Implications of Stroke Risk Criteria on the Anticoagulation Decision in Nonvalvular Atrial Fibrillation

The Anticoagulation and Risk Factors In Atrial Fibrillation (ATRIA) Study

Alan S. Go, MD; Elaine M. Hylek, MD, MPH; Kathleen A. Phillips, BA; Leila H. Borowsky, MPH; Lori E. Henault, MPH; YuChiao Chang, PhD; Joe V. Selby, MD, MPH; Daniel E. Singer, MD

Background—Warfarin dramatically reduces the risk of stroke in patients with nonvalvular atrial fibrillation (NVAF) but increases the likelihood of bleeding. Accurately identifying patients who need anticoagulation is critical. We assessed the potential impact of prominent stroke risk classification schemes on this decision in a large sample of patients with NVAF.

Methods and Results—We used clinical and electrocardiographic databases to identify 13,559 ambulatory patients with NVAF from July 1996 through December 1997. We compared the proportion of patients classified as having a low enough stroke risk to receive aspirin using published criteria from the Atrial Fibrillation Investigators (AFI), American College of Chest Physicians (ACCP), and the Stroke Prevention in Atrial Fibrillation Investigators (SPAF). In this cohort, AFI criteria classified 11% as having a low stroke risk, compared with 23% for ACCP and 29% for SPAF (κ range, 0.44 to 0.85). This 2- to-3-fold increase in low stroke risk patients by ACCP and SPAF criteria primarily resulted from the inclusion of many older subjects (65 to 75 years: men >75 years) with no additional clinical stroke risk factors.

Conclusions—The age threshold for assigning an increased stroke risk has a dramatic impact on whether to recommend warfarin in populations of patients with NVAF. Large, prospective studies with many stroke events are needed to precisely determine the relationship of age to stroke risk in AF and to identify which AF subgroups are at a sufficiently low stroke risk to forego anticoagulation. (Circulation. 2000;102:11-13.)

Key Words: fibrillation ■ anticoagulants ■ risk factors ■ stroke

Warfarin substantially decreases the risk of stroke in patients with nonvalvular atrial fibrillation (NVAF), but it increases the risk of major bleeding.1,2 To optimize the use of warfarin in patients with NVAF, it is critical to accurately identify which patients are at an increased risk for stroke and would benefit most from anticoagulation therapy and which patients are at a low enough risk for stroke to safely avoid the risks of anticoagulation.

Stroke risk classification schemes have been proposed by the Atrial Fibrillation Investigators (AFI), who performed a pooled analysis of 5 primary prevention trials3; the American College of Chest Physicians’ Consensus Conference on Antithrombotic Therapy (ACCP), which used expert committees who reviewed available published literature4; and the Stroke Prevention in Atrial Fibrillation Investigators (SPAF), who analyzed patients from a series of clinical trials.4 These risk classification schemes were based primarily on post hoc analyses of randomized trial populations. Resulting treatment recommendations overlap but have several differences (Table). The implications of these differences for the use of warfarin therapy in “real world” populations of NVAF patients are unknown.

To address this issue, we evaluated the impact of these 3 stroke risk classification schemes on the anticoagulation decision in a large cohort of ambulatory patients with NVAF.

Methods

Study Population
The cohort assembly has been described previously.5 Briefly, we constructed a cohort of patients with NVAF between July 1, 1996
A total of 13,559 patients met the criteria for NVAF during the study period. Their mean age was 71.6 years, and 43% were women. More than 75% of the cohort was ≥65 years, and 45% was ≥75 years.

Overall, 9% of patients had a previous ischemic stroke, 31% had previously diagnosed heart failure, 51% had hypertension, 17% had diabetes, and 29% had known coronary disease. Compared with patients in the first 5 primary prevention trials for AF, our cohort was older, had a higher proportion of women, and had a higher prevalence of stroke-related comorbidities.

Comparison of Stroke Risk Criteria

We compared the proportion of NVAF patients who would be categorized as having a “low stroke risk,” in which aspirin would be a reasonable alternative to warfarin, across the 3 stroke risk criteria (Figure). The AFI criteria classified 10.5% (n=1426) as having a low stroke risk, compared with 23.3% (n=3155) for the ACCP criteria and 29.3% (n=3973) for the SPAF criteria (Figure). Inclusion of patients with hyperthyroidism did not change the results significantly. There was fair agreement between AFI and ACCP (κ=0.56) and AFI and SPAF (κ=0.44) and excellent agreement between ACCP and SPAF (κ=0.85). More than 90% of the difference in the proportion of patients considered to have a low stroke risk by the ACCP and SPAF criteria compared with AFI was explained by the inclusion of older patients (65 to 75 years and men >75 years) with no other stroke risk factors.

**Discussion**

Despite demonstrated efficacy in reducing stroke, controversy persists over which NVAF patients would benefit most...
from warfarin. Using the largest sample reported to date, we assessed the clinical implications of 3 prominent stroke risk classification schemes designed to guide the use of anticoagulants in NVAF. Comparing these criteria, we found up to 3-fold differences in the proportion of patients considered to have a low enough stroke risk to recommend aspirin over warfarin. Differences were primarily explained by whether certain age or age/sex categories (65 to 75 years and men over 75 years) were thought to increase the risk of stroke independently.

Previous studies have reported varying estimates of the proportion of patients who should be considered for warfarin therapy, but they were hampered by relatively small sample sizes or by using randomized trial populations, which are not representative of NVAF patients in actual clinical care. The predictive ability of existing stroke risk criteria are based primarily on data from randomized trials that included relatively few stroke events. These classification schemes were variably effective in predicting stroke risk in one relatively small population-based AF cohort. We showed that the choice of stroke risk criteria can have substantial impact on treatment recommendations within a large, ambulatory population of NVAF patients in usual clinical care.

Our study had limitations. We approximated 2 of the SPAF criteria (systolic blood pressure>160 mm Hg and left ventricular dysfunction) using diagnoses of hypertension and heart failure, respectively. However, this likely served to categorize fewer patients at low risk than if explicit SPAF criteria were used, which suggests even greater differences exist between the various schemes. We lacked echocardiographic data, which can provide additional relevant clinical information, but its marginal benefit above clinical risk factors for determining stroke risk remains unclear. It is possible that the exclusion of patients without health plan membership or outpatient follow-up care may affect the generalizability of our results. Finally, we could not distinguish between paroxysmal and persistent/permanent AF, but previous studies suggest that the risk of stroke is similar in these subgroups.

In conclusion, prominent risk stratification schemes for NVAF patients differ substantially in the proportion of patients considered to have a low enough risk of stroke to recommend aspirin instead of warfarin. These differences depend primarily on whether the age 65 to 75 years, by itself, is viewed as a sizable risk factor for stroke in NVAF. These differences have important implications for the thousands of Americans with NVAF. Depending on the risk criteria, the number of US NVAF patients considered at low risk would range from 225,000 to nearly 650,000. Further compounding this problem is the more marked variation in locally produced treatment guidelines for AF. Therefore, large, prospective studies with many stroke events are needed to precisely specify the risk of stroke associated with increasing age and its interaction with other stroke risk factors in the setting of NVAF.

Acknowledgments
Supported by Public Health Services research grant AG15478 from the National Institutes on Aging.

References
Implications of Stroke Risk Criteria on the Anticoagulation Decision in Nonvalvular Atrial Fibrillation: The Anticoagulation and Risk Factors In Atrial Fibrillation (ATRIA) Study
Alan S. Go, Elaine M. Hylek, Kathleen A. Phillips, Leila H. Borowsky, Lori E. Henault, YuChiao Chang, Joe V. Selby and Daniel E. Singer

Circulation. 2000;102:11-13
doi: 10.1161/01.CIR.102.1.11

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/102/1/11

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/