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.

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

Atrial fibrillation (AF) is common in patients with ischemic stroke. Strokes caused by AF are associated with increased mortality as compared to strokes of other etiologies [1]. Paroxysmal AF (PAF) is self-terminating and can be missed when patients are not adequately monitored. Cryptogenic stroke is a stroke of unknown cause. Undetected AF is a possible cause of cryptogenic stroke. Two studies involving patients with implantable devices showed that subclinical atrial arrhythmias occurred frequently in patients with pacemakers and were associated with a significantly increased risk of ischemic stroke or systemic embolism [2,3]. A more recent study showed that AF in patients with ischemic stroke was better detected with an implantable cardiac monitor than standard monitoring [4]. According to the guidelines, patients with AF and a CHA2DS2-VASc score ≥ 2 should be on anticoagulant therapy [5]. Brief episodes of atrial tachycardia (with a discernible P wave) are a common finding in the Holter monitor recordings of elderly patients [Figure 1]. Episodes of atrial tachycardia may cause remodeling of the atria and may convert to AF [6]. The current guidelines do not recommend anticoagulant therapy in patients with atrial tachycardia and risk factors for embolism.

The aim of this study was to assess the incidence of atrial tachycardia during a 24 hour Holter monitor recording in patients admitted to the hospital with ischemic stroke. Another goal was to address the issue of initiating prophylactic anticoagulant therapy in patients with atrial tachycardia and a CHA2DS2-VASc score ≥ 2.

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

Figure 1. A run of atrial tachycardia of 7 beats in a patient who suffered a stroke

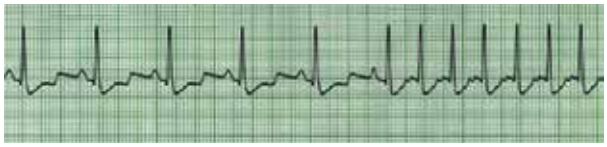

Table 1. Patient's characteristics

	Study group N=134	Control group N=68	*P* value
Age (mean ± SD)	75.6 ± 6.9	75.1 ± 6.9	NS
Female (N)	48% (65)	43% (29)	NS
Smoking (N)	22% (22)	33% (13)	NS
Hypertension (N)	86% (115)	72% (49)	0.018
Diabetes (N)	34% (46)	28% (19)	NS
Coronary artery disease (N)	27% (36)	22% (15)	NS
CHA2DS2-VASc score › 2 (N)	81% (109)	69% (47)	0.05
Creatinine (mean)	1.03 ± 0.66	0.97 ± 0.39	NS

Table 2. Echocardiographic findings

	Study group N=68	Control group N=66	*P* value
LA diameter (≥ 40 mm)	43%	36%	NS
IVS (› 10 mm)	88%	80%	NS
PW (› 10 mm)	53%	45%	NS
LVEDD (≥ 54 mm)	7%	3%	NS
LVESD (≥ 40 mm)	4%	3.0%	NS
LVEF (mean ± SD)	56 ± 8	59 ± 5	0.033
Diastolic dysfunction (yes)	62%	64%	NS
MR (mild to mod, mod)	13%	6%	NS
TR (mild to mod, mod)	13%	17%	NS
AI (mild to mod, mod)	9%	12%	NS
AS (mild to mod, mod)	7%	2%	NS
SPAP (mean ± SD, mmHg)	34 ± 9	33 ± 8	NS

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

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 syncope were selected for the control group because all had a Holter monitor placed for 24 hours during their hospitalization.

The inclusion criteria included age over 60 and admission to the hospital with a clinical picture of acute stroke. A head CT was performed in the study group patients on admission to hospital. Only patients with an abnormal CT scan were included in the study group. Also included were patients with a definite clinical presentation of stroke who received thrombolytic therapy. The exclusion criteria for both the study group and the control group were: history of AF, antiarrhythmic drug therapy, anticoagulant therapy, pulmonary fibrosis, meningioma, valvular 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.

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. Altogether, 387 patients were excluded from the study group because of a variety of 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. Seventy patients were excluded from the control group due to verious exclusion criteria as detailed in the Methods section. 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

Table 3. Holter findings

	Study group N=134	Control group N=68	*P* value
Minimum HR (mean ± SD)	56 ± 10	57 ± 11	NS
Maximum HR (mean ± SD)	90 ± 16	93 ± 16	NS
APC (≥ 500)	16%	22%	NS
AT runs-% (N)	32% (43)	23% (16)	NS
AT number of beats	6 ± 4	6 ± 4	NS
VPC (≥ 500)	15%	12%	NS
NSVT runs	7%	10%	NS

HR = heart rate, APC = atrial premature contraction, AT = atrial tachycardia, VPC = ventricular premature contraction, NSVT = non-sustained ventricular tachycardia

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 > 2 but did not have more episodes of atrial arrhythmias compared to the control group.

In the TRENDS study, 40 patients suffered a stroke, most of whom had no atrial tachycardia/atrial fibrillation burden within 30 days prior to the stroke [3]. In a TRENDS substudy, continuous monitoring detected new atrial tachycardia or fibrillation in 28% of 163 patients with previous thromboembolic events [11,12]. Similar findings were reported by other investigators [13-16]. In a recent meta-analysis, Kishore et al. [17] showed that the detection rate of AF after ischemic stroke was 11.5%. The study by Wallmann and co-authors [18] noted that atrial premature beats predicted AF in patients who suffered a stroke. We could not demonstrate such an association in our study. There are studies reporting a higher incidence of atrial arrhythmias after an ischemic stroke, especially in patients with anterior circulation infarction [19-21]. This could indicate a cerebrogenic source of cardiac arrhythmias [22]. Additionally, data from the SPAF studies show that about 30% of strokes in AF patients are not cardioembolic [23]. The association between the CHADS2 score and left atrial function in patients with coronary heart disease was also investigated. The CHADS2 score was associated with left atrial dysfunction even in patients without baseline atrial fibrillation [24]. Data from the Heart and Soul study showed that among patients with coronary artery disease, the CHADS2 score predicts ischemic stroke in the absence of atrial fibrillation [25]. The event rate in non-AF patients with a CHADS2 score of 5-6 was comparable to published rates in AF patients with moderate CHADS2 scores of 1-2. It is conceivable that atrial fibrillation is a marker for a systemic illness, which increases the risk for a thromboembolic event.

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.

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