

Stroke

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Heart Association



JOURNAL OF THE AMERICAN HEART ASSOCIATION

Stroke and atrial fibrillation

TO Cheng

Stroke 1991;22;1086

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214
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1524-4628

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Stroke and Atrial Fibrillation*To the Editor:*

It is most interesting to note that two articles^{1,2} in the same issue of *Stroke* on atrial fibrillation and stroke reported opposite results. Candelise et al¹ found that atrial fibrillation is a negative prognostic factor, independent of age. On the other hand, Friedman² found that the apparently poorer survival in those patients with atrial fibrillation could be explained by factors other than cardiac arrhythmia, and that atrial fibrillation was not an independent predictor of survival after stroke. Both articles dealt with elderly subjects, but their ages were comparable (73.6±9.5¹ vs. 75.2±7.5² years). It seems obvious that the issue of mortality in stroke with atrial fibrillation is far from being settled and further study is needed.

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References

1. Candelise L, Pinardi G, Morabito A, and the Italian Acute Stroke Study Group: Mortality in acute stroke with atrial fibrillation. *Stroke* 1991;22:169-174
2. Friedman PJ: Atrial fibrillation after stroke in the elderly. *Stroke* 1991;22:209-214

*The following is in response:**To the Editor:*

Professor Cheng has raised an interesting question when he asks why the study by Candelise and colleagues¹ reached different conclusions from the study I reported.² I will try to shed some light on this matter.

Candelise's subjects were much younger than mine: the differences in mean age were 3.8 years for those in atrial fibrillation and 8.0 years in the remaining subjects. Candelise excluded subjects with intracerebral hematoma as well as subjects in deep coma, whereas I did not. Probably the most important difference between the two studies was in statistical methods. Candelise used logistic regression to analyze 1- and 6-month survival. In contrast, I used proportional hazards, which analyzes all survival data as opposed to data at one or two arbitrary points in time. My subjects were followed for a mean of 18 months after stroke.

Another important difference between the two studies was the choice of possible predictor variables used in statistical analysis. Candelise used five possible predictor variables: gender (male/female), age (>75 versus ≤75), neurological score (≤3 versus >3), computed tomographic scan (infarct versus no infarct), and cardiac rhythm (atrial fibrillation versus other rhythm). I used two of the same predictors (gender and cardiac rhythm) as well as two other predictors in a different form. I analyzed age as a continuous rather than a categorical variable and used level of consciousness and limb power scores as separate variables. More importantly, I added a host of other variables not examined by Candelise.

In an attempt to reconcile the difference between the two studies, I applied the same statistical method as Candelise: logistic regression for 1- and 6-month survival. Cardiac rhythm was a significant univariate predictor of 6- but not 1-month survival. In multiple logistic regression, however, cardiac rhythm was not a significant predictor of survival.

Perhaps Candelise and colleagues could reanalyze their survival data using a proportional hazards model with the predictor variables I found to be most strongly related to survival: Mini-Mental State Examination score, level of consciousness on admission, age, and interstitial edema on admission chest radiograph.

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1. Candelise L, Pinardi G, Morabito A, and the Italian Acute Stroke Study Group: Mortality in acute stroke with atrial fibrillation. *Stroke* 1991;22:169-174
2. Friedman PJ: Atrial fibrillation after stroke in the elderly. *Stroke* 1991;22:209-214

*The following is in response:**To the Editor:*

We appreciate Dr. Cheng's interest and comments on two papers recently published in the same issue of *Stroke*.^{1,2} In our study,¹ a series of 1,048 patients with acute cerebral infarction, including 211 (20%) with atrial fibrillation, were followed up for 6 months. The 30-day and the 6-month case fatality rates were significantly higher in atrial fibrillation cases compared to those with sinus rhythm. Atrial fibrillation, together with age, neurological severity, and computed tomographic scan were independent significant predictors of mortality on multifactorial linear regression analysis.

Dr. Friedman² studied 354 stroke patients, including 82 (23%) with atrial fibrillation, and followed them for a mean of 18 months. He used a multivariate proportional survival method in which only Mini-Mental State Examination score, level of consciousness, age, and pulmonary interstitial edema contribute to explain mortality and to which cardiac rhythm does not contribute significantly. In our series, we considered only patients with very recent first hemispheric stroke, so that clinical, electrocardiographic, and CT scan evaluations could be performed at the same early point in the natural history of the disease.

The outcome was very different from the Friedman series of stroke cases evaluated within 1-3 days after onset of symptoms, in which CT scan confirmation of diagnosis was obtained in only 30% of cases. The clinical differences among the patients evaluated could explain the contrasting results between the two studies. In fact, it is always difficult to draw generalizable conclusions when a hospital-based rather than population-based series is analyzed. Otherwise, since ours was a multicenter series, the sample is large enough and quite representative of hospitalized stroke patients, at least in Italy.

A second major difference between the two studies is due to the length of follow-up. The Italian study concentrated mostly on short-term and the New Zealand study on long-term follow-up evaluation. It may be that atrial fibrillation could influence the outcome more in the acute phase of the disease, when the most important cause of death is cerebral, than in the chronic phase, when other causes are more frequent.

In conclusion, there is quite good evidence from ours and other studies that atrial fibrillation is associated with an increase in short-term mortality rate. Moreover, we agree with Dr. Cheng that the independent long-term predictive value of atrial fibrillation must still be confirmed.

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1. Candelise L, Pinardi G, Morabito A, and the Italian Acute Stroke Study Group: Mortality in acute stroke with atrial fibrillation. *Stroke* 1991;22:169-174
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Procoagulant States and Stroke*To the Editor:*

Attention has recently been given to the relationship between procoagulant states and stroke, with Coull and Goodnight¹ pro-