationship of Aging and Incident Comorbidities to Stroke Risk in Patients With Atrial Fibrillation

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ABSTRACT

BACKGROUND When assessing ischemic stroke risk in patients with atrial fibrillation (AF), the CHA_2DS_2-VASc score is calculated based on the baseline risk factors, and the outcomes are determined after a follow-up period. However, the stroke risk in patients with AF does not remain static, and with time, patients get older and accumulate more comorbidities.

OBJECTIVES This study hypothesized that the "Delta CHA_2DS_2-VASc score," which reflects the change in score between baseline and follow-up, would be more predictive of ischemic stroke compared with the baseline CHA_2DS_2-VASc score.

METHODS A total of 31,039 patients with AF who did not receive antiplatelet agents or oral anticoagulants, and who did not have comorbidities of the CHA_2DS_2-VASc score except for age and sex, were studied. The Delta CHA_2DS_2-VASc scores were defined as the differences between the baseline and follow-up CHA_2DS_2-VASc scores. During 171,956 person-years, 4,103 patients experienced ischemic stroke. The accuracies of baseline, follow-up, and Delta CHA_2DS_2-VASc scores in predicting ischemic stroke were analyzed and compared.

RESULTS The mean baseline CHA_2DS_2-VASc score was 1.29, which increased to 2.31 during the follow-up, with a mean Delta CHA_2DS_2-VASc score of 1.02. The CHA_2DS_2-VASc score remained unchanged in only 40.8% of patients. Among 4,103 patients who experienced ischemic stroke, 89.4% had a Delta CHA_2DS_2-VASc score ≥1 compared with only 54.6% in patients without ischemic stroke, and 2,643 (64.4%) patients had ≥1 new-onset comorbidity, the most common being hypertension. The Delta CHA_2DS_2-VASc score was a significant predictor of ischemic stroke that performed better than baseline or follow-up CHA_2DS_2-VASc scores, as assessed by the C-index and the net reclassification index.

CONCLUSIONS In this AF cohort, the authors demonstrated that the CHA_2DS_2-VASc score was not static, and that most patients with AF developed ≥1 new stroke risk factor before presentation with ischemic stroke. The Delta CHA_2DS_2-VASc score, reflecting the change in score between baseline and follow-up, was strongly predictive of ischemic stroke, reflecting how stroke risk in AF is a dynamic process due to increasing age and incident comorbidities.
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Atrial fibrillation (AF) is associated with significant morbidity, mortality, and socioeconomic burden, particularly from stroke and systemic thromboembolism (1). The latter risks are not homogeneous, and are dependent on patients' age and the presence or absence of various stroke risk factors, which have resulted in the development of clinical scores to aid risk stratification for patients with AF. Currently, the CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years [2 points], diabetes mellitus, previous stroke or transient ischemic attack [2 points], vascular disease, age 65 to 74 years, female) is recommended by guidelines for stroke risk assessment in AF (2–4).

When assessing the risk of ischemic stroke of patients with AF, the CHA_2DS_2-VASc score is conventionally calculated based on the baseline risk factors, and the outcomes are determined after a follow-up period, anything between 1 and 10 years (or more) in an intention-to-treat approach. The reality is that the patient risk does not remain static, because with time patients get older and accumulate more comorbidities. This is highly relevant when assessing risks in an AF population, which usually includes older adults and has multiple comorbidities.

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In this study, we focused on the changes in CHA_2DS_2-VASc score in patients with AF as a predictor of ischemic stroke. Because the CHA_2DS_2-VASc score would change over the follow-up period, we hypothesized the risk change (Delta CHA_2DS_2-VASc score) could have greater predictive value by assessing stroke risk factor(s) with a dynamic assessment for new and/or incident comorbidities. Second, we investigated the slope of the increment of the CHA_2DS_2-VASc score, and hypothesized when the score changed rapidly, the risk of ischemic stroke became higher.

METHODS

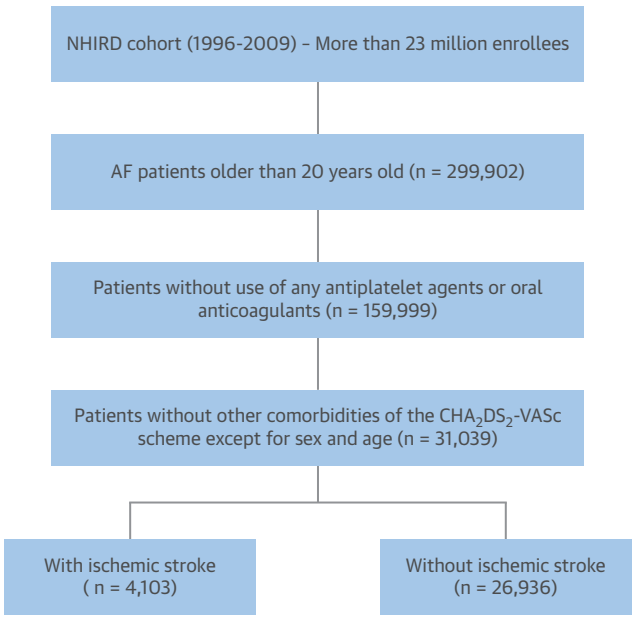
This study used the National Health Insurance Research Database (NHIRD), released by the Taiwan National Health Research Institutes. The National Health Insurance (NHI) system is a mandatory universal health insurance program that offers comprehensive medical care coverage to all Taiwanese residents. NHIRD consists of detailed health care data from >23 million enrollees, representing >99% of the population of Taiwan. In this cohort data set, the original identification numbers of the patients have been encrypted to protect their privacy, but the encrypting procedure is consistent, so that a linkage of the claims belonging to the same patient was feasible within the NHI database and can be followed continuously.

STUDY COHORT AND STUDY DESIGN. The study protocol of the present study was similar to our previous studies (5–11). From January 1, 1996 to December 31, 2009, a total of 299,902 patients with AF aged ≥20 years were identified from the NHIRD as the study population. AF was diagnosed using the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM) code (427.31). To ensure the accuracy of diagnosis, we defined patients with AF only when this was a discharge diagnosis or confirmed for ≥2 times in the outpatient department. The diagnostic accuracy of AF using this definition in NHIRD has been validated previously (12,13). Among the study population, there were 159,999 patients who did not use antiplatelet agents or oral anticoagulants (OACs), and 31,039 of them did not have any comorbidities of the CHA_2DS_2-VASc scheme, except for age

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation
AUC = area under the receiver-operating characteristic curve
CI = confidence interval
HR = hazard ratio
IQR = interquartile range
NHI = National Health Insurance
NHIRD = National Health Insurance Research Database
NRI = net reclassification index
OAC = oral anticoagulant
ROC = receiver-operating characteristic

FIGURE 1 A Flowchart of the Enrollment of the Study Cohort



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