MAYO CLINIC

ORIGINAL ARTICLE

Impact on Outcomes of Changing Treatment Guideline Recommendations for Stroke Prevention in Atrial Fibrillation: A Nationwide Cohort Study

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Abstract

Objective: To investigate the impact on outcomes of changing treatment guideline recommendations by comparing the proportion of patients with atrial fibrillation (AF) recommended oral anticoagulants (OACs) under the 2011 and 2014 American College of Cardiology/American Heart Association (ACC/AHA) guidelines.

Patients and Methods: We used the "National Health Insurance Research Database" in Taiwan, which included 354,649 patients with AF from January 1, 1996 through December 31, 2011. Patients with a $CHADS_2$ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke or transient ischemic attack) score of 2 or more and a CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65-74 years, female sex category) score of 2 or more were considered to have a definitive indication for receiving OACs according to the 2011 and 2014 ACC/AHA guidelines, respectively.

Results: The percentages of patients with AF recommended OACs increased from 69.3% (n=245,598) under the 2011 guideline to 86.7% (n=307,640) under the new 2014 guidelines, an increment of 17.5% (95% CI, 17.4-17.6). Most women with AF (94.1%) and patients older than 65 years (97.2%) would receive OACs on the basis of the 2014 guidelines. Among patients previously not being recommended OACs in older guidelines, OAC use under the new guidelines was associated with a lower risk of adverse outcomes (ischemic stroke or intracranial hemorrhage or bleeding requiring blood transfusion or mortality) with an adjusted hazard ratio of 0.89 (95% CI, 0.85-0.94).

Conclusion: In this nationwide cohort study, use of the 2014 guidelines led more patients with AF to receive OACs for stroke prevention, and this increased OAC use was associated with better outcomes. Better efforts to implement guidelines would lead to improved outcomes for patients with AF.

 ■ Mayo Clin Proc. 2016;■■(■):1-8

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia that increases the risk of ischemic stroke by 5-fold.[1] The AF-related stroke can be effectively prevented by the appropriate use of oral anticoagulants (OACs), either with warfarin or with non−vitamin K antagonist oral anticoagulants (NOACs). A key step in the prevention of AF-related stroke is effective risk stratification and application of treatment guidelines.

The $CHADS_2$ (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke or transient ischemic attack [TIA]) score was recommended by the 2006 (and subsequent 2011 focused update) American College of Cardiology/American Heart Association (ACC/AHA) AF guidelines.[2] The 2014 ACC/AHA AF guidelines recommend the use of CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or TIA, vascular disease,

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age 65-74 years, female sex category) score instead of the older $CHADS_2$ score, whereby OACs should be prescribed for patients with AF with a CHA_2DS_2-VASc score of 2 or more (with a Class I recommendation).[3] Therefore, the 2014 new AF guidelines would probably recommend more patients with AF to receive OACs for stroke prevention compared with the older guidelines. However, how many patients would have their treatment recommendation changed to receive OACs under the 2014 guildelines and the impact on overall prognosis remain unclear.

In the present study, first, we investigated the impact on outcomes of changing treatment guideline recommendations by comparing the proportion of patients with AF recommended OACs under the 2011 and 2014 guidelines. Second, we studied the overall outcomes (ischemic stroke or intracranial hemorrhage or bleeding requiring blood transfusion or mortality) of these patients with or without OAC use.

PATIENTS AND METHODS

This study used the "National Health Insurance Research Database (NHIRD)" released by the Taiwan National Health Research Institutes. The National Health Insurance system is a mandatory universal health insurance program that offers comprehensive medical care coverage to all Taiwanese residents. The NHIRD consists of detailed health care data from more than 23 million enrollees, representing more than 99% of Taiwan's population. In this cohort dataset, the patients' original identification numbers have been encrypted to protect their privacy, but the encrypting procedure was consistent, so that a linkage of the claims belonging to the same patient was feasible within the National Health Insurance database and can be followed continuously. The large sample size of this database provided a good opportunity to study the impact on outcomes of changing treatment guideline. However, the important limitation of the registry database is that the diagnoses of diseases were based on the diagnostic codes registered by the physicians responsible for the treatments of patients. Therefore, the types of AF were uncertain, and detailed information of clinical examinations, such as electrocardiography and imaging studies of brain, which could be useful to further confirm the diagnoses of AF, ischemic stroke, and intracranial hemorrhage, was not available.

Study Cohort

The study protocol of the present study was similar to that of our previous studies.[4-6] From January 1, 1996, to December 31, 2011, a total of 354,649 patients 20 years or older newly diagnosed with AF were identified from the NHIRD as the study population. Atrial fibrillation was diagnosed using the *International Classification of Diseases, Ninth Revision, Clinical Modification* codes (427.31). To ensure the accuracy of diagnosis, we defined patients with AF only when it was a discharge diagnosis or confirmed more than twice in the outpatient department.[4-7] The diagnostic accuracy of AF using this definition in the NHIRD has been validated previously.[8,9] The $CHADS_2$ score was calculated for each patient by assigning 1 point each for age 75 years or more, hypertension, diabetes mellitus, and congestive heart failure and 2 points for previous stroke/TIA.[10] The CHA_2DS_2-VASc score was calculated for each patient by assigning 1 point each for age between 65 and 74 years, history of hypertension, diabetes, recent cardiac failure, and vascular disease (myocardial infarction or peripheral artery disease), and female sex, and 2 points each for a history of a stroke/TIA or age 75 years or more.[11]

Study Population and Definitions of Clinical End Point(s)

Patients with a $CHADS_2$ score of 2 or more (n=245,598 [69.3%]) and a CHA_2DS_2-VASc score of 2 or more (n=307,640 [86.7%]) were considered to have a *definitive indication* for receiving OACs according to the 2011 and 2014 ACC/AHA guidelines, respectively (Figure 1).[2,3] Among 109,051 patients with a $CHADS_2$ score of 0 to 1, 56.9% (n=62,042; 17.5% of study cohort) had a CHA_2DS_2-VASc score of 2 or more (Figure 1). These 62,042 patients previously not being recommended OACs by the 2011 guidelines but now recommended to receive OACs by the 2014 guidelines were defined as the study population. A 90-day observation period after AF was diagnosed was adopted to determine the strategy about stroke prevention. Among the study population, the overall risk of