Silent Cerebral Infarction in Chronic Atrial Fibrillation

Palle Petersen, MD, Erling Birk Madsen, MD, PhD, Birgitte Brun, MD, Flemming Pedersen, MD, Carsten Gyldensted, MD, PhD, and Gudrun Boysen, MD, PhD

Atrial fibrillation (AF) is associated with an increased risk of stroke. In AF patients with acute stroke, cerebral computed tomography (CT) often reveals old asymptomatic infarcts. To investigate the frequency of such lesions, 29 AF patients and 29 controls in sinus rhythm without history of cerebrovascular disease were CT scanned. Fourteen patients with AF (48%) had abnormal CT scans with areas of low density with sharp demarcation from surrounding tissue compared with 8 patients in sinus rhythm (28%) (p > 0.10). However, the number of abnormal areas with apparent tissue loss was significantly higher in the AF group (39 lesions) compared with the control group (16 lesions) (p = 0.033). The lesions were mainly located in the cortex with no significant difference in lesion size between AF patients and controls. The abnormal areas probably reflected small, clinically silent infarcts. We conclude that these lesions are present in AF patients without history of cerebrovascular events and occur more frequently than in controls without atrial fibrillation. (Stroke 1987;18:1098-1100)

Subjects and Methods

The study included 30 consecutive patients (17 women and 13 men, median age 73, range 57–87 years) with electrocardiographic (ECG)-confirmed AF of >1 year’s duration. The patients were prospectively and consecutively selected from patients referred to the outpatient clinic by their general practitioner for routine ECG.

Only patients without history of cerebrovascular disease with normal neurologic examination performed by one of the authors were included. None were treated with anticoagulants or aspirin or had history of alcohol abuse. Cardiac history with respect to chest pain, hypertension, and heart failure graded by New York Heart Association (NYHA) criteria was obtained. Diagnostic criteria concerning etiologies in the AF patients have been described elsewhere. The studies comprised laboratory tests for thyrotoxicosis, chest x-ray, echocardiography for detecting left atrial thrombosis, and CT scan of the brain (using an EMI model 1010, Medical Hounslow, United Kingdom) without contrast injection.

The control group consisted of 30 healthy individuals who had previously participated in the Copenhagen City Heart Study, a population study in which nearly 20,000 persons were invited to have a cardiovascular examination during the years 1976–78 and 1981–83. Each control was selected to match a patient by age and sex and had normal sinus rhythm. None of the controls had history of cerebrovascular events or cardiovascular or endocrinologic disease, and all controls had normal physical and neurologic examinations before entering the study. The same studies were performed as in patients with AF. The study protocol was approved by the local ethical committee, and all participants gave informed consent.

All CT scans were evaluated blindly by 2 consultant neuroradiologists with special attention to the number and size of low-density areas. Lesion size was measured by ruler to the nearest half-millimeter in 2 dimensions and multiplied by the thickness of the slice (10 mm). The echocardiograms were studied by 2 cardiologists without knowledge of the CT results.

Statistical analyses were performed using the χ² test and the Mann-Whitney rank sum test for unpaired data with correction for ties. Only p values <0.05 were considered significant.
Results

Among the 30 patients with AF, 22 had atherosclerotic and/or hypertensive heart disease (73%), 5 AF alone (17%), 2 thyrotoxicosis (7%), and 1 rheumatic heart disease (3%). Four patients had experienced myocardial infarction previously, and 4 had exercise-induced angina. Seventeen patients (57%) had slight heart failure (NYHA Class I), 4 (13%) moderate heart failure (NYHA Class II), and the rest (30%) no heart failure. No patients had left atrial thromboses by echocardiography.

One CT scan each in the AF and sinus rhythm groups were excluded from analysis for technical reasons. Among 29 patients with AF, 14 (48%) had 1 or more low-density areas on CT scan compared with 8 of the 29 controls in sinus rhythm (28%) (Figures 1 and 2); this difference was not significant (p > 0.10) (Table 1). The total number of low-density areas was significantly greater in the AF group (39) compared with controls in sinus rhythm (16) (p = 0.033) (Table 1). Further CT analysis showed no difference in the size of low-density areas between AF patients and controls. The median volume of the areas was 944 mm$^3$ in both groups with a range of 148–4,486 mm$^3$ in AF patients and 370–2,544 mm$^3$ in controls. There was no correlation of the low-density lesions with age independent of rhythm disturbance.
due to the increasing elderly population and the fre-
tions. It is important to identify possible subgroups
among AF patients with particularly high risk of
stroke. In such subgroups, treatment with coumarin
drugs or aspirin could be suggested.

It is unknown whether patients with AF and silent
cerebral infarction are more prone to develop stroke
and whether AF is associated with higher frequency
of silent cerebral infarction compared with sinus rhythm.
In an uncontrolled study of 85 patients with embolic
stroke, 15 patients (18%) had experienced clinically
silent cerebral infarction. Our finding of a high inci-
dence of low-density areas in patients with AF is in
accordance with that study.

The CT scans were evaluated blindly by 2 neurora-
diologists with no bias regarding AF or sinus rhythm.
Whether the low-density areas identified in the present
study represented localized atrophy. However, we found
more low-density areas in AF patients compared with con-
trols, suggesting that AF in some patients leads to
localized tissue loss. This finding stresses the need for
randomized controlled studies of prophylaxis against
thromboembolism in AF patients.

Discussion

AF is of considerable interest in stroke prophylaxis
due to the increasing elderly population and the fre-
quent and often serious cerebral embolic complica-
tions. It is important to identify possible subgroups
among AF patients with particularly high risk of
stroke. In such subgroups, treatment with coumarin
drugs or aspirin could be suggested.

It is unknown whether patients with AF and silent
cerebral infarction are more prone to develop stroke
and whether AF is associated with higher frequency
of silent cerebral infarction compared with sinus rhythm.
In an uncontrolled study of 85 patients with embolic
stroke, 15 patients (18%) had experienced clinically
silent cerebral infarction. Our finding of a high inci-
dence of low-density areas in patients with AF is in
accordance with that study.

The CT scans were evaluated blindly by 2 neurora-
diologists with no bias regarding AF or sinus rhythm.
Whether the low-density areas identified in the present
study represented cerebral infarction or localized atro-
phy is an open question. Some cerebrovascular events
in patients with AF are caused by thrombosis rather
than embolism, and although our controls were
healthy, the low-density areas demonstrated by CT
scan may reflect thrombotic events caused by athero-
sclerosis in elderly persons. The higher frequency of
lesions in AF could be explained by cardiac emboliza-
tion although echocardiography detected no left atrial
thromboses in either group.

The study was designed to include 30 patients in
each group, one group with AF and one group in sinus
rhythm. The limited number of subjects may explain
why the difference in number of subjects with abnor-
mal CT scans among patients with AF (48%) com-
pared with controls (28%) was not significant. How-
ever, the difference in number and distribution of
low-density areas was significant, 39 in AF patients
and only 16 in controls (Table 1). The increased risk of
such lesions with AF was expected, but the relatively
high frequency among healthy individuals in sinus
rhythm was not.

CT findings in elderly individuals are only sparsely
studied and have mostly correlated degree of atrophy
and psychological impairment without description of
structural lesions. Other studies of normal elderly
people have also focused on the degree of cerebral
atrophy without further characterization of focal le-
isons. It is possible that no focal lesions were iden-
tified or that they were classified as localized atrophy.

In the present study some low-density areas could
represent localized atrophy. However, we found more
low-density areas in AF patients compared with con-
trols, suggesting that AF in some patients leads to
localized tissue loss. This finding stresses the need for
randomized controlled studies of prophylaxis against
thromboembolism in AF patients.

Acknowledgments

We are thankful to statistician Jørgen Nyboe for
performing the statistical analyses, to secretary Pia
Poulsen for typing the manuscript, and to laboratory
assistant Annette Gerlach for performing the labora-
tory analyses.

References

1. Wolf PA, Dawber TR, Thomas HE Jr, Kannel WB: Epidemi-
ologic assessment of chronic atrial fibrillation and risk of
2. Petersen P, Godtfredsen J: Embolic complications in paroxys-
mal atrial fibrillation. Stroke 1986;17:622–626
3. Norrving B, Nilsson B: Cerebral embolism of cardiac origin;
the limited possibilities of secondary prevention (abstract).
Third Scandinavian Meeting on Cerebrovascular Disease, Hel-
1986;73:520
Arch Neurol 1984;41:707
5. The Criteria Committee of the New York Heart Association:
Nomenclature and Criteria for Diagnosis of Diseases of the
Heart and Great Vessels, ed 8. New York, New York Heart
Association, Inc, 1979
6. Godtfredsen J: Atrial Fibrillation. Etiology, Course and Prog-
nosis. A Follow-up Study of 1,212 Cases. Copenhagen,
Munksgaard, 1975
7. Sørensen PS, Bojesen G, Jensen G, Schnohr P: Prevalence of
stroke in a district of Copenhagen. Acta Neuro Scand 1982;66:
68–81
1979;34:59–66
9. Fox JH, Topel JL, Huchman MS: Use of computerized tomog-
raphy in senile dementia. J Neurol Neurosurg Psychiatry
1975;38:948–953
10. Huchman MS, Fox J, Topel JL: The validity of criteria for the
evaluation of cerebral atrophy by computerized tomography.
Neuroradiology 1975;16:85–92
11. Gonzalez CF, Lantieri RL, Nathan RJ: The CT scan appear-
ce of the brain in the normal elderly population: A corre-
the elderly: The normal population. Br J Psychiatry 1980;136:
249–255

Table 1. Distribution of Number of Cerebral Low-Density
Areas in Subjects With Atrial Fibrillation and Sinus Rhythm

<table>
<thead>
<tr>
<th>No. of low-density areas</th>
<th>No. of subjects</th>
<th>Total low-density areas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AF</td>
<td>SR</td>
</tr>
<tr>
<td>0</td>
<td>15</td>
<td>21</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>

AF, atrial fibrillation; SR, sinus rhythm. Significant difference between total low-density areas in subjects with AF and SR, p = 0.033.

KEY WORDS • atrial fibrillation • stroke
Silent cerebral infarction in chronic atrial fibrillation.
P Petersen, E B Madsen, B Brun, F Pedersen, C Gyldensted and G Boysen

Stroke. 1987;18:1098-1100
doi: 10.1161/01.STR.18.6.1098

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1987 American Heart Association, Inc. All rights reserved.
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/18/6/1098

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke 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 Stroke is online at:
http://stroke.ahajournals.org/subscriptions/