CLINICAL RESEARCH STUDY

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Absence of Oral Anticoagulation and Subsequent Outcomes Among Outpatients with Atrial Fibrillation

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ABSTRACT

BACKGROUND: Prior studies have shown a treatment gap in oral anticoagulation (OAC) use among patients with atrial fibrillation yet have incompletely characterized factors associated with failure to treat and subsequent outcomes in contemporary practice.

METHODS: Using data collected between June 2010 and August 2011 from 174 ambulatory care sites in the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation, we identified factors associated with absence of OAC via stratified logistic regression. Using weighted Cox regression, we assessed the association between OAC non-use and subsequent outcomes over 2.5 years.

RESULTS: Among 9553 patients, 2202 (23.0%) were not on OAC. Among OAC nonrecipients, 1846 (83.8%) had a CHA_2DS_2-VASc score $\geq$2. Factors independently associated with OAC non-use included atrial fibrillation type (paroxysmal odds ratio [OR] 0.73, 95% confidence interval [CI] 0.54-0.99; persistent OR 0.14, 95% CI 0.10-0.21; permanent OR 0.35, 95% CI 0.25-0.49; reference = new-onset), left atrial diameter enlargement (mild OR 0.80, 95% CI 0.66-0.97; moderate 0.58, 95% CI 0.47-0.73; severe 0.53, 95% CI 0.42-0.68; reference = normal diameter), and age >80 years (OR 1.04, 95% CI 1.02-1.08). Untreated patients had a higher risk of death (adjusted hazard ratio [HR] 1.22, 95% CI 1.05-1.41), a lower bleeding risk (adjusted HR 0.35, 95% CI 0.15-0.81), and a nonsignificant trend toward higher risk of stroke/non-central nervous system embolism/transient ischemic attack than those treated (adjusted HR 1.18, 95% CI 0.91-1.54).

CONCLUSIONS: A majority of atrial fibrillation patients not treated with an OAC in current community practice meet guideline indications for treatment. Atrial fibrillation burden, chronicity, and comorbidity are associated with nontreatment. Untreated patients are at increased risk for adverse outcomes.

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Oral anticoagulation (OAC) prevents stroke and improves all-cause survival in patients with atrial fibrillation. In historical clinical trials, vitamin K antagonists reduced the risk of thromboembolism by 64% and all-cause death by 26%, with an acceptable increase in bleeding risk compared with no treatment.[1] Trials of non-vitamin K OACs have demonstrated efficacy and safety equivalent or superior to vitamin K antagonism.[2-5]

Clinical guidelines recommend that atrial fibrillation patients who are at moderate to high risk of stroke without a known contraindication should be treated with OAC.[6-8] Despite demonstrated efficacy and professional guideline recommendations, OAC treatment rates are generally below 60%[9] and have remained low over time.[10] However, factors underlying absence of OAC therapy and associated outcomes in the current therapeutic era are incompletely understood. Accordingly, the present analysis sought to identify factors associated with the absence of OAC therapy in US clinical practice. Additionally, we sought to describe outcomes in patients who were not treated with OAC in contemporary US outpatient practice.

CLINICAL SIGNIFICANCE

- In ORBIT-AF, a national, ongoing registry of outpatients with atrial fibrillation, a majority of atrial fibrillation patients not treated with oral anticoagulation meet guideline indications for treatment.
- Atrial fibrillation burden, chronicity, and comorbidity are associated with nontreatment.
- Untreated patients are at elevated risk for death.
- Future quality improvement initiatives should emphasize appropriate risk stratification and underscore the survival benefit of oral anticoagulation use.

METHODS

Data Source

Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) is a national registry of US outpatients with atrial fibrillation. The rationale, study design, data collection, and methods have been described previously.[11] The primary dataset for the present analysis consisted of baseline data collected from 174 primary care, cardiology, or electrophysiology sites between June 2010 and August 2011. Trained personnel abstracted data on eligible atrial fibrillation outpatients and submitted them to the ORBIT-AF registry by means of a Web-enabled case report form. Data included demographic and clinical characteristics, medical history, heart rhythm history, and pharmacologic treatment, including OAC use. The Duke Clinical Research Institute serves as the data and coordinating center for the registry.

Study Population

A total of 10,135 patients aged ≥18 years with electrocardiographically documented atrial fibrillation were enrolled in ORBIT-AF. For the present analysis, patients with an absolute contraindication to OAC use, including prior intracranial hemorrhage, allergy, and pregnancy, were excluded (n = 89). Those missing data on OAC status at baseline (n = 1) or without any follow-up (n = 329) were also excluded. In an analysis dedicated to patients with unequivocal American Heart Association/American College of Cardiology/Heart Rhythm Society guideline indications for OAC,[8] we excluded patients with a CHA_2DS_2-VASc (**C**ongestive heart failure; **H**ypertension; **A**ge ≥75 years; **D**iabetes mellitus; prior **S**troke, TIA, or thromboembolism; **V**ascular disease; **A**ge 65-74 years; **S**ex **c**ategory) score <2 (n = 930). To identify factors associated with non-use of OAC, sites with >95% OAC use and/or <20 patients were excluded (n = 2564). For the purpose of the outcomes assessment among patients with a CHA_2DS_2-VASc score <2, sites with >95% OAC use and/or <20 patients were included.

Outcome Measures

The condition of interest was OAC use at baseline. Outcomes of interest included all-cause death, stroke or systemic embolism, and major bleeding. In ORBIT-AF, patients were evaluated every 6 months, and the time and date of intervening cardiovascular events were recorded, including but not limited to stroke, bleeding events, and death. Stroke was defined as a new, sudden, focal neurologic deficit that persisted beyond 24 hours and was not due to a readily identifiable, nonvascular cause (eg, seizure). All stroke and systemic embolism events were verified and adjudicated using source documentation. Major bleeding was defined according to the International Society of Thrombosis and Haemostasis criteria.[12] International Society of Thrombosis and Haemostasis acute major bleeding events were those that were fatal; occurred in a critical area or organ such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, or intramuscular with compartment syndrome; and/or led to a fall in hemoglobin level of 2 g/L or more, leading to transfusion of 2 or more units of whole or red blood cells.[12]

Statistical Analysis

In the overall study population, we compared the baseline characteristics of patients who did not receive OAC with those of patients who did, using χ^2 tests for categorical variables and Wilcoxon rank-sum tests for continuous variables. Percentages for categorical variables and medians and interquartile ranges (IQRs) for continuous variables are reported. An analysis of only patients with guideline indications for OAC was performed among patients with a CHA_2DS_2-VASc score ≥2.