

**ORIGINAL ARTICLE**

**ARAŞTIRMA YAZISI**

**THE RELATIONSHIP BETWEEN CLINICAL AND DEMOGRAPHIC DATA AND CHA2DS2-VASc SCORE OF PATIENTS WITH STROKE OF UNKNOWN SOURCE, WHO HAD PAF ON 24-HOUR RHYTHM HOLTER ECG**

**Aygül TANTİK PAK, Zahide MAİL GÜRKAN, Yıldızhan ŞENGÜL**

**Gaziosmanpaşa Taksim Research and Training Hospital, Neurology Clinic, İstanbul, TURKEY**

**ABSTRACT**

**INTRODUCTION=** The cause of approximately 25% of ischemic strokes is unknown. In many studies, paroxysmal atrial fibrillation (PAF) was found in 11-30% of stroke of unknownsource. Compared to the general population, the risk of stroke is twice as high in patients with PAF. CHA2DS2VAS score is used to determine the risk of stroke in patients with AF. In this study, we aimed to investigate the relationship between clinical and demographic data and CHA2DS2VAS score of patients with stroke of unknownsource who had PAF on 24-hour rhythm holter electrocardiography (ECG).

**METHODS:** Patients who were diagnosed with ischemic stroke in our clinic between 2017-2019 and whose etiology could not be determined and who had PAF on 24-hour rhythm holter ECG were included in the study. Demographic data were recorded, CHA2DS2VAS score, NIHSS (National Institute of Health Stroke Scale Scores), ASPECT (The Alberta Stroke Program Early CT Score) values, mRS (modified Rankin Scale) were calculated. The relationship between demographic, clinical and imaging data and CHA2DS2VAS score was compared.

**RESULTS:** The mean age of the 48 patients included in our study was 67.10 ± 12.05. 52.1% (n=25) of the patients were female and 48.9% (n=23) were male. The most frequent complaints of the patients were weakness of the arm and leg, impaired speech, and impaired consciousness. Congestive heart failure (CHF) in 6.3% (n=3), diabetes mellitus (DM) in 29.2% (n=14), hypertension (HT) in 75% (n=36), 27.1% (n=13) had vascular disease. The effect of age on the CHA2DS2VAS score was most prominent ( $\beta$ : 0.676,  $p < 0.01$ ), followed by a high rate of effect on DM and CHF.

**DISCUSSION and CONCLUSION:** In our study, age was the most effective factor on CHA2DS2VAS score. This shows that the rate of PAF detection on 24-hour rhythm holter ECG was increases with age.

**Keywords:** Atrial fibrillation, CHA2DS2-VASc score, stroke, paroxysmal atrial fibrillation, stroke of unknownsource, rhythm holter.

**NEDENİ BİLİNMEYEN İNME GEÇİRMİŞ HASTALARDAN 24 SAATLİK RİTİM HOLTER EKG KAYDINDA PAF SAPTANANLARIN KLİNİK VE DEMOGRAFİK VERİLERİNİN CHA2DS2-VASC SKORUYLA İLİŞKİSİ**

**ÖZET**

**GİRİŞ ve AMAÇ:** İskemik inmelerin yaklaşık %25'inin nedeni bilinmemektedir. Birçok çalışmada nedeni bilinmeyen inmelerin %11-30'da paroksizmal atriyal fibrilasyonu (PAF) saptanmıştır. Genel topluma göre inme geçirme riski PAF olanlarda iki kat fazladır. Atriyal fibrilasyonu olan hastalarda CHA2DS2VAS skoru inme riskini belirlemede kullanılır. Bizde bu çalışmada nedeni bilinmeyen inme geçiren ve 24 saatlik ritim holter elektrokardiyografi (EKG)'de PAF saptadığımız hastaların klinik ve demografik verilerinin CHA2DS2VAS skoru ile ilişkisini araştırmayı amaçladık.

**YÖNTEM ve GEREÇLER:** Çalışmaya 2017-2019 yıllarında iskemik inme tanısıyla servisimizde yatırılan etiyolojisi belirlenemeyen ve 24 saatlik ritim holter EKG'de PAF saptanan hastalar dahil edildi. Demografik verileri kaydedilerek, CHA2DS2VAS skoru, NIHSS (National Institutes Of Health Stroke Scale Scores) değerleri, ASPECT (The Alberta Stroke Program Early CT Score) değerleri, mRS (modifiye Rankin Skalası) hesaplandı. Demografik, klinik ve görüntüleme verilerinin CHA2DS2VAS skoru ile ilişkisi karşılaştırıldı.

**BULGULAR:** Çalışmamıza katılan 48 hastanın yaş ortalaması 67.10 ±12,05 idi. Hastaların %52,1 (n=25)'i kadın, %48,9 (n=23)'ü erkekti. Hastaların en sık geliş şikayetleri kol ve bacakta güçsüzlük, konuşmada bozulma, bilinç bozukluğunun olmasıydı. Hastaların %6,3 (n=3)'ünde konjestif kalp yetmezliği (KKY), %29,2 (n=14)'sinde diyabetes mellitus (DM), %75

**Corresponding author:** Aygül Tantik Pak, MD. Gaziosmanpaşa Taksim Research and Training Hospital, Neurology Clinic, İstanbul, TURKEY.

**Telephone:** +902129453000

**E-mail:** aa.aygultantik@hotmail.com

**Received:** 05.09.2019

**Accepted:** 27.11.2019

**This article should be cited as following:** Tantik Pak A, Mail Gürkan Z, Şengül Y. The relationship between clinical and demographic data and CHA2DS2-VASc score of patients with stroke of unknownsource who had PAF on 24-hour rhythm holter ECG. Turkish Journal of Cerebrovascular Diseases 2019; 25 (3): 150-154. doi: 10.5505/tbdhd.2019.46338

(n=36)'inde hipertansiyon (HT), %27,1 (n=13)' inde vasküler hastalık vardı. CHA2DS2VAS skoru üzerinde yaşın etkisi en belirgindi ( $\beta$ : 0,676,  $p<0,01$ ), ardından DM ve KKY'nin etki oranı yüksek olarak saptandı.

**TARTIŞMA ve SONUÇ:** Çalışmamızda CHA2DS2VAS skoru üzerinde en etkili faktörün yaş olduğu saptandı. Bu da nedeni bilinmeyen inme hastalarında 24 saatlik ritim holter EKG de PAF saptama oranının yaş arttıkça arttığını göstermekteydi.

**Anahtar Sözcükler:** Atriyal fibrilasyon, CHA2DS2-VASc skoru, inme, nedeni bilinmeyen inme, paroksizmal atriyal fibrilasyon, ritim holter.

## INTRODUCTION

Of the ischemic strokes, 14-30% are cardio-embolic strokes. Atrial fibrillation (AF) is an important risk factor for ischemic stroke and transient ischemic attack (1). Approximately 25% of ischemic strokes is of unknown source (2). Undetectable paroxysmal atrial fibrillation (PAF) may be the cause of cryptogenic ischemic strokes (3). In many studies, PAF was detected in 11-30% of strokes of unknown cause (4-5). In the general population, the risk of stroke is twice in PAF patients (6). PAF is a self-terminating and recurrent cardiac arrhythmia, sometimes in the form of a single attack, sometimes in clusters at varying periods. PAF accounts for 25-62% of AF patients (7). The self-terminating nature of PAF leads to inadequate diagnosis and maltreatment in ischemic stroke patients. Some treatment guidelines have emphasized the importance of detecting PAF to determine the correct treatment after an ischemic stroke or transient ischemic stroke (8). Therefore, both the diagnosis of atrial fibrillation and effective anticoagulation are extremely important in ischemic stroke patients. The CHA2DS2-VASc score is used to determine the risk of thromboembolism in patients with atrial fibrillation. The total score that can be taken is in the range of 0-9, and anticoagulation is recommended in patients with a score  $\geq 2$ . The CHA2DS2-VASc score is evaluated as follows: congestive heart failure:1 point, hypertension=1 point, 75 years and older:2 points, diabetes mellitus:1 point, stroke or transient ischemic attack:2 points, vascular disease:1 point, 65-74 years of age:1 point, female:1 point (9-10).

This study aims to investigate the effect of demographic and clinical data of the patients with stroke of unknown source, who had PAF in 24-hour rhythm Holter ECG, on their CHA2DS2-VASc scores. Thus, it was aimed to draw attention to the fact that atrial fibrillation should be checked in cryptogenic stroke patients.

## MATERIAL AND METHODS

This study was approved by the Taksim Training and Research Hospital Clinical Research Ethics Committee (no: 120 dated: August 21, 2019). The study was conducted with 48 patients with PAF out of 104 patients who underwent 24-hour Holter electrocardiography (ECG), among 310 patients hospitalized in the neurology service with a diagnosis of ischemic stroke, between January 2017 and July 2019. Since the study was conducted retrospectively, no written or oral consent was obtained from the patients. The inclusion criteria of the study: Being over 18 years of age, having had cerebral infarction or transient ischemic stroke, detection of PAF attacks over 30 seconds on a 24-hour Holter ECG examination. Exclusion criteria Presence of chronic atrial fibrillation, carotid stenosis over 70% in the symptomatic side detected by color Doppler ultrasonography or extracranial angiography through computed tomography, presence of lacunar and small vascular disease.

Demographic data, clinical data, and comorbid diseases of the patients were recorded. The patients' CHA2DS2-VASc score was calculated. The National Institutes of Health Stroke Scale (NIHSS) scores were given according to the presenting neurological examinations. NIHSS is a neurological examination scale for stroke patients, consisting of 15 items with a minimum score of 0 and a maximum score of 42 (11). "The Alberta Stroke Program Early CT Score" (ASPECT) values were calculated by examining their brain tomographies (12). ASPECT is a scale consisting of 10 areas used to determine the damaged volume of the middle cerebral artery irrigation area by brain tomography, with values ranging from minimum 0 points to maximum 10 points. Modified Rankin Scale (mRS) was calculated according to pre-discharge examinations (13). The modified Rankin scale is a 6-item scale that measures the disability status of a stroke patient

with a minimum score of 0 and a maximum score of 6.

We compared the relationship of demographic and clinical data of patients with CHA2DS2-VASc score. Effects comorbid diseases on CHA2DS2-VASc score, NIHSS, ASPECT and mRS were evaluated. The correlation between CHA2DS2-VASc score and NIHSS, ASPECT and mRS was examined.

**Statistics:** IBM SPSS Version 20.0 statistics package program was used with the number and percentages for categorical of measurements, and mean and standard deviation (where necessary with median and minimum-maximum) was used for numerical measurements together with descriptive statistical methods. Pearson correlation analysis was used for data with a normal distribution, and Spearman correlation analysis was used for the data with non-normal distribution in order to evaluate the relationship between CHA2DS2-VASc score and NIHSS, ASPECT and mRS. Multiple regression analysis and logistic regression analysis were used to determine the relationship between CHA2DS2-VASc score and clinical and demographic data.  $P < 0.05$  was taken as the statistical significance level of the tests.

## RESULTS

Of the 310 hospitalized patients admitted to our clinic with ischemic stroke, 104 had a rhythm Holter EKG due to unknown etiology of the stroke. PAF was identified in 48 of these patients. The demographic and clinical data of 48 patients included in our study are presented in detail in Table I. The mean age of the patients was  $67.10 \pm 12.05$ . Of the patients 52.1% was female, and 48.9% was male.

The most common presenting symptoms of the patients were weakness in the arms and legs, speech impairment, and impaired consciousness. Other presenting symptoms include senseless behavior, hiccups, difficulty in swallowing, dizziness, numbness in the arm, difficulty in walking and seizures. All patients had either ischemic stroke or transient ischemic stroke. Of the patients, 6.3% ( $n=3$ ) had CHF, 29.2% ( $n=14$ ) had DM, 75% ( $n=36$ ) had HT, and 27.1% ( $n=13$ ) had vascular disease.

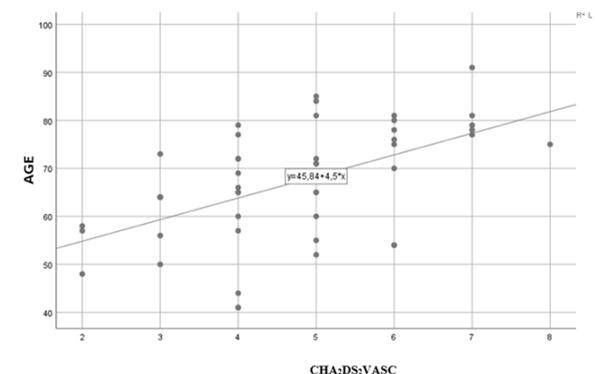
The effect of age on CHA2DS2-VASc score was most prominent ( $\beta: 0.574, p < 0.01$ ) (Figure I), followed by the effect of DM ( $\beta: 0.355, p < 0.01$ ), and CHF ( $\beta: 0.321, p < 0.01$ ).

Hypertension ( $\beta: 0.285, p < 0.01$ ) and gender ( $\beta: 0.255, p < 0.01$ ) were found to have a significant effect on CHA2DS2-VASc score (Table II).

**Table I.** Demographic data of the patients.

Age	67.10±12.05
Gender	52.1% (25 females) 48.9% (23 males)
Presenting complaints	
Speech impairment	43.8% (n=21)
Weakness in the left leg	25% (n=12)
Weakness in the right arm and leg	12.5% (n=6)
Impaired consciousness	10.4%
CHF*	6.3% (n=3)
DM†	29.2% (n=14)
HT‡	75% (n=36)
Vascular disease	27.1% (11=CAD§, 1=PAH  , 1=SVT¶)
Site of infarct	
Supratentorial	35 (72.9%)
Infratentorial	13 (27.1%)

\*Congestive heart failure, †Diabetes mellitus, ‡Hypertension, §Coronary artery disease, ||Peripheral artery disease, ¶Sinus vein thrombosis.



**Figure I.** Effect of age on the CHA2DS2-VASc score.

**Table II.** Relationship of comorbid diseases with CHA2DS2-VASc score.

	$\beta$ value	p value
Gender	0.254	<0.001
Age	0.676	<0.001
CHF*	0.298	<0.001
DM†	0.344	<0.001
HT‡	0.298	<0.001
Vascular disease	0.234	<0.001
Recurrent stroke	0.071	0.245

\*Congestive heart failure, †Diabetes mellitus, ‡Hypertension.

There was no significant relationship between recurrent stroke and CHA2DS2-VASc score ( $p > 0.05$ ). There was no significant correlation between CHA2DS2-VASc score and NIHSS, ASPECT and mRS ( $p > 0.05$ ). However, there was a significant relationship between NIHSS and ASPECT and mRS ( $p < 0.05$ ) (Table III).

**Table III.** Correlation between CHA<sub>2</sub>DS<sub>2</sub>-VASc and NIHSS, ASPECT and mRS.

	CHA <sub>2</sub> DS <sub>2</sub> -VASc	NIHSS*	ASPECT†	mRS‡
CHA <sub>2</sub> DS <sub>2</sub> -VASc				
r value	1.000	0.030	-0.128	0.180
p value	.	0.841	0.387	0.220
NIHSS*				
r value	0.030	1.000	-0.459	0.764
p value	0.841	.	0.001	0.000
ASPECT†				
r value	-0.128	-0.459	1.000	-0.439
p value	0.387	0.001	.	0.002
mRS‡				
r value	0.180	0.764	-0.439	1.000
p value	0.220	0.000	0.002	.

\*National Institutes of Health Stroke Scale Scores, †The Alberta Stroke Program Early CT Score, ‡Modified Rankin Scale

## DISCUSSION

This study was planned to determine the demographic and clinical data that have a significant correlation with CHA<sub>2</sub>DS<sub>2</sub>-VASc score in cryptogenic stroke patients with PAF detected by 24-hour Holter ECG. In our study, the relationship of advanced age with CHA<sub>2</sub>DS<sub>2</sub>-VASc score was found to be the most significant.

In the multi-centered Stroke and Monitoring for PAF in Real Time (SMART) study, PAF was found in 29 (12%) of 239 patients with cryptogenic stroke according to a 30-day ECG record (4). In another study, patients with acute ischemic stroke or transient ischemic attack were followed by continuous cardiac monitoring during their hospitalization, and AF was detected as a new diagnosis in 21 (13.5%) of 155 patients. These AF attacks were paroxysmal and had a duration of less than one hour (14). In our study, PAF was identified in 14.88% (48/310) of patients according to their 24-hour rhythm Holter ECG records.

In one study, 1239 of 3480 patients with transient ischemic stroke and ischemic infarction underwent a 24-hour rhythm Holter ECG, and PAF was found in 237 (19%), and sinus rhythm in 1002 (81%) patients. Increased age, female gender, previous ischemic stroke, myocardial infarction, pathological troponin levels, embolic stroke and infarction in different arterial areas were important indicators for PAF prediction ( $p < 0.01$ ) (15). Although our research design was different from their study, it was found that female gender and advanced age were the most effective factors in CHA<sub>2</sub>DS<sub>2</sub>-VASc score in PAF patients.

In another study, which investigated the reliability of STAF (Score for the Targeting of Atrial Fibrillation) score, PAF was detected in 30 (22.6%) of 133 patients with cryptogenic stroke. The use of the STAF score for AF detection in stroke patients was found to be limited in these patients, but it was found that age and gender den be used as independent markers ( $p < 0.01$ ) (6). In another study of similar design, 183 (31.3%) of 584 stroke patients were diagnosed with AF, and age, NIHSS, left atrial dilation and lack of vascular etiology was reported to be superior to the STAF score, as independent markers in predicting AF (16).

In our study, CHA<sub>2</sub>DS<sub>2</sub>-VASc score was found to have a significant relation to increased age and female gender ( $p < 0.01$ ). This finding was associated with the effect of age on the score. In our study, CHF, DM and HT were also found to have a significant effect on CHA<sub>2</sub>DS<sub>2</sub>-VASc score. In this study, however, the relationship between previous stroke and PAF diagnosis was not significant ( $p > 0.05$ ). The reason for this difference was believed to be the low number of our patients with recurrent ischemic stroke.

The limitations of our study include the single-centered approach, and the inclusion of PAF-only patients. Future studies with a research design that compares PAF/non-PAF patients and their data will shed more light to the PAF prediction.

In this study, PAF was more frequent in older age and female patients with stroke of unknown cause. However, there was no correlation between CHA<sub>2</sub>DS<sub>2</sub>-VASc score and stroke scores (NIHSS, ASPECT and mRS) in our patients with PAF. As a result, recording a long-term Holter ECG or planning repeated Holter ECG in stroke patients in the older age female population will be beneficial in determining stroke etiology.

## REFERENCES

1. Arboix, Adria, and Josefina Alioc. "Cardioembolic stroke: clinical features, specific cardiac disorders and prognosis." *Current cardiology reviews* 2010; 6:150-161.
2. Hart, R. G., Diener, H. C. and Coutts, S. B., et al. "Embolic strokes of undetermined source: the case for a new clinical construct." *The Lancet Neurology* 2014; 13: 429-438.
3. Seet, Raymond CS, Paul A. Friedman, and Alejandro A. Rabinstein. "Prolonged rhythm monitoring for the detection of occult paroxysmal atrial fibrillation in ischemic stroke of unknown cause." *Circulation* 2011; 124:477-486.

4. Flint, A. C., Banki, N. M. and Ren, X., et al. "Detection of paroxysmal atrial fibrillation by 30-day event monitoring in cryptogenic ischemic stroke: the Stroke and Monitoring for PAF in Real Time (SMART) Registry." *Stroke* 2012; 43: 2788-2790.
5. Rizos T, Güntner J. and Jenetzky E, et al. Continuous stroke unit electrocardiographic monitoring versus 24-hour Holter electrocardiography for detection of paroxysmal atrial fibrillation after stroke. *Stroke* 2012; 43: 2689-94
6. Göksu, E. Ö., Yüksel, B., Esin, M., et al. "The value of STAF (Score for the Targeting of Atrial Fibrillation) in Patients with Cryptogenic Embolic Stroke." *Archives of Neuropsychiatry* 2019; 56:119.
7. Levy, S., Novella, P. and Ricard, P., et al. "Paroxysmal Atrial Fibrillation= A Need for Classification." *J Cardiovasc Electrophysiol* 1995; 6:69-74.
8. Furie, K. L., Kasner, S. E., Adams, R. et al. "Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association." *Stroke* 2011; 42:227-276.
9. Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137:263-272.
10. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace* 2016; 18:1609-1678.
11. Brott, T., Adams Jr, H. P., Olinger, C. P. et al. "Measurements of acute cerebral infarction= a clinical examination scale." *Stroke* 1989; 20:864-870.
12. J. H. Warwick Pexman, Philip A. Barber, Michael D. Hill, et al. Stroke Program Early CT Score (ASPECTS) for Assessing CT Scans in Patients with Acute Stroke. *AJNR American journal of neuroradiology* 2001; 22:1534-1542.
13. Quinn, T. J., J. Dawson, and M. Walters. "Dr John Rankin; his life, legacy and the 50th anniversary of the Rankin Stroke Scale." *Scottish medical journal* 2008; 53.1:44-47.
14. Sposato, L. A., Klein, F. R., Jáuregui, A., et al. "Newly diagnosed atrial fibrillation after acute ischemic stroke and transient ischemic attack: importance of immediate and prolonged continuous cardiac monitoring." *Journal of Stroke and Cerebrovascular Diseases* 2012; 21:210-216.
15. Naess, H., Andreassen, U. W., Thomassen, L., et al. A score for paroxysmal atrial fibrillation in acute ischemic stroke. *International Journal of Stroke* 2018; 13:496-502.
16. Horstmann, S., Rizos, T. And Güntner et al. "Does the STAF score help detect paroxysmal atrial fibrillation in acute stroke patients?." *European journal of neurology* 2013; 20:147-152.