Factors Associated with Anticoagulation Delay Following New-Onset Atrial Fibrillation

Shaan Khurshid, MD[a], Lu-Chen Weng, PhD[b], Olivia L. Hulme, BA[b], Patrick T. Ellinor, MD, PhD[b,c], and Steven A. Lubitz, MD, MPH[b,c,*]

Oral anticoagulation (OAC) is effective yet reportedly underutilized for stroke prevention in atrial fibrillation (AF). Factors associated with delayed OAC after incident AF are unknown. Using a large electronic medical record, we identified incident episodes of AF diagnosed in 2006 to 2014 using a validated algorithm. Among patients with a Congestive heart failure, Hypertension, Age, Diabetes, and Stroke ($CHADS_2$) score ≥1 started on OAC within 1 year, we examined baseline characteristics at AF diagnosis and their association with time to OAC using multivariable Cox proportional hazards modeling. Of 4,388 patients with incident AF and $CHADS_2$ score ≥1 who were started on OAC within 1 year, the mean age was 72.6, and 41% were women. Median time to OAC was 5 days (interquartile range 1 to 43), and most patients received warfarin (86.3%). Among patients without prevalent stroke, 98 strokes (2.2% of the sample) occurred between AF diagnosis and OAC initiation. In multivariable analyses, several factors were associated with delayed OAC including female gender (hazard ratio [HR] 1.08, 95% confidence interval [CI] 1.01 to 1.15), absence of hypertension (HR 1.15, 95% CI 1.03 to 1.27), previous fall (HR 1.53, 95% CI 1.08 to 2.17), and chronic kidney disease (HR 1.12, 95% CI 1.04 to 1.21). Among women, OAC prescription at 1, 3, and 6 months was 70.0%, 81.7%, and 89.5%, respectively, whereas for men, OAC prescription was 73.4%, 84.0%, and 91.5%, respectively. Most patients with new AF and elevated stroke risk started on OAC receive it within 1 week, although the promptness of initiation varies. The stroke rate is substantial in the period between AF diagnosis and OAC initiation. Interventions targeting identified risk factors for delayed OAC may result in improved outcomes. **(Am J Cardiol 2017;120:1316–1321)**

Atrial fibrillation (AF) is a prevalent arrhythmia associated with significant stroke risk.[1–3] Oral anticoagulation (OAC) with either warfarin (a vitamin K antagonist) or a novel oral anticoagulant (NOAC) is effective in reducing the risk of stroke associated with AF.[4] As a result, consensus guidelines recommend treatment with either warfarin or NOAC in patients with moderate to high stroke risk, a population that includes the majority of AF patients.[5,6] Despite this recommendation, evidence repeatedly demonstrates that up to 50% of patients with an indication for OAC do not receive it.[7,8] Although previous studies have exposed clinical factors associated with a lower incidence of OAC such as female gender and older age,[8] to date studies have not focused on factors relating to a potential delay in the initiation of OAC therapy after a new diagnosis of AF. Indeed, consideration of factors related to delayed OAC initiation may expose patient, provider, or other systemic characteristics that could be targeted to reduce the total time AF patients are exposed to elevated stroke risk through lack of thromboembolism prophylaxis. In this study, we leveraged a large hospital-based electronic medical record (EMR) to identify cases of incident AF. We then sought to identify clinical factors associated with delayed OAC among the AF patients at elevated stroke risk who ultimately received anticoagulation.

Methods

The Partners HealthCare EMR utilized in this study has been described previously.[9] Briefly, the Partners HealthCare EMR is a large medical record utilized by 7 Massachusetts hospitals. Using the Research Patient Database Query Tool, a large database of detailed Partners HealthCare EMR data, we applied a validated electronic AF ascertainment algorithm[9] to identify unique cases of AF. Briefly, the AF algorithm utilizes diagnostic, procedure, electrocardiographic, and medication data to ascertain the presence of atrial flutter or fibrillation.

To identify potential patients with AF, we first identified all individuals with at least 1 International Statistical Classification of Diseases, ninth revision code for AF at Massachusetts General Hospital from 2006 to 2014 (n = 46,151). To ensure that we captured only new AF diagnoses, we limited the sample to patients who had an independent encounter within 3 to 24 months before AF

[a]Division of Cardiology, Massachusetts General Hospital, Boston, Massachusetts; [b]Cardiovascular Research Center, Massachusetts General Hospital, Boston, Massachusetts; and [c]Cardiac Arrhythmia Service, Massachusetts General Hospital, Boston, Massachusetts. Manuscript received May 2, 2017; revised manuscript received and accepted July 5, 2017.

See page 1320 for disclosure information.

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*Corresponding author: Tel: 617-643-7339; fax: 617-726-3852.
E-mail address: slubitz@mgh.harvard.edu (S.A. Lubitz).

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diagnosis in which they did not meet algorithm criteria for AF. To ensure reliable follow-up during which we could ascertain the presence of OAC, we required patients to have separate contact 3 to 24 months after AF diagnosis. We chose 2006 as the start date as this was the first year the American College of Cardiology/American Heart Association AF management guidelines recommended the use of the Congestive heart failure, Hypertension, Age, Diabetes, and Stroke ($CHADS_2$) prediction tool for stroke risk stratification in AF.[10] As we were interested in patients with new AF at an elevated stroke risk with an indication for OAC, we excluded patients with a $CHADS_2$ score of 0. We also excluded patients exposed to OAC before an AF diagnosis as well as patients who were not started on OAC within 1 year of AF diagnosis given our intent to identify factors associated with de novo OAC initiation. As we hypothesized that algorithm performance may be affected by the removal of patients with previous OAC exposure, we performed manual adjudication of AF in a subset of 100 records in which algorithm PPV was found to be 97%.[9] Manual adjudication of AF date in an independent subset of 100 records demonstrated median discrepancy of 0 days (interquartile range 0 to 18.3). In total, we included 4,388 individuals with new AF in the analysis (Figure 1).

For each patient with AF, we extracted clinical characteristics present at AF diagnosis. Demographic information including age, gender, and race were extracted directly from the EMR. Encounter-level factors, including insurance provider and clinic location, were obtained from billing data coded at the index AF encounter. Co-morbidities prevalent at AF diagnosis were defined using the presence of at least 1 International Statistical Classification of Diseases, ninth revision, code for a given condition at any time before the index AF encounter in a manner similar to that used in previous studies.[8,11] Baseline medication use was defined as the presence of a medication prescription within 30 days prior to AF diagnosis. Reversible AF was defined as the concomitant presence of AF with an International Statistical Classification of Diseases, ninth revision, code diagnosis corresponding to cardiac surgery or thyroid disease. To enable consideration of the total number of medications a patient is prescribed, we tabulated the number of medications prescribed to each individual within 90 days of the AF diagnosis and termed this the Medication Burden Index (MBI). For each patient, we then determined whether they were above (high MBI) or below (low MBI) the median of the MBI distribution and utilized this binary value for subsequent analyses.

For each AF patient, we calculated time to OAC as the number of days between the date of AF diagnosis and the first appearance of OAC (warfarin or NOAC) in the medical record. To determine independent clinical factors associated with increased time to OAC following AF diagnosis, we performed multivariable Cox proportional hazard regression with time to OAC as the outcome of interest. Variables included in the multivariable models were year of AF diagnosis, age, gender, race, hypertension, heart failure, diabetes, previous stroke or transient ischemic attack, vascular disease, reversible AF, dementia, previous fall, previous bleed or thrombocytopenia, aspirin use, P2Y12 inhibitor use, dual antiplatelet therapy use (aspirin and P2Y12 inhibitor), malignancy, liver disease, pulmonary disease, rheumatic disease, weakness/paralysis, chronic kidney disease, insurance carrier, MBI, and provider specialty (medicine, nonmedicine, emergency, or cardiology) at AF diagnosis. To account for the varying baseline propensity to receive OAC that may be confounded by frequent health-care encounters, we tabulated the total number of billed encounters before AF diagnosis and divided the distribution into quartiles, and then stratified the Cox models by quartiles.

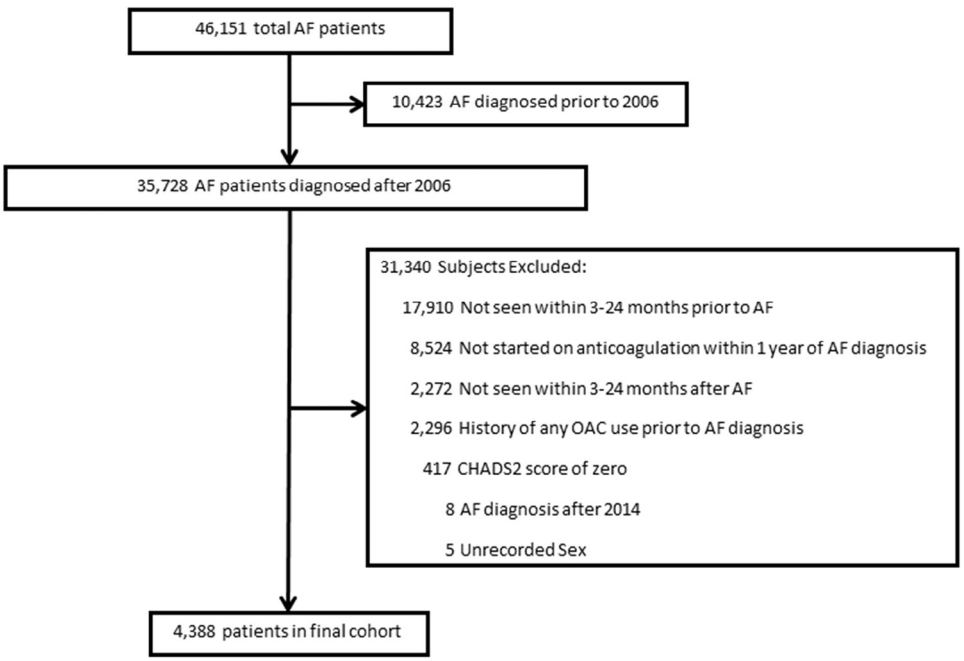

Figure 1. Study design. Graphic depiction of study design. AF = atrial fibrillation; $CHADS_2$ = Congestive heart failure, Hypertension, Age, Diabetes, and Stroke; OAC = oral anticoagulant.