CLINICAL RESEARCH STUDY

Underuse of Oral Anticoagulants in Atrial Fibrillation: A Systematic Review

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ABSTRACT

BACKGROUND: Atrial fibrillation is associated with substantial mortality and morbidity from stroke and thromboembolism. Despite an efficacious oral anticoagulation therapy (warfarin), atrial fibrillation patients at high risk for stroke are often under-treated. This systematic review compares current treatment practices for stroke prevention in atrial fibrillation with published guidelines.

METHODS: Literature searches (1997-2008) identified 98 studies concerning current treatment practices for stroke prevention in atrial fibrillation. The percentage of patients eligible for oral anticoagulation due to elevated stroke risk was compared with the percentage treated. Under-treatment was defined as treatment of <70% of high-risk patients.

RESULTS: Of 54 studies that reported stroke risk levels and the percentage of patients treated, most showed underuse of oral anticoagulants for high-risk patients. From 29 studies of patients with prior stroke/ transient ischemic attack who should all receive oral anticoagulation according to published guidelines, 25 studies reported under-treatment, with 21 of 29 studies reporting oral anticoagulation treatment levels below 60% (range 19%-81.3%). Subjects with a $CHADS_2$ (congestive heart failure, hypertension, age >75 years, diabetes mellitus, and prior stroke or transient ischemic attack) score ≥2 also were suboptimally treated, with 7 of 9 studies reporting treatment levels below 70% (range 39%-92.3%). Studies (21 of 54) using other stroke risk stratification schemes differ in the criteria they use to designate patients as "high risk," such that direct comparison is not possible.

CONCLUSIONS: This systematic review demonstrates the underuse of oral anticoagulation therapy for real-world atrial fibrillation patients with an elevated risk of stroke, highlighting the need for improved therapies for stroke prevention in atrial fibrillation.

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KEYWORDS: Atrial fibrillation; Current treatment practices; Guidelines; Oral anticoagulant therapy; Stroke risk

Atrial fibrillation, the most common significant cardiac rhythm disorder, is associated with substantial mortality and morbidity from stroke and thromboembolism.[1] Incidence of atrial fibrillation in the general population ranges from 0.85 to 4.1 per 1000 person-years,[2-4] and increases substantially with age.[2,5] Atrial fibrillation patients are at higher risk of stroke, and cardiovascular- and stroke-related death than the general population.[6-8] However, this elevated risk of stroke is not homogeneous and is increased by the presence of additional risk factors including prior stroke, transient ischemic attack, hypertension, increasing age, and diabetes.[9,10]

Published guidelines for stroke prevention in atrial fibrillation patients recommend treatment with oral anticoagu-

lants for patients at moderate or high risk of stroke, and aspirin or no antithrombotic therapy for patients at moderate or low risk.[11-15] Guidelines tend to differ over stroke risk stratification due to variations in the categorization of risk factors (Table 1, online). A recent review concluded that while all the schemes stratified stroke risk, the absolute stroke rates varied widely.[16] Observed stroke rates for those categorized as low risk ranged from 0% to 2.3% per year while rates for those categorized as high risk ranged from 2.5% to 7.9% per year.[16] When applied to the same representative cohort, the percentage of patients categorized as low risk by the different schemes varied from 9% to 49%, and the percentage categorized as high risk varied from 11% to 77%.[16] In addition, the ability of commonly used risk stratification schemes to predict stroke in atrial fibrillation patients is limited. Gage and colleagues[17] reported that risk schemes had only fair discriminating ability (c-statistic: 0.56 to 0.62; ideal is 1), while Baruch et al[18] reported that only 3 schemes—CHADS$_2$ (congestive heart failure, hypertension, age >75 years, diabetes mellitus, and prior stroke or transient ischemic attack) score,[17,19] Stroke Prevention in Atrial Fibrillation,[20] and Framingham score[21]—had greater predictive accuracy for stroke than chance.[18] Substantial, clinically relevant differences exist among published schemes that may lead to inconsistent stroke risk estimates for atrial fibrillation patients, resulting in confusion among clinicians and nonuniform use of anticoagulation therapy.[16]

This study systematically reviews the literature concerning stroke prevention in high-risk atrial fibrillation patients to examine the use of oral anticoagulants in current practice with respect to guidelines for prophylaxis.

PATIENTS AND METHODS

Literature Search
An extensive search of recent biomedical literature was performed using PubMed for studies pertaining to current treatment practices for stroke prevention for atrial fibrillation patients; the search was limited to studies on humans, published after May 1997. Combinations of the following search terms were used: practices, treatment, atrial fibrillation, stroke, antithrombotics, antiplatelets, oral anticoagulants, warfarin, and vitamin K antagonist. Studies were excluded if no stroke risk stratification was available for the whole patient population or if treatment details were not available for patients with prior stroke. Clinical trials were

> **CLINICAL SIGNIFICANCE**
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> - Underuse of oral anticoagulants for high-risk atrial fibrillation patients was found in most of the 54 studies (1998-2008) reporting both patient stroke risk and patients treated.
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> - Over two thirds of studies of atrial fibrillation patients with prior stroke or transient ischemic attack reported treatment levels of under 60% of eligible patients.
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> - Most studies based on CHADS$_2$ (congestive heart failure, hypertension, age >75 years, diabetes mellitus, and prior stroke or transient ischemic attack) score reported oral anticoagulant treatment levels of high-risk subjects below 70%.

excluded because they contained no treatment data from "real life" clinical settings. English language articles were primarily reviewed, with promising articles in other languages as practical. Bibliographies of retrieved articles and abstracts returned as "related articles" from PubMed were screened to identify additional sources. All world regions were explored. Analyses were conducted by 2 independent investigators.

Analysis of Current Treatment Practices for Stroke Prevention in High-risk Atrial Fibrillation Patients
The following data were systematically extracted; patient population, study setting (general practice or hospital), risk stratification scheme or treatment guideline applied, relevant risk criteria, and proportion of patients treated with oral anticoagulation therapy or antiplatelet agents. Because the recommended treatment for atrial fibrillation is dependent on patient risk for stroke, only articles that reported treatment levels of atrial fibrillation patients at high risk of stroke were included. High-risk categories for this literature review include: atrial fibrillation patients with prior ischemic stroke or transient ischemic attack; patients with a CHADS$_2$ score of 2 or more;[17,22] and patients designated high risk by any other risk stratification scheme (American College of Cardiology/American Heart Association/European Society of Cardiology guidelines, and others).[23,24] Only patients at a high risk of stroke were included in the analysis.

The following values were extracted or calculated from data presented in the literature selected. Firstly, the proportion of the study population with prior stroke/transient ischemic attack, who are all considered to be eligible for oral anticoagulation treatment according to all published guidelines, was captured. Secondly, the percentage of patients eligible for oral anticoagulation treatment according to the relevant risk stratification scheme or treatment guideline used to classify patients in that study was recorded. Thirdly, the percentage of patients actually treated with oral anticoagulation was noted. If data were available only for subpopulations (eg, men and women separately), an overall weighted average was calculated. Data on contraindications to oral anticoagulation therapy were captured if available. From values collected, we calculated the proportion of atrial fibrillation patients eligible for oral anticoagulation treatment—due to either the presence of prior stroke/transient ischemic attack or a high risk designation from a risk strat-