Stroke in Thyrotoxicosis With Atrial Fibrillation

Palle Petersen, MD, and Jens Mølholm Hansen, MD

Chronic atrial fibrillation is associated with an increased risk of stroke. In elderly patients with thyrotoxicosis, atrial fibrillation is frequently encountered, and the true risk of cerebrovascular events in these patients is controversial. We retrospectively studied 610 patients with initially untreated thyrotoxicosis, 91 (14.9%) of whom had atrial fibrillation, with the highest frequency in the elderly patients. The risk of cerebrovascular events, with special attention to the first year after the diagnosis of thyrotoxicosis, was calculated using logistic regression methods with age, sex, and atrial fibrillation as independent variables. Only age was an important risk factor (p<0.005), whereas sex and atrial fibrillation were not significant (p = 0.09 and p = 0.17, respectively) as independent risk factors. This is contrary to other studies of patients with thyrotoxic atrial fibrillation, and the need for further clarification of this issue is clear. From our study the indication for prophylactic treatment with anticoagulants for prevention of stroke in thyrotoxic atrial fibrillation seems doubtful, especially as no controlled studies of such treatment in patients with atrial fibrillation are currently available. (Stroke 1988;19:15-18)

Subjects and Methods

Our study was retrospective and included a total of 610 consecutive patients with thyrotoxicosis admitted from 1976 to 1985 to a department of internal medicine and endocrinology in a hospital in Copenhagen. All patients had the diagnosis of thyrotoxicosis made according to established criteria. All except one patient had the type of goiter confirmed by thyroid scintigraphy, and all patients had an electrocardiogram (ECG) on admission. The patients were followed in the out-patient clinic at scheduled intervals, and they were examined by the same consultant physician. Patients followed for <1 year (n = 57) were excluded from the statistical analysis of cerebrovascular events, as were patients receiving anticoagulant treatment (n = 2). None of these excluded patients had cerebrovascular events during follow-up.

The criteria for cerebrovascular events were clinical signs or a medically confirmed history of the acute onset of a neurologic deficit of presumed vascular origin. The patients were grouped as having had a transient ischemic attack (TIA) if an episode of focal ischemia had clinically resolved within 24 hours and as having had a stroke if the neurologic deficit exceeded 24 hours.

According to ECG, the patients were also classified as having sinus rhythm, paroxysmal atrial fibrillation (PAF), or chronic atrial fibrillation (CAF). As the study was retrospective and based on out-patients, a further detailed analysis of the number of PAF episodes and the duration of PAF was impossible to calculate. Accordingly, the diagnosis of CAF was made when no episode of sinus rhythm was registered at any time on ECG during follow-up. If no episode of AF was noticed on admission or during follow-up, the patient was classified as having sinus rhythm.

There were 527 women (86.4%) and 83 men (13.6%). The mean age was 54 (range 13–93) years. The mean follow-up was 39 (range 0–108) months. On admission, 91 of the 610 patients (14.9%) had AF (75 women [82.4%], 16 men [17.6%]). The mean duration before the patients became euthyroid was 10 weeks.

The statistical analysis of cerebrovascular events within the first year after admission was based on logistic regression methods with age, sex, and AF as independent variables. The Goodman-Kruskal y test was used for the analysis of stroke versus TIA in the two groups of patients.

Results

Of the 610 patients, 91 (14.9%) had AF. The frequency of AF rose with increasing age, being higher after 60 years of age, when >25% of the patients had...
Table 1. Atrial Fibrillation in 610 Patients With Thyrotoxicosis and Reversion to Sinus Rhythm During Antithyroid Treatment

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Total patients</th>
<th>With atrial fibrillation</th>
<th>Without reversion</th>
<th>With reversion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No. %</td>
<td>No. %</td>
</tr>
<tr>
<td>0-50</td>
<td>235</td>
<td>2</td>
<td>0.9</td>
<td>0</td>
</tr>
<tr>
<td>51-60</td>
<td>138</td>
<td>18</td>
<td>13.0</td>
<td>4</td>
</tr>
<tr>
<td>61-70</td>
<td>132</td>
<td>34</td>
<td>25.8</td>
<td>16</td>
</tr>
<tr>
<td>71-80</td>
<td>88</td>
<td>32</td>
<td>36.4</td>
<td>19</td>
</tr>
<tr>
<td>&gt;80</td>
<td>17</td>
<td>5</td>
<td>29.4</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>610</td>
<td>91</td>
<td>14.9</td>
<td>42</td>
</tr>
</tbody>
</table>

AF. In patients <50 years of age, AF was found infrequently; i.e., only 0.9% had AF (Table 1). (Table 2 shows the ECG diagnoses in the patients excluded from the statistical analysis of cerebrovascular events.) In 46% of the AF patients sinus rhythm developed after treatment of thyrotoxicosis (Table 1), but the frequency of reversion to sinus rhythm varied from 100% in the youngest patients to 25% in the elderly patients. No patient was electrically converted to sinus rhythm.

A total of 27 cerebrovascular events occurred in the 610 patients, 12 in those having AF and 15 in patients in sinus rhythm (Table 3). Thirteen events occurred during the first year, 5 in the AF and 8 in the sinus rhythm class (Table 4). All these 13 events occurred before the patients became euthyroid. As the majority of the 610 patients were in sinus rhythm, the results in Table 3 may give the impression that AF carried a higher risk of cerebrovascular events. However, that study included no control group. Twenty-one patients had AF, and 5 of these had systemic emboli. Hurley et al13 found 8 arterial embolic episodes (6 cerebral) in 68 patients with thyrotoxic AF. Seventeen embolic events were cerebral, underscoring the serious character of the events. However, that study included no control group. The study of Yuen et al12 included 210 patients with thyrotoxicosis, but no comparisons were made with a control group. Twenty-one patients had AF, and 5 of these had systemic emboli.

Table 2. Patients Excluded From the Study

<table>
<thead>
<tr>
<th>Classification</th>
<th>Patients followed &lt;1 year</th>
<th>Patients on anticoagulation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>11</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>46</td>
<td>0</td>
<td>46</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>2</td>
<td>59</td>
</tr>
</tbody>
</table>

Two patients in sinus rhythm died subsequent to the cerebrovascular event.

Table 3. Cerebrovascular Events in 610 Patients With Thyrotoxicosis

<table>
<thead>
<tr>
<th></th>
<th>Within first year</th>
<th>After first year</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>5</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>8</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>14</td>
<td>27</td>
</tr>
</tbody>
</table>

Discussion

It is well established that AF carries an increased risk of stroke. In the Framingham study,12 CAF was associated with an increased risk of stroke. AF in the absence of rheumatic heart disease (RHD) was associated with a more than fivefold increase in stroke incidence, whereas AF with RHD had a 17-fold increase compared with controls without AF. In that study the frequency of thyrotoxicosis was not calculated, but there was a high frequency of strokes in so-called lone AF, which may have included some patients with thyrotoxicosis. During the last decade several studies11-14 have found an increased stroke risk in thyrotoxicosis with AF, contrary to older studies18,19 in which the rarity of embolism in thyrotoxic AF was commented upon.

In our study we found a tendency toward more cerebrovascular events in AF but without statistical evidence of AF being an independent risk factor during the first year after the diagnosis of thyrotoxicosis; age was the only significant risk factor. This is in contrast with the study of Staffurth et al,13 in which 26 episodes of arterial embolism were found in 262 patients with thyrotoxic AF. Seventeen embolic events were cerebral, underscoring the serious character of the events. However, that study included no control group. The study of Yuen et al12 included 210 patients with thyrotoxicosis, but no comparisons were made with a control group. Twenty-one patients had AF, and 5 of these had systemic emboli. Hurley et al13 found 8 arterial embolic episodes (6 cerebral) in 68 patients with AF and thyrotoxicosis, but insufficient data were provided on the 311 patients with thyrotoxicosis and in sinus rhythm. Recently Bar-Sela et al14 found 12 embolic complications in 30 patients with thyrotoxic AF and no episodes in 112 patients in sinus rhythm. However, this might be explained by the fact that the mean ages in the AF and sinus rhythm classes were markedly
increased compared with age-matched controls with thyrotoxicosis and in sinus rhythm, and since the cost/
benefit ratio of anticoagulation in AF with or without thyrotoxicosis has not been established, we suggest
that recommendation of such treatment should await further studies of stroke occurrence in thyrotoxic AF
and the results of controlled studies of anticoagulants for prevention of stroke in patients with AF.

Acknowledgments

The authors wish to thank the statistician Svend Kreiner, MSc, for performing the statistical analyses
and Pia Poulsen for typing the manuscript.

References

1. Ostrander LD Jr, Brandt RL, Kjelsberg MO, Epstein FH: Electrocardiographic findings among the adult population of a total
natural community, Tecumseh, Michigan. Circulation 1965; 31:888-898
2. Kulbertus HE, Leval-Ruten FD, Bartsch P, Petit J: Atrial fibrillation in elderly, ambulatory patients, in Kulbertus HE,
Molndal, Sweden, AB Hälse, 1982, pp 148-157
Am Heart J 1972;84:120-131
Munksgaard, 1976
5. Sawyer CG, Bolin LB, Stevens EL, Daniel LB, O'Neill ND, Hayes DM: Atrial fibrillation: its etiology, treatment and asso-
ciation with embolization. South Med J 1958;51:84-93
6. Åberg H: Atrial fibrillation. A review of 463 cases from Phila-
1968;184:425-431
7. Cramér G: Early and late results of conversion of atrial fibrilla-
tion with quinidine. A clinical and hemodynamic study. Acta
8. Wolf PA, Kannel WB, McGeel DL, Meeks SL, Bhanche NE,
McNamara PM: Duration of atrial fibrillation and imminence
9. Hart GR, Easton JD, Sherman DG: Duration of non-valvular
atrial fibrillation and stroke (letter). Stroke 1983;14:827
10. Symons C: Thyroid heart disease. Br Heart J 1979;41:257-262
11. Staffurth JS, Gibberd MC, Tang Fui SNG: Arterial embolism
690
12. Yuen RWM, Gutteridge DH, Thompson PL, Robinson JS:
Embolism in thyrotoxic atrial fibrillation. Med J Aust 1979;1:
630-631
13. Hurley DM, Hunter AN, Hewett MJ, Stockig JR: Atrial fibril-
lion and arterial embolism in hypothyroidism. Aust NZ J
Med 1981;11:391-393
in thyrotoxicosis with atrial fibrillation. Arch Intern Med
1981;141:1191-1192
therapy in atrial fibrillation. Chest 1986;89(suppl):68-81
Endocrinol 1983;19:603-607
17. Wolf PA, Dawber TR, Thomas HE, Kannel WB: Epidemi-
ologic assessment of chronic atrial fibrillation and risk of stroke:
Saunders, 1967, p 546
Livingstone, 1976
20. Stensgaard Hansen B, Marquardsen J: Incidence of stroke in
Frederiksborg, Denmark. Stroke 1977;8:663-665

Table 5. Significance of Risk Factors for Cerebrovascular
Events During First Year in 551 Patients With Thyrotoxicosis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Sex</td>
<td>0.09</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0.17</td>
</tr>
</tbody>
</table>

*Significance assessed using logistic regression methods.

different, 56 and 39 years, respectively. The results of these studies indicate that thyrotoxic AF is associated
with a high risk of embolism.

The results of our study seem to indicate that AF in
untreated thyrotoxicosis is not complicated by an ex-
cess of embolic events when compared with age-
matched controls with thyrotoxicosis and in sinus
rhythm. However, the frequency of events in the first
year in thyrotoxicosis and sinus rhythm was slightly
increased compared with epidemiologic studies with-
out thyrotoxicosis and AF. Since all cerebrovascu-
lar events when compared with age-
untreated thyrotoxicosis is not complicated by an ex-
crement of ECG results. It is known that some patients with
became euthyroid, we suggest that efforts should be
directed to treating thyrotoxicosis promptly, regardless
of ECG results. It is known that some patients with
thyrotoxicosis and AF develop sinus rhythm after ade-
quate treatment; i.e., they have PAF. The risk of
stroke in PAF has long been a matter of controversy,
but recently a study of 426 patients with initial PAF has
demonstrated a low frequency of stroke in PAF,
whereas the stroke rate increased significantly in pa-
patients who later developed CAF. In our study there
was no significant difference in the number of embolic
events in patients with CAF and PAF, indicating that
even CAF was associated with a low risk of cerebro-
vascular events. However, there was a tendency to-
ward more events in the AF class, although the differ-
ence was not significant. This could be explained by
the relatively small number of AF patients in our study
as the yearly frequency of events (Table 4) was close to
that found in studies of AF including different etiol-
o logies. Moreover, we found more strokes in patients
with AF was not significantly in-

Table 6. Type of Cerebrovascular Events in 610 Patients
With Thyrotoxicosis

<table>
<thead>
<tr>
<th>Stroke</th>
<th>Transient ischemic attack</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Chronic</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Paroxysmal</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sinus rhythm</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>14</td>
</tr>
</tbody>
</table>


**Key Words** • thyrotoxicosis • cerebrovascular disorders • atrial fibrillation
Stroke in thyrotoxicosis with atrial fibrillation.
P Petersen and J M Hansen

Stroke. 1988;19:15-18
doi: 10.1161/01.STR.19.1.15
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1988 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/19/1/15

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/