BRIEF REPORTS

Stroke Risk in an Elderly Population with Atrial Fibrillation

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Patients with nonvalvular atrial fibrillation (AF) have an increased risk of stroke, but the absolute rate of stroke varies widely depending on coexistent vascular disease. We assessed the stroke rate and predictive value of two published schemes for stroke risk stratification in a population-derived cohort of 259 elderly people with nonvalvular AF followed for a median of 5.3 years. The rate of ischemic stroke was 2.8% per year (95% confidence interval [CI] 1.9, 3.9). Thirty-one percent were predicted to be at low risk, and their stroke rate was 1.7% per year (95% CI 0.6, 3.8). Many people with AF in this population-derived cohort had relatively low rates of stroke. Further studies to reliably stratify stroke risk in patients with AF are needed.

KEY WORDS: atrial fibrillation; aged; risk factors; stroke; cerebrovascular disease.

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Atrial fibrillation (AF) is an independent risk factor for stroke,¹ but the absolute rate of stroke varies widely depending on coexistent vascular disease. Stroke rates range from less than 0.5% per year in patients with AF under age 60 years old without cardiopulmonary disease ("lone AF")^{2,3} to 12% per year for those with prior stroke.^{4,5} Risk stratification schemes for stroke in patients with AF have been derived from participants in randomized clinical trials.^{3,6} However, participants with AF in these trials were, on average, younger and more often men than patients with AF in population-based cohorts.⁷ The fre-

quency and predictive value of thromboembolic risk factors in a population-derived cohort have not been examined previously.

We determined the stroke rate of participants with AF in the Cardiovascular Health Study (CHS),^{8,9} categorized AF participants as being at low, moderate, or high risk of stroke using two published risk stratification schemes,^{10,11} and then assessed whether these schemes successfully predicted stroke during follow-up.

METHODS

The CHS is a multicenter, longitudinal observational study of a population-based sample of 5,201 adults over age 65 at entry recruited from four communities. Details of study design and recruitment, which commenced in 1989, have been published.^{8,9} At CHS entry, 277 participants (5.3%) were identified as having AF on the basis of entry electrocardiograms or through self-report confirmed by review of medical records. Excluding 18 people with prosthetic cardiac valves or mitral stenosis, the remaining 259 participants with nonvalvular AF are considered here. Antithrombotic therapy during follow-up was determined by their personal physicians.

We assessed thromboembolic risk factors associated with stroke in two published risk stratification schemes (Table 1).^{10,11} Definitions of clinical characteristics of CHS participants have been reported.¹² A history of hypertension was defined as systolic blood pressure of 160 mm Hg or higher, diastolic blood pressure of 90 mm Hg or higher, or self-reported hypertension with current use of antihypertensive medication. Prevalent myocardial infarction, angina pectoris, congestive heart failure, stroke, and transient ischemic attack (TIA) were identified by interview with subsequent confirmation from medical records.

Antithrombotic therapy was recorded at study entry and at yearly follow-up visits (participants brought all medications to annual clinic visits).¹³ For sensitivity analysis, exposure while receiving warfarin but not aspirin was excluded by censoring exposure at the time it was ascertained that warfarin was used, providing warfarin use was recorded prior to stroke. This was done because anticoagulation with warfarin is highly (about 70%) efficacious for reducing stroke in patients with AF.^{3–5} Censored follow-up during warfarin use accounted for 14% of all follow-up and

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Table 1. Risk Stratification Schemes

Risk	Atrial Fibrillation Investigators/American College of Chest Physicians Consensus Conference ^{3,10}			Stroke Prevention in Atrial Fibrillation III Study ^{6,11*}		
	Clinical Features	Proportion of Patients, %	Annual Stroke Rate, %	Clinical Features	Proportion of Patients, %	Annual Stroke Rate, %
High	History of hypertension Diabetes Prior stroke or TIA Coronary artery disease Congestive heart failure	73	≈6	Systolic BP >160 mm Hg Left ventricular dysfunction† Prior stroke or TIA Women >75 years old	48	≈6
Moderate	Age ≥65, no high-risk features	16	≈2‡	History of hypertension, no high-risk features	23	≈3
Low	None of the above	11	≈1	None of the above	29	≈1

*Stroke rate while receiving aspirin.

†Defined as fractional shortening of <25% by m-mode echocardiography or recent (within 3 months) congestive heart failure.

‡In the AFI/ACCP Consensus Conference scheme, the ischemic stroke rate in those without high-risk features was 1.6% per year in the age group 60–69, 2.1% in those age 70–79, and 3.0% in those over age 80.³

was evenly distributed over the risk categories. Strokes were identified during annual follow-up examinations and at 6-month interim telephone contacts. Ischemic strokes included both those presumed to be cardioembolic and noncardioembolic. Potential stroke cases were adjudicated by a committee of neurologists and internists using information from patient interviews, medical records, and brain-imaging studies.

The log rank test from a Cox proportional regression was used to compute the association of risk stratification categories with subsequent stroke. Stroke rates were calculated based on person-years of observation, with confidence intervals determined from the Poisson distribution.

RESULTS

Of 259 CHS participants (5.0% of the cohort) with nonvalvular AF, the mean age was 74 ± 6 years, and 50% were women. Among these participants with AF, hypertension, coronary artery disease, diabetes, congestive heart failure, and prior stroke or TIA, were present in 51%, 42%, 28%, 16%, and 7%, respectively, and fractional shortening

below 25% by echocardiography occurred in 9%. At study entry in 1989–1990, 6% were receiving warfarin and 31% were taking aspirin regularly. After 4 years of follow-up, 24% were receiving warfarin and 37% were taking aspirin.

During follow-up, 21 participants with AF without incident stroke died, and 3 (1%) had incomplete follow-up after an average of 3 years of observation (i.e., over 99% complete for observable person-years). During follow-up, 33 strokes (of which one was hemorrhagic) yielded a rate of 2.8% per year (95% confidence interval [CI] 1.9, 3.9). Excluding follow-up during anticoagulation, the rate was 2.6% per year (95% CI 1.7, 3.8). The overall rate of stroke among all CHS participants was 1.5% per year during a median follow-up of 5.3 years (range 4–6 years).

Risk Stratification

Age above 65 years conferred moderate risk by Atrial Fibrillation Investigators/American College of Chest Physicians (AFI/ACCP) criteria (Table 1), and hence all CHS participants with AF were at least at moderate risk. Applying the AFI/ACCP criteria, 76% of the CHS cohort were

Table 2. Risk Status and Rates of Stroke

Criteria	% of CHS Cohort (n)	% with Strokes (n)	% Given Warfarin* (n)	Annual Stroke Rate (All Follow-up), %	Annual Stroke Rate (Not Anticoagulated),† % (95% CI)
AFI/ACCP Consensus Conference‡					
Moderate risk	24 (62)	10 (6)	24 (15)	2.0	2.4 (0.9, 5.1)
High risk	76 (197)	14 (27)	17 (34)	3.1	2.7 (1.7, 4.1)
SPAF III Study‡					
Low risk	31 (80)	9 (7)	17 (14)	1.8	1.7 (0.6, 3.8)
Moderate risk	24 (62)	10 (6)	24 (15)	2.0	2.0 (0.7, 4.7)
High risk	45 (117)	17 (20)	17 (20)	4.0	3.7 (2.1, 5.8)

*Any time during follow-up prior to the occurrence of stroke.

†Stroke rate while not receiving warfarin.

‡AFI/ACCP indicates Atrial Fibrillation Investigators/American College of Chest Physicians; SPAF, Stroke Prevention in Atrial Fibrillation. In the AFI/ACCP Consensus Conference scheme, the ischemic stroke rate in those without high-risk features was 1.6% per year in the age group 60–69, 2.1% in those age 70–79, and 3.0% in those over age 80.

at high risk while 24% were at moderate risk of stroke (Table 2); these proportions are similar to those in the original AFI/ACCP cohort (Table 1). By the Stroke Prevention in Atrial Fibrillation (SPAF) III Study criteria, 45% of the cohort were classified as high risk, 24% as moderate risk (i.e., a history of hypertension without other high-risk variables), and 31% were low risk; these proportions are similar to those in the original SPAF III cohort (Table 1). Warfarin use during follow-up, determined by the individual participant's personal physician, was similar in all risk categories (Table 2).

The difference in absolute stroke rates between those categorized as moderate versus high risk by the AFI/ACCP criteria was small (Table 2, $p = .79$). The SPAF III Study criteria showed somewhat larger differences between those classified as high versus low or moderate risk (Table 2, $p = .05$), with those classified as low risk by SPAF III criteria having a stroke rate of 1.7% per year (95% CI 0.6, 3.8). Those classified as either low or moderate risk had a stroke rate of 1.9% per year (95% CI 0.9, 3.3), significantly different ($p = .05$) from high risk participants (3.7% per year).

DISCUSSION

Reliable risk stratification would contribute to identification of patients with AF according to their potential benefit from lifelong anticoagulation. Our findings show substantial limitations in available methods for risk stratification. Cardiovascular Health Study patients with AF categorized as low-to-moderate risk by either scheme were observed to have stroke rates between 1.7% and 2.4% per year. The 95% CIs around the observed rates were wide, however, with the upper limits including substantial rates of stroke (e.g., 4%–5% per year), and patients categorized as high risk by the AFI/ACCP and SPAF III schemes had rates of stroke that were only slightly higher (2.7% per year and 3.7% per year, respectively).

The observed rate of stroke (2.6% per year) among CHS participants with AF who were not anticoagulated was lower than that in pooled analysis of first-generation clinical trials (average stroke rate of 4.5% per year overall, and 4% per year excluding those with prior stroke)³ and another population-based study (3.8% per year).¹⁴ Three more recent clinical trials reported stroke rates between 1.9% and 3.0% per year in patients receiving aspirin or no antithrombotic therapy.^{15–17} Aspirin use by nearly a third of CHS participants with AF may also have contributed to the relatively low stroke rate.¹⁸

Considering AF patients classified as low or moderate risk by the SPAF III Study criteria, the observed rate of stroke in CHS (1.9% per year) was similar to that in the SPAF I and II studies (1.9% per year; 95% CI 1.2, 2.9)¹¹ and in the SPAF III study (2.0% per year; 95% CI 1.5, 2.8)⁶ given aspirin. Given the consistency, it seems likely that AF patients with stroke rates of about 2% per year while taking aspirin can be identified, although further studies are needed.

Prolonged follow-up, averaging over 5 years, may have diminished the predictive power of variables defined at study entry. Assessment of the AFI/ACCP scheme was compromised because no CHS participants were classified as low risk due to age criteria, and a third of follow-up occurred during aspirin therapy. Conversely, CHS participants with AF had clinical features similar to those of AF patients seen in general clinical practice, supporting the generalizability of the findings.^{19–21}

Our findings support the need for further studies of stroke and predictors of stroke risk in patients with AF outside clinical trials. These results suggest that many AF patients in population-based cohorts have relatively low risks of stroke. Reliable identification of such low-risk patients could improve management.

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