Atrial Tachycardia in Patients with Cryptogenic Stroke: Is there a Need For Anticoagulation?

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ABSTRACT:

Background: Brief episodes of atrial tachycardia are a common finding in the Holter monitor recordings of elderly patients. Episodes of atrial tachycardia may convert to atrial fibrillation. Current guidelines do not recommend anticoagulant therapy in patients with atrial tachycardia and risk factors for embolism.

Objectives: To assess the incidence of atrial tachycardia in a 24 hour Holter monitor recording of patients admitted to hospital with ischemic stroke.

Methods: The patient cohort included two groups: 134 patients admitted with a diagnosis of ischemic stroke (the study group), and 68 consecutive patients with a diagnosis of syncope (the control group). Both groups used a Holter monitor.

Results: There was no difference in the incidence of atrial tachycardia runs between the groups. Patients who suffered a stroke were more likely to be hypertensive (P < 0.05) and more likely to have a CHA²DS²-VASc score of ≥3 (P = 0.05).

Conclusions: Atrial tachycardia as recorded on a Holter monitor was not more prevalent in patients presenting with ischemic stroke. The occurrence of atrial tachycardia is not an indication for systemic anticoagulation.

KEY WORDS: cryptogenic stroke, atrial tachycardia, CHA²DS²-VASc score, syncope

Patients and Methods

We reviewed the medical records of the neurology service and the internal medicine wards at Assaf Harofeh Medical Center for the period January 2010 to July 2012. The patient cohort comprised two groups: 134 patients admitted with a diagnosis of ischemic stroke (study group), and 68 consecutive patients admitted with a diagnosis of syncope (control group). Both groups used a Holter monitor. For this study atrial tachycardia was defined as rapid arrhythmia, usually 110–200 per minute, of at least three consecutive beats, originating from an atrial focus or possibly from the pulmonary veins.

A cranial computed tomography (CT) scan was performed in all study group patients on admission to the hospital. The strokes were differentiated by CT scan according to the TOAST criteria [7,8]. All patients who were admitted to the hospital...
with an ischemic stroke or syncope had a Holter monitor. The Holter tracings were analyzed and all the arrhythmias were counted. The demographics of the patients in the two groups are detailed in Table 1. An echocardiogram was performed after admission to hospital in about 50% of those admitted with stroke, and in 97% of patients in the control group during their hospitalization [Table 2]. The CHA2DS2-VASc score was calculated from the patients’ data prior to the stroke and therefore the true score should be 2 points higher. Patients with the control group showed brief runs of AF without discernible P waves. Altogether, 387 patients were excluded from the study group because of a history of AF and another 5 patients were excluded because the Holter monitor showed brief runs of AF without discernible P waves. Seventy patients were excluded from the control group due to a history of AF, antiarrhythmic drug therapy, anticoagulant therapy, pulmonary fibrosis, meningioma, valvar heart disease (moderate to severe), pacemaker, hemocystinuria, left ventricular ejection fraction < 30%, thrombocytosis, cold agglutinins, carotid disease, polycythemia vera, macroglobulinemia, hypertrophic cardiomyopathy, hemodialysis, malignancy, thrombocytosis, patent foramen ovale, use of illicit drugs, endocarditis and pulmonary embolism. Also excluded from the study group were patients admitted with a clinical picture of stroke or transient ischemic attack who were not treated with thrombolytic therapy and who had two consecutive normal CT scans during their hospitalization. Patients admitted with syncope who had a history of stroke were excluded from the control group. The study was approved by the institutional review board of Assaf Harofeh Medical Center and the need for patients’ consent was waived.

### Table 1. Patient's characteristics

<table>
<thead>
<tr>
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<th>Study group N=134</th>
<th>Control group N=68</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>75.6 ± 6.9</td>
<td>75.1 ± 6.9</td>
<td>NS</td>
</tr>
<tr>
<td>Female (%)</td>
<td>48% (65)</td>
<td>43% (29)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>22% (22)</td>
<td>33% (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>86% (115)</td>
<td>72% (49)</td>
<td>0.018</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>34% (48)</td>
<td>28% (19)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>27% (36)</td>
<td>22% (15)</td>
<td>NS</td>
</tr>
<tr>
<td>CHA2DS2-VASc score &gt; 2 (%)</td>
<td>81% (109)</td>
<td>69% (47)</td>
<td>0.05</td>
</tr>
<tr>
<td>Creatinine (mean)</td>
<td>1.03 ± 0.66</td>
<td>0.97 ± 0.39</td>
<td>NS</td>
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</table>

### Table 2. Echocardiographic findings

<table>
<thead>
<tr>
<th></th>
<th>Study group N=68</th>
<th>Control group N=66</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA diameter (≥ 40 mm)</td>
<td>43%</td>
<td>36%</td>
<td>NS</td>
</tr>
<tr>
<td>IVS (≥ 10 mm)</td>
<td>88%</td>
<td>80%</td>
<td>NS</td>
</tr>
<tr>
<td>PW (≥ 10 mm)</td>
<td>53%</td>
<td>45%</td>
<td>NS</td>
</tr>
<tr>
<td>LVEDD (≥ 54 mm)</td>
<td>7%</td>
<td>3%</td>
<td>NS</td>
</tr>
<tr>
<td>LVESD (≥ 40 mm)</td>
<td>4%</td>
<td>3.0%</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF (mean ± SD)</td>
<td>56 ± 8</td>
<td>59 ± 5</td>
<td>0.033</td>
</tr>
<tr>
<td>Diastolic dysfunction (yes)</td>
<td>62%</td>
<td>64%</td>
<td>NS</td>
</tr>
<tr>
<td>MR (mild to mod, mod)</td>
<td>13%</td>
<td>6%</td>
<td>NS</td>
</tr>
<tr>
<td>TR (mild to mod, mod)</td>
<td>13%</td>
<td>17%</td>
<td>NS</td>
</tr>
<tr>
<td>AI (mild to mod, mod)</td>
<td>9%</td>
<td>12%</td>
<td>NS</td>
</tr>
<tr>
<td>AS (mild to mod, mod)</td>
<td>7%</td>
<td>2%</td>
<td>NS</td>
</tr>
<tr>
<td>SPAP (mean ± SD, mmHg)</td>
<td>34 ± 9</td>
<td>33 ± 8</td>
<td>NS</td>
</tr>
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LA = left atrial, IVS = interventricular septum, PW = posterior wall, LVEDD = left ventricular end-diastolic diameter, LVESD = LV end-systolic diameter, LVEF = LV ejection fraction, MR = mitral regurgitation, mod = moderate, TR = tricuspid regurgitation, AI = aortic insufficiency, AS = aortic stenosis, SPAP = systolic pulmonary arterial pressure

### Statistical Analysis

Statistical analysis was performed using SPSS version 20 software. Data are expressed as mean ± standard deviation. Differences between means were assessed by the t-test. Differences between proportions were assessed with the chi-square test. A two-tailed P value < 0.05 was considered statistically significant.

### Results

During the period January 2010 to July 2012, 644 patients were admitted to the hospital with an ischemic stroke; all had a Holter monitor and a CT scan as part of the clinical workup. Of these, 134 were found eligible for the study group. Screening for the control group yielded 181 patients of whom 68 patients were eligible. A total of 118 patients were excluded from the study group because of a history of AF and another 5 patients were excluded because the Holter monitor showed brief runs of AF without discernible P waves. Seventy patients were excluded from the control group due to various exclusion criteria as detailed in the Methods section. Forty patients were excluded from the control group because of a history of AF and an additional 3 patients were excluded because the Holter monitor showed brief runs of AF without discernible P waves. There was no statistically significant difference between patients who suffered a stroke and patients in the control group in terms of age, gender, smoking history, diabetes, coronary artery disease, and renal function. Patients who suffered a stroke were more likely to be hypertensive (P < 0.05) and were more likely to have a CHA2DS2-VASc score ≥ 3 (P = 0.05) [Table 1]. There was no significant difference in the echocardiographic parameters except for left ventricular ejection fraction, which was lower in the study group [Table 2]. There was no difference
in the occurrence of atrial tachycardia runs between the study group and the control group [Table 3]. There was no difference in the occurrence of atrial tachycardia in hypertensive and normotensive patients between the study group and the control group, or in the occurrence of atrial premature beats between the study group and the control group.

DISCUSSION

Ischemic stroke may be the first presentation in patients with undetected atrial fibrillation. Much effort has been invested in the search for screening techniques to identify patients at risk of ischemic stroke. Our study showed that atrial tachycardia as recorded on a 24 hour Holter monitor was not more prevalent in patients presenting with ischemic stroke.

According to the recently published Crystal AF and EMBRACE studies, a prolonged monitoring period is necessary for detecting episodes of AF [9,10]. Both studies showed that the detection rate of AF was about fourfold higher in the intervention compared to the study group.

In the ASSERT study, subclinical atrial tachyarrhythmias occurred frequently in patients with pacemakers and were associated with a significantly increased risk of ischemic stroke or systemic embolism [2]. The patients in the ASSERT study had various atrial arrhythmias which lasted at least 6 minutes. That patient population was different from ours: our study excluded patients who had AF on their Holter and included only patients with atrial tachycardia of 3 beats or longer. The minimum atrial rate and duration of an atrial tachyarrhythmia that are thrombogenic are not known. The ASSERT study did show that patients with a CHAD2 score > 2 and subclinical atrial arrhythmias had a higher risk of suffering a stroke. In our study, patients with a stroke were more likely to have a CHA2DS2-VASc score ≥ 4 regardless of the presence of atrial tachycardia or fibrillation.

The main limitation of our study is that it was based on a 24 hour Holter monitor. Continuous monitoring of patients who suffered a stroke could reveal a higher incidence of atrial arrhythmias. Another limitation is the etiology of stroke. It is possible that some of the strokes were not embolic and therefore were not related to an atrial arrhythmia. Additionally, before any firm conclusions can be reached, prospective studies to evaluate the risk associated with the occurrence of AT in a Holter monitor are warranted.

CONCLUSIONS

Atrial tachycardia as recorded on a Holter monitor was not more prevalent in patients presenting with ischemic stroke. The occurrence of atrial tachycardia is not an indication for systemic anticoagulation. Further research is needed to justify the initiation of antithrombotic therapy in patients with a CHA2DS2-VASc score ≥ 4 regardless of the presence of atrial tachycardia or fibrillation.
References
4. Diener HC. To monitor or to not monitor for paroxysmal atrial fibrillation after transient ischemic attack or stroke: this is the question. Stroke 2014; 45: 355-6.

Capsule
Anticoagulant “mors” into pneumonia therapy
Pneumonia can cause lung cell death, yet the mechanisms by which infection reduces cell viability are unclear. Zou et al. found that a poorly described protein, Morf411L, triggers cell death in mice with pneumonia. The half-life of Morf411L – normally a short-lived protein – was increased in the context of pneumonia. The anticoagulant drug Argatroban blocked half-life extension as well as the injurious actions of Morf411L, thus prolonging the survival of mice with experimental pneumonia. Sci Transl Med 2015; 7: 311ra171
Eitan Israeli

Capsule
A close-up view of retrovirus spreading
Viral infections typically begin with a small number of viral particles gaining access to the host at a specific tissue site. But how do viruses that cause systemic infections, such as HIV, spread more widely? Sewald et al. visualized how the retroviruses murine leukemia virus (MLV) and HIV spread within lymph nodes in mice. Specific macrophages that line the lymph-draining sinuses in lymph nodes first captured the virus using the carbohydrate-binding protein CD169. These macrophages subsequently transferred virus to the B1 subclass of B lymphocytes, which migrated further into the lymph node, disseminating the virus more widely. Science 2015; 350: 563
Eitan Israeli