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ORIGINAL ARTICLE

Factors driving the use of warfarin and non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

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KEYWORDS
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Background/purpose: In the past, warfarin was the drug of choice for stroke prevention in patients with atrial fibrillation (AF). Recently, non-vitamin K antagonist oral anticoagulants (NOACs) have been approved as an alternative to warfarin in nonvalvular AF. However, there is a limited amount of real-world data on how NOACs are currently being used in Taiwan. This study was conducted to investigate the factors driving the initiation of anticoagulants and the selection of different anticoagulants in patients with AF.

Methods: We used National Taiwan University Hospital's electronic database to identify all nonvalvular AF patients from January 1, 2007 to December 31, 2013. Multivariate logistic regression models were used to examine the factors driving the initiation of anticoagulants and the selection of different anticoagulants.

Results: Among AF patients, 66.4% of anticoagulants users used NOACs instead of warfarin after the era of NOACs. Patients with female sex, hypertension, ischemic heart disease, cancer, hepatic disease, renal disease, bleeding history, and aspirin use were less likely to be anticoagulant users but are more likely to be anticoagulant users with a history of stroke (odds ratio = 2.64; 95% confidence interval, 2.02–3.45). Older age, ischemic heart disease, and

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aspirin use were the factors associated with NOACs usage, whereas hepatic disease showed the opposite results (odds ratio = 0.09; 95% confidence interval, 0.02—0.42).
Conclusion: Stroke history was associated with anticoagulant use, whereas comorbidities associated with increased risk of bleeding showed the opposite result. Patients with hepatic disease were less likely to use NOACs.

Introduction

Atrial fibrillation (AF) is a common arrhythmia encountered in clinical practice. Stroke is one of the complications of AF, which results in serious disability and increased economic burden for patients and their families. In the past, warfarin was the drug of choice for stroke prevention in AF patients, especially for those at higher risk.[1] However, reports showed underuse of warfarin.[2,3] Nearly 28% of AF patients received warfarin in the Taiwan Stroke Registry from 2006 to 2008.[4] Only 24.7% of AF patients received appropriate antithrombotic therapy according to treatment guideline in a study performed using the National Health Insurance Research Database (NHIRD) between 2003 and 2004.[5]

Non-vitamin K antagonist oral anticoagulants (NOACs), including dabigatran, rivaroxaban, apixaban, and edoxaban, have shown more encouraging efficacy and safety profiles compared to warfarin.[6—10] Current treatment guidelines suggest NOACs as alternatives to warfarin in nonvalvular AF.[11,12] Some reports from Denmark have explored the use of NOACs and factors associated with the use of NOACs after they were approved for release on the market.[13,14] Since 2012, NOACs have been available in Taiwan. So far, there is limited real-world data on how NOACs are currently being used as well as factors driving the initiation and selection of anticoagulants. The objective of our study is to investigate factors driving the initiation of anticoagulants (anticoagulant vs. no anticoagulant) and the selection of different anticoagulants (warfarin or NOACs) in Taiwan.

Methods

Data source

We used National Taiwan University Hospital's (NTUH) electronic database from 2006 to 2013 as our data source. NTUH is a 2500-bed tertiary medical center that serves 2000 inpatients and 8000 outpatients daily. The database provides information from outpatient, inpatient, and emergency departments with the disease diagnosis according to International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes as well as surgery and procedure records for the patients. All prescription records are available from the pharmacy department. Using specified identification code for each patient, all information can be linked together. Our study was approved by the institutional review board of the NTUH.

Study design

We first identified newly diagnosed AF patients from 2007 to 2013. Newly diagnosed was defined as no AF disease codes (ICD-9-CM code 427.31) present in the database from outpatient, inpatient, or emergency department in 2006. Patients with at least three AF disease codes from January 1, 2007 to December 31, 2013 were recruited into study. Individuals with no age record or younger than 20 years were excluded. Patients with valvular AF (history of rheumatic heart disease, or had undergone valve repair or replacement), history of pulmonary embolism or deep vein thrombosis, or had undergone hip or knee replacement within 1 year prior to study entry were excluded. Anticoagulant users were grouped according to the first anticoagulant prescription record after AF was first diagnosed. Dabigatran (110 mg; available since February 1, 2013) and rivaroxaban (20 mg; available since November 1, 2013) were the two available NOACs during the study period. For patients with no anticoagulant treatment throughout study, the date when AF was first diagnosed served as their index date. The date of the first anticoagulant prescription was defined as the index date for anticoagulant users.

Definition for variables

Records related to comorbidities, surgeries, and concomitant medications were collected within 12 months prior to the index date. Comorbidities were defined as ICD-9-CM codes present in the hospital database within 1 year prior to the index date. The ICD-9-CM codes used in our study are shown in Appendix 1. Information related to valve repair, valve replacement, and hip or knee replacement were defined using the codes for surgery and physician orders provided by the Information Technology Center from NTUH. The codes are listed in Appendix 2. Generic names for concomitant medications used in the study are given in Appendix 3. The $CHADS_2$ score indicates congestive heart failure, hypertension, age $\geq$75 years, diabetes mellitus, prior stroke or TIA (transient ischemic attack) or TE (thromboembolism) score; CHA_2DS_2-VASc score for congestive heart failure, hypertension, age $\geq$75 years, diabetes mellitus, prior stroke or TIA or TE, vascular disease, age 65—74 years, sex category point score systems; HAS-BLED score for hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR (international normalized ratio), age older than 65 years, concomitant use of drugs or alcohol. Calculations for the scoring systems mentioned above were made using

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