Atrial fibrillation (AF) is associated with an increased risk of stroke. The Framingham study\(^1\) found a fivefold increased risk of stroke in nonrheumatic chronic AF and a 17-fold increased risk in rheumatic AF compared with controls without AF. A recent study showed a 2% yearly incidence of stroke in paroxysmal AF and a 5% yearly incidence in patients with chronic AF.\(^2\)

Recently, an uncontrolled study detected a high frequency of silent cerebral infarction in AF patients with cerebral embolism.\(^3\) Computed tomography (CT) has been recommended in patients with AF for identifying low-density areas of previous cerebral infarction. Patients with such areas probably are at increased risk of subsequent cerebral embolization.\(^4\)

The aim of the present study was to evaluate whether silent cerebral infarction occurs more frequently in persons with chronic AF compared with a control group in sinus rhythm.

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 out-patient 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\(^5\) was obtained. Diagnostic criteria concerning etiologies in the AF patients have been described elsewhere.\(^6\) 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,\(^7\) 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 \(\chi^2\) 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.
Discussion

AF is of considerable interest in stroke prophyaxis due to the increasing elderly population and the frequent and often serious cerebral embolic complications. 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 incidence of low-density areas in patients with AF is in accordance with that study. The CT scans were evaluated blindly by 2 neuroradiologists with no bias regarding AF or sinus rhythm. Whether the low-density areas identified in the present study represented cerebral infarction or localized atrophy 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 atherosclerosis in elderly persons. The higher frequency of lesions in AF could be explained by cardiac embolization 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 abnormal CT scans among patients with AF (48%) compared with controls (28%) was not significant. However, 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 lesions. It is possible that no focal lesions were identified 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 controls, 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

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References


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>
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<tbody>
<tr>
<td></td>
<td>AF</td>
<td>SR</td>
</tr>
<tr>
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<td>21</td>
</tr>
<tr>
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</tr>
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<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.
Silent cerebral infarction in chronic atrial fibrillation.
P Petersen, E B Madsen, B Brun, F Pedersen, C Gyldensted and G Boysen

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