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Holter Monitorisation Results in Early Period of Acute Ischemic Stroke

Akut İskemik İnmenin Erken Döneminde Holter Monitörizasyon Sonuçları

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ABSTRACT

Introduction: Paroxysmal atrial fibrillation (PAF) has a similar risk with persistent AF for ischemic stroke. Holter monitorization (HM) and other long-term monitorization methods increased the detection of PAF and short-lasting runs of tachyarrhythmias. Their classification as PAF and roles in the etiology of ischemic stroke is controversial. In this study, we aimed to investigate the frequency of any duration of PAF and clinical characteristics of the patients with acute ischemic stroke who have undergone 24-hrs HM.

Methods: Patients with acute ischemic stroke and transient ischemic attack (TIA) hospitalized in the Neurology ward and undergone 24-hrs of HM during their hospital stay were included in the study. HM reports, clinical, and laboratory characteristics were analyzed, retrospectively. Patients were grouped into three based on HM: 1st group, without PAF; 2nd group, PAF >30 seconds (s) and 3rd group, PAF<30s.

Results: PAF of any duration was detected in 18.8% (n=49) of 261 patients. The duration of PAF was <30s in 16.1% (n=42) and >30s in 2.7% (n=7) of the patients. The mean age, left atrium diameter and CHA2DS2-VASc scores of the second group were significantly higher than the first group (p<0.001, p<0.001 and p=0.007; respectively). The mean age, left atrium diameter, modified Rankin Scores (MRS), and CHA2DS2-VASc scores of the third group were significantly higher than the first group (p<0.001; for all). There was no difference between the second and the third groups in means of mean age, left atrial diameter, MRS, and CHA2DS2-VASc scores (p<0.017, for all).

Conclusion: In this study, 24-hrs HM in the early period of acute ischemic stroke results yielded a high frequency of PAF<30s and predictive features were in parallel with the literature.

Keywords: Holter monitorisation, atrial fibrillation, stroke, brain ischemia

ÖZ

Amaç: Paroxismal atrial fibrilasyon (PAF) inme etyolojisinde kalıcı AF ile benzer riski paylaşmaktadır. Holter Monitorizasyon (HM) ve diğer taşınabilir uzun süreli monitorizasyon yöntemleri ile PAF saptama imkanı artarken kısa süreli taşiaritmileri de görünür kılmıştır. Bu kısa süreli taşiaritmilerin PAF olarak kabul edilip edilemeyeceği veya inme etyolojisindeki yeri tartışmalıdır. Çalışmadaki amacımız 24 saat HM uygulanan akut iskemik inme hastalarında PAF görülme sıklığını ve klinik inme özelliklerini araştırmaktır.

Yöntem: Bu çalışmaya, akut iskemik inme ve geçici iskemik inme (GİA) tanılarıyla nöroloji kliniğinde yatırılarak izlenen ve yatış süreleri içerisinde 24 saatlik HM yapılan hastalar dahil edilmiştir. Hastaların HM sonuçları, klinik özellikleri ve laboratuvar sonuçları retrospektif olarak değerlendirilmiştir. HM sonuçlarına göre hastalar 1. "PAF saptanmayanlar", 2. "PAF süresi >30 sn olanlar" ve 3. "PAF süresi <30 sn olanlar" olarak üç gruba ayrılarak incelenmiştir.

Bulgular: Çalışmaya dahil edilen 261 hastanın %18,8'inde (n=49) PAF saptanmıştır. Olguların %16,1'inde (n=42) PAF süreleri < 30 sn, %2,7'sinde (n=7) ise >30 sn idi. İkinci grubun yaş ortalaması , sol atrium çap ortalaması ve CHA2DS2-VASc skoru ortalaması PAF olmayan gruba göre istatistiksel olarak anlamlı şekilde yüksek bulundu (sırasıyla; p<0,001, p<0,001 ve p=0,007). Üçüncü grubun yaş ortalaması, sol atrium çap ortalaması, modifiye rankin skoru (MRS) ve CHADS2-VASc skoru ortalaması PAF olmayan gruba göre istatistiksel olarak anlamlı şekilde yüksek bulundu (p<0,001). İkinci ve üçüncü gruplar arasında yaş, sol atrium çapı, MRS ve CHA2DS2-VASc skoru ortalamalarında birbirleriyle karşılaştırılmasında istatiksel farklılık saptanmadı (p<0,017)

Sonuç: Bizim çalışmamızda akut iskemik inme sonrası erken dönemde yapılan 24 saatlik HM ile < 30 sn PAF görülme oranı yüksek bulunmuştur ve prediktif bulguları literatürle uyumlu özellikler göstermektedir.

Anahtar kelimeler: Holter monitorizasyon, atrial fibrilasyon, inme, beyin iskemisi

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INTRODUCTION

Paroxysmal atrial fibrillation (PAF) is associated with a similar risk for ischemic stroke (1) as permanent or sustained atrial fibrillation (AF). It was reported that in some patients cryptogenic stroke has a cardioembolic etiology (2,3). In addition,stroke can have multiple etiologies and stroke of a non-embolic etiology might be due to an unknown cardioembolic etiology (4). Recent guidelines suggest anticoagulant treatment for secondary prophylaxis in stroke patients with AF (5). Anticoagulant treatment provides 40% more protection against stroke than anti-aggregant treatment; as such, the detection of AF is quite important (6).

Attacks of PAF are short lasting and generally asymptomatic, and therefore, cannot be detected, which causes insufficient secondary prophylaxis. Holter monitorization (HM) and other monitorization methods are used to detect PAF in stroke patients (7). The PAF detection rate is reported to be 2%-25% (8,9,10,11,12,13). The primary cause for this variability is differences between methods and the definition of PAF. In studies that defined atrial tachyarrhythmia of any duration as PAF the PAF detection rate was higher (14,15,16). Clinical guidelines define PAF as atrial tachyarrhythmia lasting >30 s; however, the risk of stroke and the need for anticoagulation treatment in patients with tachyarrhythmia <30 s remain unclear (17). The present study aimed to determine the PAF detection rate and PAF distribution based on the duration of, and demographics and clinical findings in patients with acute ischemic stroke (AIS) or transient ischemic attack (TIA) that were hospitalized and had undergone 24-h HM during the early post-stroke period.

METHODS

This study included patients with AIS and TIA without AF (based on routine electrocardiography [ECG]) that were hospitalized and had undergone 24-h HM. The Institutional Ethics Committee at Haseki Training and Research Hospital approved the study. Patient records were anonymized and de-identified prior to analysis, therefore patient consent was not obtained. Ischemic stroke was defined as a focal neurologic deficit lasting >24 h and/or detection of an acute ischemic lesion via cranial CT or MRI. TIA was defined as a neurologic deficit lasting <24 h without detection of an ischemic lesion via cranial CT or MRI. HM was performed for 24 h using 3 electrodes. AF was defined as the absence of p waves or irregular ventricular with fibrillation waves. AF of any duration was accepted as PAF. Transthoracic echocardiography (TTE), including the left atrial diameter (LAD) and left ventricular ejection fraction (LEF), was performed while the patients were hospitalized.

Patient age, gender, and risk factors for stroke were analyzed. Risk factors for stroke included hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), smoking, and history of stroke. Among the laboratory tests performed, total cholesterol, low-density lipoprotein (LDL), triglyceride (TG), and HbA1c were added to the data. HT was defined as systolic blood pressure >140 mmHg, diastolic blood pressure >90 mmHg, or use of antihypertensive medication. DM was defined as fasting blood glucose >126 mg/dL or receipt of anti-diabetic treatment. Oxfordshire Community Stroke Project (OCSP) classification was used (18). Disability was assessed using the modified Rankin Scale (mRS). In addition, the CHA2DS2-VASc score was calculated in each patient.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences for Windows v.15.0 (SPSS, Inc., Chicago, IL, USA). Categorical variables are shown as number and percentage, and numerical variables are shown as mean ± SD and median. Comparison of >2 independent data groups not normally distributed was performed using the Kruskal-Wallis test. Subgroup analysis was performed via the parametric Mann-Whitney U test with Bonferroni correction. The chi square test was used to compare groups with categorical variables. In all other instances, Monte Carlo simulation was used. The level of statistical significance was set at $p<0.05$.

RESULTS

The study included 261 patients (145 male and 116 female). In total, 49 (18.8%) patients had PAF. PAF duration was <30 s in 42 (85.7%) patients and >30 s in 7 (12.3%). The patients were grouped as follows: group 1: no PAF; group 2: PAF duration >30 s; group 3: PAF duration <30 s. The timing of 24-h HM did not differ between the groups (p=0.961). Patient demographics, and clinical and laboratory findings are shown in Table 1. There weren't any significant differences in mean HT, DM, CAD, history of stroke, anti-aggregant and/or anticoagulant use, HbA1c, TG, or EF between the groups (p>0.05). Total cholesterol, LDL, and the number of smokings were significantly higher in the patients without PAF (of any duration) compared to the patients with PAF (p=0.008, p=0.044, and p=0.007, respectively).

Table 1. Clinical and laboratory findings

	Group 1 (no PAF)	Group 2 (PAF >30 s)	Group 3 (PAF <30 s)	P
n (%)	212 (81.2)	7 (2.7)	42 (16.1)	
Age (years), mean±SD	63.7±12.2	73.1±7.0	74.4±9.3	<0.001
Males, n (%)	123 (58.0)	4 (57.1)	18 (42.9)	0.135
Females, n (%)	89 (42.0)	3 (42.9)	24 (57.1)	
Smokers, n (%)	81 (38.2)	0 (0.0)	8 (19.0)	0.007
Holter Timing (mean±SD)	5.0±3.7/4	5.7±4.6/3.5	5.8±6.2/4	0.961
HT, n (%)	163 (76.9)	6 (85.7)	36 (85.7)	0.398
DM, n (%)	74 (34.9)	3 (42.9)	17 (40.5)	0.679
HbA1c (mean±SD)	6.7±1.8	6.7±2.4	7.4±2.4	0.358
Total Cholesterol (mean±SD)	206.1±52.1	159.9±41.5	186.7±47.0	0.008
LDL (mean±SD)	131.1±44.2	99.9±37.5	117.2±36.5	0.044
TG (mean±SD)	178.7±147.0	136.0±66.0	145.8±86.5	0.088
LAD (mean±SD)	34.8±3.7	41.7±1.6	40.6±2.0	<0.001
LEF (mean±SD)	57.8±5.6	57.1±3.9	56.5±5.5	0.122
mRS score (mean±SD)	2.1±1.2	2.4±1.6	3.0±1.6	0.003
CHA2DS2-VASc score (mean±SD)	3.0±1.7	4.9±1.3	4.5±1.4	<0.001
CAD, n (%)	44 (20.8)	2 (28.6)	7 (16.7)	0.717
History of Stroke, n (%)	39 (18.4)	3 (42.9)	12 (28.6)	0.113
Anti-aggregant and/or anticoagulant use, n (%)	51 (24.1)	3 (42.9)	12 (28.6)	0.460
Infarct subtypes and TIA, n (%)				
LACI	40 (18.9)	0 (0.0)	2 (4.8)	0.273
PACI	101 (47.6)	4 (57.1)	24 (57.1)	
POCI	54 (25.5)	2 (28.6)	11 (26.2)	
TACI	13 (6.1)	1 (14.3)	4 (9.5)	
TIA	4 (1.9)	0 (0.0)	1 (2.4)	

HT: hypertension; DM: diabetes mellitus; HbA1c glycosylated hemoglobin; LDL: low-density lipoprotein; TG: triglyceride; LAD: left atrial diameter; LEF: left ejection fraction; mRS: modified Rankin Scale; CHA2DS2-VASc (C: congestive heart failure; H: hypertension; A: age; D: diabetes mellitus; S: stroke/TIA/systemic emboli; V: vascular disease; A: age; Sc: sex category); CAD: coronary heart disease; TIA: transient ischemic attack; LACI: lacunar infarct; PACI: partial anterior cerebral infarct; POCI: posterior cerebral infarct; TACI: total anterior cerebral infarct

Table 2. Group comparisons with posthoc tests

		Age	Total Cholesterol	TG	LDL	LAD	mRS Score	CHA2DS2-VASc
Group 1	Group 3	<0.001	0.026	0.047	0.066	<0.001	0.001	<0.001
Group 1	Group 2	<0.001	0.021	0.267	0.068	<0.001	0.627	0.007
Group 2	Group 3	0.431	0.125	0.919	0.350	0.118	0.405	0.387

TG: triglyceride; LDL: low-density lipoprotein; LAD: left atrial diameter; mRS: modified Rankin Scale; CHA2DS2-VASc (C: congestive heart failure; H: hypertension; A: age; D: diabetes mellitus; S: stroke/TIA/systemic emboli; V: vascular disease; A: age; Sc: sex category). Mann-Whitney U test with Bonferroni correction (p<0.017).

There weren't any significant differences in mean age, total cholesterol, TG, LDL, LAD, mRS score, or CHA2DS2-VASc score between groups 2 and 3 (p>0.017). Age, LAD, and CHA2DS2-VASc score in group 2 were significantly higher than in group 1 (p<0.001, p<0.001, and p=0.007, respectively). Age, LAD, mRS score, and CHA2DS2-VASc score in group 3 were higher than in group 1 (p<0.001, p<0.001, p=0.001, and p<0.001, respectively) (Table 2).

DISCUSSION

The present study's most import finding is the high frequency of PAF with a duration <30 s during the early post-stroke period detected using 24-h HM. The PAF rate was 18.8% and the duration of PAF was <30 s in 87.7% of cases. Mean age, LAD, and CHA2DS2-VASc score were higher in groups 2 and 3 than in group 1. The mRS score was significantly higher in group 3 (PAF <30 s) than in group 1 (no PAF), but was similar in group 2 (PAF >30 s) and group 1. The present findings are similar to those of some earlier studies. Alhadramy et al. (11) reported that the frequency of PAF was 10% and that in 72% of the cases PAF duration was <30 s. Rabinstein et al. (12) observed a PAF frequency of 19.5% and that 80% of the cases had PAF duration <30 s. Khan et al. (13) reported a PAF frequency of 15% and that 65% of the cases had PAF duration <30 s.

The risk of stroke and systemic embolism is not affected by the type of AF (16). The mechanism of embolism associated with AF is not fully understood. One theory is that AF might cause mechanical atrial dysfunction and thrombus formation. As such, the duration and timing of AF defines the risk of stroke and AF develops just before the thromboembolic event. Another theory is that AF is not a direct consequence of mechanical dysfunction; fibrosis and inflammation cause atrial dysfunction and the myopathic process, resulting in AF. According to this hypothesis, there isn't a temporal relationship between thromboembolic events and arrhythmia (12). This hypothesis is supported by the TRENDS study findings (17).

The PAF duration threshold of 30 s is included in the American Heart Association (AHA) 2006 guidelines (14). According to 2007 Heart Rhythm Society consensus criteria, post-ablation of AF recurrence was considered significant only if the episode was >30 s in duration (18). Newer guidelines did not focus on the treatment approaches for the episodes <30 s in duration. Rabinstein et al. (12) reported that attacks of asymptomatic PAF frequently occur during the post-stroke period in elderly patients, but that there is no consensus concerning whether or not anticoagulant treatment should be used. Khan et al. (13) reported that cardiologists prefer to use anticoagulation for PAF >30 s PAF twice more; however, there was no difference in the preferences of non-cardiologists, according to the duration of PAF. Manina et al. (10) reported administering anticoagulant treatment in all patients with PAF, regardless of duration. Doliwa Sobocinski et al. (19) suggest that short-lasting tachyarrhythmia might be a precursor of permanent AF and that anticoagulation treatment should be considered as prophylaxis for stroke. Alhadramy et al. (11) posited that prospective studies are needed to determine the long-term risk of ischemic stroke in patients with PAF <30 s and reported that they routinely initiate anticoagulation in such patients. Arsava et al. (20) reported that PAF <30 s represents an intermediate clinical form that differs from permanent AF and, therefore, suggest that anticoagulation be withheld.

Increasing age and LAD are the primary predictive factors in patients with PAF (21,22). The CRYSTAL AF study showed than an increase in the CHA2DS2-VASc score is also predictive (23). In the present study patients with PAF <30 s and PAF >30 s were similar in terms of age, LAD, and CHA2DS2-VASc score, whereas they differed from patients without PAF in terms of the same parameters; therefore, we think that anticoagulation treatment should be a consideration in patients with PAF <30 s.

The timing, method, and duration of monitorization for the detection of AF during the post-stroke period are not standardized. Long-term monitorization was reported to increase the AF detection rate (9), but patient compliance was low (16). The European Stroke Organization and American Heart Association (AHA) suggest 24-h HM for the detection of PAF (24). Detection of PAF during the early post-stroke period is important for secondary prophylaxis of stroke. Based on the present findings, we recommend 24-h monitorization in patients with stroke of unknown etiology. In conclusion, the frequency of PAF <30 s detected via 24-h HM in the present study was high and the factors that were predictive of PAF were similar to those reported earlier. Echocardiographic findings and the CHA2DS2-VASc score can help clinicians decide if anticoagulant treatment is warranted in such patients.

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