Reviewing a Clinical Decision Aid for the Selection of Anticoagulation Treatment in Patients With Nonvalvular Atrial Fibrillation: Applications in a US Managed Care Health Plan Database

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ABSTRACT

Purpose: The Clinical Decision Aid was created to assist in selecting anticoagulant therapies for patients with nonvalvular atrial fibrillation. The aid incorporates a patient's absolute risk for stroke and bleeding, relative stroke risk reduction, and increase in relative bleeding risk to identify the agent with the lowest net risk. We describe theoretical implications of utilizing the aid at a US managed care population level.

Methods: This retrospective study used claims data from a large US managed care database including enrollees in commercial and Medicare Advantage plans. The distribution of patients across each possible combination of scores on the HAS-BLED scale (evidence of hypertension, abnormal renal or liver function, stroke, bleeding, labile INR, age >65 years, and drugs or alcohol abuse or dependence) and the CHA_2DS_2-VASc scale ($CHADS_2$ [congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism] with additional nonmajor stroke risk factors, including age 65–74 years, female sex, and vascular disease) was generated. We assessed the correlation between the HAS-BLED and CHA_2DS_2-VASc scores and derived the optimal treatment options based on various bleeding ratios.

Findings: Data from 48,260 patients were included in the analysis. The MAPD subset had a higher mean HAS-BLED score (2.17 vs 1.39; $P < 0.001$) and a higher mean CHA_2DS_2-VASc score (3.35 vs 2.05; $P < 0.001$) than did the commercial subset. Pearson coefficients suggested a moderate to strong positive correlation between the HAS-BLED and CHA_2DS_2-VASc scores among the commercial (0.730; $P < 0.001$) and MAPD (0.568; $P < 0.001$) enrollees. Based on a 2:1 bleeding-to-stroke risk ratio, 70.50% of patients would be recommended treatment with apixaban; 25.86%, no treatment; 3.62%, acetylsalicylic acid; and 0.01%, dabigatran 150 mg, if the Clinical Decision Aid were to be used for anticoagulant treatment selection.

Implications: Evidence-based clinical decision–making tools utilizing risk assessment for recommending a treatment may be valuable for not only health care providers but also health care payers in optimizing care at the population level. (*Clin Ther.* 2014;36:1566–1573)

Key words: anticoagulation therapy, antithrombotic therapy, atrial fibrillation, bleeding, stroke.

INTRODUCTION

Although warfarin is effective in reducing the risk for thromboembolism in patients with nonvalvular atrial fibrillation (NVAF), it has been associated with several shortcomings, such as the need for regular monitoring of the international normalized ratio (INR), a narrow therapeutic range of INR, and multiple interactions with drugs and food. A few novel oral anticoagulants (NOACs)—apixaban, dabigatran, and rivaroxaban—have recently been approved in the United States as

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alternatives to warfarin for reducing the risks for stroke and systemic embolism (SSE) in patients with NVAF. Unlike warfarin, NOACs have more predictable dose responses, fewer drug and food interactions, and no requirement for laboratory monitoring.[1–3] Each of these medications demonstrates a unique risk–benefit profile and certain advantages versus warfarin. In the absence of head-to-head comparisons among the NOACs, it is challenging for clinicians to determine the best treatment option among the available choices.

A Clinical Decision Aid was created by LaHaye et al[4] to assist clinicians in selecting anticoagulant therapy at the point of care. The aid compares the following treatment options: no treatment, acetylsalicylic acid (ASA), ASA plus clopidogrel 75 mg once daily (ASA + clopidogrel), warfarin, dabigatran 110 mg BID (dabigatran 110), dabigatran 150 mg BID (dabigatran 150), rivaroxaban 20 mg once daily (rivaroxaban), and apixaban 5 mg BID (apixaban). The key feature of the aid is that it addresses the importance of considering the risks for both stroke and major bleeding in determining the optimal anticoagulant option for individual patients with NVAF. It incorporates a patient's absolute risk for stroke, absolute risk for bleeding, the relative stroke risk reduction, and the increased relative risk for bleeding associated with each anticoagulant agent to identify the agent with the lowest *net risk*. To estimate the absolute risk for stroke, the tool utilizes the stroke risk assessment schema, CHA_2DS_2-VASc,[5–7] and to estimate the absolute risk for major bleeding, it utilizes the bleeding risk assessment schema (evidence of hypertension, abnormal renal or liver function, stroke, bleeding, labile INR, age >65 years, and drugs or alcohol abuse or dependence; HAS-BLED).[5,8,9] The baseline risks and relative risks for stroke and major bleeding of each treatment choice were determined based on a variety of evidence sources, including observational research from a large-scale patient registry, meta-analyses, and randomized clinical trials. For each combination of HAS-BLED and CHA_2DS_2-VASc scores of a patient, the Clinical Decision Aid calculates the net risk for every anticoagulant treatment option and compares it with the net risk of no treatment to determine the option with the lowest net risk. LaHaye et al[4] explain, "Net risk is defined as the annual absolute risk of *either* SSE *or* Major Bleeding, and is calculated as 1 minus the risk of *neither* SSE *nor* Major Bleeding, where the risk of *neither* SSE *nor* Major Bleeding is equal to the product of the risk of no SSE and the risk of no Major Bleeding" (page 2165). Using warfarin as an example:

$$\text{Net Risk}_{\text{warfarin}} = 1 - [(1 - \text{TRS}_{\text{warfarin}}) \times (1 - \text{TRB}_{\text{warfarin}})] \quad (1)$$

where TRS_{warfarin} is a patient's annual absolute risk for SSE with warfarin treatment, and TRB_{warfarin} is a patient's annual absolute risk for major bleeding with warfarin treatment.[4] The option with the lowest net risk is then recommended as "optimal" for the patient.

Treatments recommended by the Clinical Decision Aid may be modified by a few patient factors, the most important of which is the *bleeding ratio,* defined as the maximum number of major bleeding events that a patient is willing to experience to prevent 1 SSE. For example, a bleeding ratio of 2:1 means a patient is willing to endure 2 major bleeding events to prevent a stroke. Applying a bleeding ratio of 2:1, then the warfarin-related net risk model (mentioned earlier) would be revised such that the patient's annual absolute risk for major bleeding with warfarin treatment is divided by 2, as follows:

$$\text{Net Risk}_{\text{warfarin}} = 1 - \{[1 - \text{TRS}_{\text{warfarin}}] \times [1 - (\text{TRB}_{\text{warfarin}}/2)]\} \quad (2)$$

The goal of this report was to describe theoretical implications of utilizing the Clinical Decision Aid at a patient population level. We assessed the percentage distribution of patients with NVAF across each possible combination of HAS-BLED and CHA_2DS_2-VASc scores in a large US managed care health plan setting. We then derived the optimal anticoagulant treatment option based on the aid's recommendations.

PATIENTS AND METHODS

Study Design and Data Sources

This retrospective study was conducted using medical and pharmacy claims data from the period from January 1, 2004, to June 30, 2010, from the database of a large-scale US managed care health plan affiliated with Optum, Inc. Member coverage was geographically diverse, with coverage across all US census regions. The data were completely deidentified before receipt by the investigators. The study was conducted in accordance with the International Society for Pharmacoepidemiology Guidelines for Good Epidemiology Practices and applicable regulatory requirements. Because individual identities or medical records were not disclosed, and data were accessed using methods consistent with the