Net Clinical Benefits of Guidelines and Decision Tool Recommendations for Oral Anticoagulant Use among Patients with Atrial Fibrillation

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Background: The 2012 American College of Chest Physicians' Evidence-Based Clinical Practice (CHEST), the 2012 European Society of Cardiology, and the 2014 American Heart Association guidelines and published decision tools by LaHaye and Casciano offer oral anticoagulant (OAC) recommendations for patients with atrial fibrillation (AF). The aim of our study was to compare the net clinical benefit (NCB) of OAC prescribing that was concordant with these decision aids. *Methods:* A cohort study of the 2001-2013 LifeLink claims data was used. NCB in concordance with each decision aid was defined as adverse events (thromboembolic and major bleed events) prevented per 10,000 person-years. Cox proportional hazard models were used to assess the relative risk of AF adverse events associated in concordance with each decision aid adjusted for potential confounders. *Findings:* The study included 15,129 patients with AF, contributing 33,512 person-years. The NCB of the CHEST guidelines was the highest (NCB = 30.07; 95% confidence interval [CI] = 28.66, 31.49) and the European Society of Cardiology guidelines the lowest (NCB = 7.38; 95% CI = 5.97, 8.80). Significant unadjusted decreases in the risk of AF adverse events associated with concordant OAC use/nonuse were found for the CHEST guidelines (hazard ratio [HR] = .825; 95% CI = .695, .979), Casciano tool (HR = .838; 95% CI = .706, .995), and LaHaye tool (HR = .841; 95% CI = .709, .999); however, none were significant after multivariate adjustment. *Conclusion:* Concordant OAC use with any of the decision aids except for the aggressive LaHaye tool led to a positive NCB. The decision aids based on the CHA_2DS_2-VASc algorithm did not consistently improve the NCB compared to $CHADS_2$-based aids. Recommending OAC use when CHA_2DS_2-VASc score = 1 resulted in a lower NCB when all other factors guiding recommendations were held constant. **Key Words:** Atrial fibrillation—guideline—decision tool—concordance—net clinical benefit.

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Introduction

Atrial fibrillation (AF) is a cardiac arrhythmia that increases the risk of ischemic stroke (IS) or thromboembolism (TE).[1] Oral anticoagulants (OACs) are often prescribed in these patients to reduce the risk of IS/TE events. Warfarin and newer OACs are more effective than aspirin in reducing the IS/TE risk but are also associated with an increased bleeding risk.[2] Therefore, evaluation of both stroke and bleeding risk is critical when considering anticoagulating patients with AF.

The treatment recommendations of contemporary AF treatment guidelines are mainly based on IS risk; only a few consider or formally incorporate bleeding risk when recommending OAC despite the availability of bleeding risk algorithms that accurately predict major bleed events.[3] Widely accepted guidelines such as the 2012 American College of Chest Physicians' Evidence-Based Clinical Practice (CHEST) Guidelines and the 2014 American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society (AHA/ACC/HRS hereafter "AHA") guidelines do not incorporate bleeding risk algorithms when making OAC treatment recommendations in patients with AF.[4,5] Likewise, the 2012 European Society of Cardiology (ESC) guidelines for the management of AF considers the HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly (> 65 years), Drugs/alcohol concomitantly) bleeding risk but only recommends caution when prescribing anticoagulants in patients with a HAS-BLED score greater than or equal to 3.[6] To address this problem, various clinical decision support tools have been developed that incorporate both the IS risk and the bleeding risk.[7-10]

Currently, limited evidence documents the overall benefit to patients in routine care when different guidelines are followed. The impact of inadequate adherence to the AF guideline recommendations was studied by Saarinen et al.[11] in 2014; however, they only assessed the AHA and ESC guideline recommendations on 3-month mortality because of ischemic and hemorrhagic strokes using a small study sample (n = 102). In the present study, we compared 2 decision tools developed and published by Casciano et al. and LaHaye et al. along with the 3 AF guidelines: the 2012 CHEST guidelines, the 2012 ESC guidelines, and the 2014 AHA guidelines (decision tools and guidelines hereafter referred to as "decision aids").[4-6,9,10] To our knowledge, no epidemiological study has been conducted to compare the clinical benefit of decision tools to AF guidelines.

The aim of our study was to compare the predictive ability of these aids by contrasting the net clinical benefit (NCB) when OAC use is concordant and discordant with each of the aids. Because AF anticoagulant decisions are not based on single-event rates such as IS or major bleed, the standard measures of model performance such as model discrimination could not be used directly. Instead, we compared composite stroke/bleed event rates of these tools when anticoagulant prescribing is concordant and when it is discordant with the treatment recommendations. This will allow clinicians to identify the differences between these aids and offer insights on which decision aid may have more clinical value in rendering anticoagulant recommendations when followed in routine care.

Methods

Study Design and Study Measures

A cohort study design using the 2001-2013 PharMetrics LifeLink claims data was used to compare the NCB of patients with AF who were concordant versus discordant with the decision aids. PharMetrics LifeLink is representative of the commercially insured population of the United States with respect to age, gender, geographic location, and the type of insurance coverage. The database includes inpatient claims, outpatient claims, prescription claims, and eligibility data. The study subjects were incident AF cases without any AF-related claims during the year before their first primary AF diagnosis. For each subject, we calculated the $CHADS_2$ (Congestive heart failure, Hypertension, Age ≥ 75, Diabetes, and Prior Stroke or transient ischemic attack),[12] CHA_2DS_2-VASc (Congestive heart failure, Hypertension, Age ≥ 75, Age 65–74 years, Diabetes, Prior Stroke or transient ischemic attack, Vascular disease, and Sex),[13] HAS-BLED,[14] ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation)[15] scores and other measures necessary for the 2012 CHEST, the 2012 ESC, the 2014 AHA guidelines, and LaHaye and Casciano tools to render an OAC recommendation. Because the AHA guidelines do not offer clear guidance when the CHA_2DS_2-VASc score = 1, we constructed 2 scenarios: AHA aggressive, which recommended OAC when CHA_2DS_2-VASc score = 1; and AHA conservative, which recommended withholding OAC when CHA_2DS_2-VASc score = 1. To operationalize recommendations of the ESC guidelines, which incorporate bleeding risk, we defined a CHA_2DS_2-VASc score equal to 1 and a HAS-BLED score greater than or equal to 3 as a recommendation to withhold OAC, and a CHA_2DS_2-VASc score equal to 1 and HAS-BLED score less than 3 as an OAC recommendation. Bleeding risk was not considered for any other levels of CHA_2DS_2-VASc scores. OAC exposure was determined within the first 90 days after the index AF diagnosis using both prescription fills (for warfarin, dabigatran, apixaban, or rivaroxaban) and inpatient/outpatient claims data (for International Normalized Ratio (INR)/ Prothrombin time (PT) testing). We compared those recommendations with actual OAC exposures to determine concordant and discordant OAC use/nonuse. When a patient's OAC exposure status was