Atrial Fibrillation After Stroke in the Elderly

Paul J. Friedman, MD, FRACP

To examine the relationship between atrial fibrillation and mortality after stroke, we studied 186 men and 167 women from the Waikato Stroke Registry whose mean age was 75.2 ± 7.5 years. Twenty-three percent (82 of 353) had atrial fibrillation or flutter on their admission electrocardiogram. This group differed significantly from that with sinus rhythm in three respects: 1) They were older (p < 0.01); 2) they had more severe current stroke deficit as evidenced by lower limb power (p < 0.05) and Mini-Mental State Score (p < 0.001), higher incidence of homonymous hemianopia (p < 0.05), and lower incidence of lacunar syndrome stroke (p < 0.001); and 3) they had a significantly higher incidence of cardiomegaly and congestive heart failure (p < 0.01). Functional outcome was insignificantly better in the group with sinus rhythm. During a mean follow-up period of 18 months, mortality was significantly higher in the group with atrial fibrillation (p = 0.001). Proportional hazards modeling, however, showed that the apparently poorer survival in those patients with atrial fibrillation could be explained by factors other than cardiac rhythm, such as age, Mini-Mental State Score, level of consciousness, and interstitial edema on admission chest radiograph. Thus, atrial fibrillation was not an independent predictor of survival after stroke. (Stroke 1991;22:209–214)

Atrial fibrillation is common among elderly people with acute stroke.1,2 The medical literature regarding atrial fibrillation and stroke has generally focused on the risk of initial and subsequent stroke in patients with atrial fibrillation. This risk is highest in people with underlying rheumatic or valvular heart disease, intermediate in those with nonvalvular atrial fibrillation, and lowest in those with lone atrial fibrillation.3,4 Patients with atrial fibrillation have a higher incidence of congestive heart failure than those with sinus rhythm.2,5 Heart failure, in turn, may contribute to the increased mortality among patients with atrial fibrillation.

Proportional hazards modeling is a powerful tool for analyzing survival and for determining factors associated with mortality. Proportional hazards modeling of survival is more informative than analysis at discrete time intervals because it uses all survival data as opposed to data at one point in time. In populations with coronary artery disease5 and elderly people living in the community,6 proportional hazards modeling has shown atrial fibrillation to be an independent predictor of mortality, even after accounting for other features of heart disease. Few studies have examined atrial fibrillation after stroke as a predictor of survival.7–10 In the only such study to use proportional hazards modeling,7 52 of the 409 patients had transient ischemic attack rather than stroke. Hence, study results may not generalize to a population of acute stroke patients. Accordingly, we have used proportional hazards modeling to examine the relationship between atrial fibrillation and mortality in the Waikato Stroke Registry population.

Subjects and Methods

We defined stroke as rapidly developing clinical signs of focal or global (if stupor or coma present) loss of brain function lasting more than 24 hours or leading to death, with no apparent cause other than cerebral infarction or intracerebral hematoma. Patients with subarachnoid hemorrhage were excluded.

We examined all patients aged 60 and above admitted to Waikato Hospital with suspected stroke, usually within 1–3 days after admission. Seventy-six percent of patients were admitted within 48 hours of stroke onset. If there was any doubt about the diagnosis of stroke, the patient did not enter the stroke registry until there was confirmation of the diagnosis by computed tomography (CT), single-photon emission computed tomography (SPECT) using [123I]iodoamphetamine, or autopsy. Probable lacunar syndrome stroke was defined by the presence of one of the lacunar syndromes11 and the absence of a larger infarction on CT, if performed.

During the 24-month patient entry period (May 1, 1987, to May 1, 1989) 388 stroke events were recorded in the Waikato Stroke Registry. We excluded

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Funded in part by grants from the New Zealand Lottery Board and the Waikato Medical Research Foundation.

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Received February 28, 1990; accepted September 7, 1990.
35 stroke events for the following reasons: 14 were recurrences in patients already part of the study, 15 had no electrocardiogram, two had a permanent pacemaker or complete heart block, and four were lost to follow-up before 120 days after stroke. Thus, the study included 353 patients—186 men and 167 women with a mean age of 75.2±7.5 years. Ninety-three percent lived at home as opposed to an institution before the current stroke.

We used minimum power in the affected limbs, graded on the Medical Research Council Scale, as the index of motor loss from stroke. We calculated arm power by averaging power scores for elbow flexion and finger abduction. Leg power was calculated by averaging power scores for hip extension, knee extension, and ankle dorsiflexion. Mini-Mental State Score was used to assess cognitive impairment. The modified Barthel activities of daily living (ADL) score† ranged from zero (totally dependent and doubly incontinent) to 20 (independent self-care abilities and continent). Prestroke Barthel score was determined from reports of the patient’s family. Maximal Barthel score was defined as the highest Barthel score from those measured on days 7, 30, 60, 90, 120, and 180 poststroke; it was thus used as a time-independent measure of maximal recovery.

We used the electrocardiogram and chest radiograph performed at the time of admission to classify cardiac rhythm and radiographic signs of heart failure. Patients with atrial fibrillation or flutter were classified as having atrial fibrillation. Those with sinus rhythm, irrespective of the presence of premature beats, were classified as having sinus rhythm. We excluded patients with permanent pacemakers or complete heart block. Cardiomegaly was defined as a cardiothoracic ratio above 0.50, pulmonary venous congestion by distention of upper lobe veins and peripheral blurring, and interstitial edema by the presence of Kerley B lines and reticular shadowing. Heart failure, myocardial infarction, hypertension, and diabetes were defined by the past or current clinical diagnoses of congestive cardiac failure, myocardial infarction, hypertension, and diabetes mellitus, respectively.

For patients who died, the principal cause of death was extracted from death certificates. Heart disease as a cause of death included myocardial infarction, congestive heart failure, sudden death, and any other cardiac disorder listed as principal cause of death.

We used Student’s t test and the χ² test when appropriate for univariate comparison of the two groups for continuous and discrete data, respectively. Ninety-five percent confidence intervals were calculated.14 We used a proportional hazards model with a Weibull distribution to analyze survival with the SAS Statistical Package procedure LIFEREG. Independent variables in the model included age, sex, prestroke Barthel ADL score, prestroke residence (home or institution), prior stroke (yes or no), level of consciousness on admission (alert or not alert) arm and leg power scores, homonymous hemianopia (present/absent), Mini-Mental State Score, stroke type (lacunar or nonlacunar), rhythm (atrial fibrillation or sinus rhythm), cardiomegaly, pulmonary venous congestion, interstitial edema (present/absent), heart failure (yes or no), myocardial infarction (yes or no), hypertension (yes or no), and diabetes (yes or no).

The study was approved by the Medical Research Ethics Committee.

### Results

Eighty-two of the 353 patients (23%) had atrial fibrillation at the time of admission. In 57% this rhythm had been documented before stroke. Ninety-six percent of patients with atrial fibrillation were considered on clinical grounds to have nonvalvular atrial fibrillation; the remaining three patients had mitral stenosis, prosthetic heart valve, and hypertrophic cardiomyopathy, respectively.

The group with atrial fibrillation differed from that with sinus rhythm in three respects: they were significantly older; they had more severe current stroke deficit as evidenced by lower incidence of lacunar syndrome stroke, lower level of consciousness on admission, lower limb power and Mini-Mental State Score, and a higher incidence of homonymous hemianopia; and they had a higher incidence of cardiome-
TABLE 2. Comparison of Patients With Atrial Fibrillation and Sinus Rhythm With Regard to Current Stroke Deficit and Admission Chest Radiographic Signs of Heart Failure

<table>
<thead>
<tr>
<th></th>
<th>Atrial fibrillation</th>
<th>Sinus rhythm</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacunar syndrome stroke</td>
<td>3/82 (4%)*</td>
<td>54/271 (20%)</td>
<td>-22% to 0%</td>
</tr>
<tr>
<td>Alert on admission</td>
<td>53/82 (65%)*†</td>
<td>207/271 (76%)</td>
<td>-20% to -2%</td>
</tr>
<tr>
<td>Arm power score</td>
<td>1.77±1.86†</td>
<td>2.33±1.90</td>
<td>-1.03 to -0.09</td>
</tr>
<tr>
<td>Leg power score</td>
<td>2.03±1.88†</td>
<td>2.62±1.84</td>
<td>-1.05 to -0.13</td>
</tr>
<tr>
<td>Homonymous hemianopia‡</td>
<td>32/68 (47%)*</td>
<td>75/239 (31%)</td>
<td>+4% to +30%</td>
</tr>
<tr>
<td>Mini-Mental State Score¶</td>
<td>10.3±10.4*</td>
<td>15.2±11.2</td>
<td>-7.8 to -2.0</td>
</tr>
<tr>
<td>(n=75)</td>
<td></td>
<td>(n=252)</td>
<td></td>
</tr>
<tr>
<td>Cardiomegaly</td>
<td>47/70 (67%)*</td>
<td>76/251 (30%)</td>
<td>+24% to +49%</td>
</tr>
<tr>
<td>Pulmonary venous congestion</td>
<td>22/70 (31%)*</td>
<td>29/251 (12%)</td>
<td>+8% to +31%</td>
</tr>
<tr>
<td>Interstitial edema</td>
<td>11/70 (16%)*§</td>
<td>12/251 (5%)</td>
<td>+2% to +20%</td>
</tr>
</tbody>
</table>

Values are mean±SD. CI, confidence interval.
* p<0.01.
† p<0.05.
‡ Excludes patients not tested or not able to be tested.
§ p<0.01.

Survival was significantly worse among those with atrial fibrillation as compared to those in sinus rhythm. Figure 1 shows that survival of the two groups continued to diverge over time; at 6, 12, and 18 months poststroke, the difference in survival between the two groups rose from 16% to 18% and 29%, respectively.

Computed tomography was performed on a greater proportion of patients with sinus rhythm than with atrial fibrillation (92 of 271 versus 15 of 82, p<0.05). The incidence of intracerebral hematoma was insignificantly higher in the group with sinus rhythm compared to those with atrial fibrillation (20% versus 7% of those undergoing CT scanning, respectively). Patients with sinus rhythm were three times more likely to have a nondiagnostic CT scan than those with atrial fibrillation (18 of 92 versus one of 15, p=NS). Patients with atrial fibrillation who had a CT scan were a selective group with much lower 90-day mortality than those who did not have a CT scan (20% versus 49%, respectively). In contrast, 90-day mortality in patients with sinus rhythm with or without CT scanning was similar (25% versus 27%). Overall, 49% of those with sinus rhythm as compared to 35% of those with atrial fibrillation had either a CT scan, a SPECT scan, or autopsy of the brain. Among patients with first-ever stroke who received CT scanning, the frequency of silent infarction on CT was 13% among those with atrial fibrillation and 10% among those with sinus rhythm.

Mean follow-up was 18 months poststroke (range, 4–35 months). Only five of the 82 patients with atrial fibrillation were treated with long-term anticoagulation. This decision was generally left to the attending physician; some physicians did not use anticoagulants on elderly patients, whereas others would use them only for those patients with excellent functional recovery after stroke.

To analyze predictors of survival, we first entered singly the independent variables shown in Tables 1 and 2 into a proportional hazards model. The best univariate predictors of mortality, ranked in order according to their χ² value from the proportional hazards model, are shown in Table 3. Cardiac rhythm was the ninth best predictor of the 12 significantly associated with survival. Variables not significantly related to survival included sex, prestroke Barthel score, prior residence, prior stroke, homonymous hemianopia, myocardial infarction, and diabetes.
To further elucidate the role of atrial fibrillation as a predictor of mortality, we entered variables that were individually predictive of survival into a multivariate proportional hazards model by forward and backward selection. Cardiac rhythm did not remain in any of the most successful models. The best model for predicting survival contained Mini-Mental State Score, level of consciousness, age, and interstitial edema. Even without any of the chest radiographic measures, cardiac rhythm did not contribute significantly to any of the multivariate models.

We repeated survival analyses for the subset of 271 patients with first-ever stroke. Results were similar to those from the entire group of 353 patients; cardiac rhythm was a univariate predictor of survival, but did not contribute to the multivariate models, particularly when one of the chest radiographic variables was included. We then repeated survival analysis for the subset of 88 patients whose CT scans showed infarcts or were nondiagnostic (i.e., excluding intracerebral hematoma). Mini-Mental State Score remained the best predictor of survival. Cardiac rhythm was not a significant predictor of survival, even in univariate analysis.

Principal cause of death from death certificates is shown in Table 4. Among patients dying within 7 days of stroke, more than two-thirds of those with sinus rhythm or atrial fibrillation died from stroke, and roughly 80% died of either stroke or pneumonia. Among patients dying 8–30 days after stroke, death from stroke was more common in the group with atrial fibrillation (Table 4). Such deaths almost always stemmed from the index stroke event rather than from a new event. Among those patients dying more than 30 days after stroke, the principal causes of death were similar in both groups; stroke was not a more common cause of death among patients with atrial fibrillation who died (Table 4). Among those who survived more than 30 days, there was no significant difference in deaths due principally to stroke. Death certificates did not distinguish cardioembolic stroke from other forms of stroke. Only one patient (who had atrial fibrillation) died of cardiac embolism to organs other than brain.

Maximal Barthel score after stroke was significantly lower in the group with atrial fibrillation as compared to those with sinus rhythm and had a higher incidence of congestive heart failure.

Although previous studies have documented the increased hospital mortality in stroke patients with atrial fibrillation,1-2 a few studies have reported survival follow-up beyond hospital discharge for as long as this report (mean, 18 months).7-9 The only such study to use proportional hazards modeling found that although atrial fibrillation was associated with increased mortality, in multivariate models it was not a predictor of mortality.7 Our results with respect to atrial fibrillation were virtually the same as those in the Swedish study. Because 13% of patients in that study had transient ischemic attack rather than stroke, results may not generalize to a population of acute stroke patients. A study of 1,484 stroke patients in Manitoba found atrial fibrillation to be associated with a slight but insignificant increase in age-adjusted mortality.9 However, proportional hazards modeling was not used to adjust for other factors influencing mortality. Solzi et al9 reported that among 1,369 patients with thrombotic stroke, admitted to a rehabilitation hospital in Israel, atrial fibrillation was a significant univariate predictor of mortality. Their study patients, however, were highly selected; those dying soon after stroke or not admitted for rehabilitation were excluded. Overall survival of their patients was much better than those in the current study. Bearing this in mind, their graph comparing survival in the groups with sinus rhythm and atrial
Atrial fibrillation showed the same continued divergence over the first 18 months poststroke as ours. Among 283 stroke patients from another Swedish study who were followed a mean of 20 months, atrial fibrillation was not a significant predictor of mortality even in univariate analysis.10

Our patients with atrial fibrillation had more severe current stroke deficit than those in sinus rhythm. In particular, they had a lower incidence of lacunar syndrome stroke, lower limb power, and Mini-Mental State Score, and a higher incidence of homonymous hemianopia. Overall, this suggests a larger volume of brain involved by the current stroke. The Stroke Data Bank reported a similar finding:15 patients with lacunar infarction had a lower incidence of atrial fibrillation than those with nonlacunar infarction (3% versus 12%). Atrial fibrillation did not influence functional recovery from stroke, as evidenced by maximal Barthel ADL score during the first 6 months after stroke.

In univariate analysis using the proportional hazards model, atrial fibrillation was one of 12 significant predictors of mortality. However, in multivariate proportional hazards analysis, atrial fibrillation dropped out of the model. The best predictors of survival were Mini-Mental State Score, level of consciousness, age, and interstitial edema. Thus, the apparent increase in mortality among patients with atrial fibrillation can be explained by other differences between that group and those in sinus rhythm. Similar results occurred when analysis was confined to patients with first-ever stroke.

Other reports have confirmed age7,9,16–18 and impaired level of consciousness7,8,10,17,18 as important predictors of mortality after stroke. A study of atrial fibrillation poststroke in Glasgow found an increased mortality compared to sinus rhythm in patients aged 60–79, but not in those aged 80 or older.1 According-ly, we reanalyzed our data using these age brackets. The hospital mortality ratio (atrial fibrillation mortality/sinus rhythm mortality) was 1.64 for age 60–79 and 1.39 for age 80 or older. Thus, our results in part support the findings from Glasgow.

Our study has two major limitations. First, and most importantly, only 30% of the study patients had CT scans. To further compound this problem, CT scanning was performed significantly more often in those patients with sinus rhythm than in those with atrial fibrillation and, when performed, showed a higher incidence of intracerebral hematoma in those with sinus rhythm (20% versus 7%, p=NS). Patients with intracerebral hematoma have a higher 30-day mortality than those with cerebral infarction.15 The proportional hazards survival model we used did not include disease (infarction versus hematoma) as an independent variable because of the low frequency of CT scanning. Had we performed CT scans on all patients, we could have either excluded those with hematoma or used disease (infarct versus hematoma) as an independent variable in survival modeling. Such analyses would have more accurately assessed the effects of cardiac rhythm on survival after stroke.

Had we excluded patients with intracerebral hematoma, the mortality difference between those in sinus rhythm and those in atrial fibrillation probably would have been greater than we observed in our patients with either cerebral infarction or intracerebral hematoma.

The second major limitation of this study was the low autopsy rate and frequent lack of documentation as to whether disease or death during follow-up was related to cardioembolic events. We had to rely on death certificates, which are frequently inaccurate, as a uniform measure to assess cause of death. Death certificates rarely distinguished cardioembolic stroke from other forms of stroke.

Results from this study can be generalized to other populations of elderly patients admitted to hospital after stroke as defined by World Health Organization criteria (excluding subarachnoid hemorrhage). Only 6% of our patients with atrial fibrillation received long-term anticoagulation poststroke. Hence, findings from this report cannot be generalized to anti-coagulated patients or to patients not admitted to hospital after stroke. Study results need to be confirmed in a patient sample undergoing universal early CT scanning to detect intracerebral hematoma.

In conclusion, atrial fibrillation poststroke occurred in one-quarter of elderly stroke registry patients. Atrial fibrillation was associated with significantly worse survival than sinus rhythm, but after adjusting for the greater age, more severe stroke deficit, and higher incidence of heart failure among patients with atrial fibrillation, we found that cardiac rhythm was no longer a significant predictor of survival. This is consistent with results from two randomized trials which found that warfarin reduced the subsequent rate of systemic emboli without altering mortality in atrial fibrillation.19,20

Acknowledgment

The author wishes to thank Dr. Harold Henderson from the Waikato Centre for Applied Statistics for his statistical advise.

References


KEY WORDS • atrial fibrillation • cerebrovascular disorders
Atrial fibrillation after stroke in the elderly.

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doi: 10.1161/01.STR.22.2.209

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/22/2/209

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