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ÖZGÜN ARAŞTIRMA / ORIGINAL RESEARCH

Periferik Arter Embolisi Geçiren Atriyal Fibrilasyonu Olan ve Olmayan Hastaların Tromboembolik Risk Düzeyi Birbirinden Farklı mıdır?

Is Thromboembolic Risk Level Different Between Patients with and without Atrial Fibrillation Suffering from Peripheral Arterial Embolism?

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Öz

Amaç: CHA2DS2-VASc [Konjestif kalp yetmezliği/sol ventrikül disfonksiyonu, hipertansiyon, yaş ≥75 yıl (çift puan), diyabet, inme (çift puan)-vasküler hastalık, 65-74 yaş ve kadın cinsiyet] skoru atriyal fibrilasyona (AF) bağlı tromboembolik komplikasyonların risk sınıflandırmasında kullanılan geçerli, pratik bir yöntemdir. Fakat klinik pratikte kullanımı daha çok inme için olmaktadır. Bu çalışmada periferik arteriyel emboli (PAE) geçiren AF'li ve AF'li olmayan hastaların CHA2DS2-VASc skoru karşılaştırılmıştır.

Gereç ve Yöntem: Bu çalışmada ocak 2011 ve aralık 2016 tarihleri arasında periferik arteryel emboli tanısı alan 150 hastanın kayıtları geriye dönük taranmıştır. Tüm hastaların olay öncesi CHA2DS2-VASc skoru hesaplanmıştır.

Bulgular: Hastaların %59'unda AF saptandı. AF'li hastaların yaş ortalaması, kadın cinsiyet, hipertansiyon , kalp yetmezliği , hiperlipidemi ve inme oranı daha yüksek izlenmiştir ($p<0,05$). AF'li hastaların ortalama CHA2DS2-VASc skoru AF'li olmayan hastalara göre daha yüksekti (5,1±1,7'e 3,5±1,8 $p<0,001$). CHA2DS2-VASc skoru 1-3 aralığında olanların oranı, AF li olmayan hastalarda daha yüksek iken (%41'e %23 $p=0,017$), CHA2DS2-VASc skoru 7-9 aralığında olanların oranı AF'li hasta grubunda daha yüksek izlenmiştir (%28'e %6 $p<0,001$). Hastane içi mortalite (%14'e %7 $p=0,235$) her iki grupta benzerdi.

Sonuç: Atriyal fibrilasyonlu hastaların CHA2DS2-VASc skor temelli tromboembolik risk düzeyi daha yüksek olmasına rağmen, PAE oranı açısından AF'li ve AF'li olmayan hastalar arasında fark izlenmemiştir.

Anahtar Kelimeler: Atriyal fibrilasyon, tromboembolizm, CHA2DS2-VASc skoru

Abstract

Objective: CHA2DS2-VASc [congestive heart failure / left ventricular dysfunction, hypertension, age≥75 years (doubled), diabetes, stroke (doubled) – vascular disease, 65–74 years of age, and female sex]is a validated , straightforward and practical stratification of thromboembolic risk score for non-valvular atrial fibrillation (NVAF). However it is usually

used for stroke. In this trial we aim to compare the CHA2DS2-VASc score between patients with and without AF suffering from peripheral arterial embolism (PAE).
Materials and Methods: We retrospectively evaluated the data registries of 150 patients who admitted to hospital due to PAE between January 2011- December 2016. CHA2DS2-VASc score was calculated for each patient
Results: Atrial fibrillation was detected 59% of patients. Patients with AF were elder, more often female gender, hypertension, heart failure, hyperlipidemia, stroke and transient ischemic attack ($p<0.05$). The rate of prior PAE was similar between two groups ($p>0.05$). Patients with AF had higher CHA2DS2-VASc score then those without AF (5.1±1.7 vs 3.5±1.8 $p<0.001$). The rate of the patients with a CHA2DS2-VASc score 1-3 was higher in non-AF group (41% vs 23% $p=0.017$). However the rate of the patients with a CHA2DS2-VASc score score 7-9 was higher in AF group (28% vs 6% $p<0.001$). In-hospital mortality was similar between groups (14% vs 7% $p=0.235$).
Conclusion: Although AF patients had higher thromboembolic risk level based on CHA2DS2-VASc score. The rate of prior PAE rate was similar between AF and non-AF groups.

Keywords: Atrial Fibrillation, Thromboembolism, CHA2DS2-VASc score

Introduction

Acute peripheral arterial embolism (PAE) is one of the most important disease leading cardiovascular mortality and morbidity. There are many major risk factors for acute PAE including hyperlipidemia, hypertension, diabetes mellitus, age, stroke, coronary artery disease. Another important risk factor for PAE is atrial fibrillation (AF) (1). Atrial fibrillation is the most commonly seen arrhythmia, affecting the 1-2% of general population (2). Although stroke is the most feared and well-known thromboembolic complication of AF, PAE of AF is also an important cause of mortality and morbidity (2,3).
Clinical trials and real world data of AF related thromboembolic complications mostly focused on stroke. The CHA2DS2-VASc score [congestive heart failure / left ventricular dysfunction, hypertension, age≥75 years (doubled), diabetes, stroke (doubled) – vascular disease, 65–74 years of age, and female sex] is validated , straightforward and practical stratification of thromboembolic risk score for AF (4). It is well known that CHA2DS2-VASc score is higher in patients with AF suffering from stroke than those without AF (4). However the risk level for thromboembolic risk level based on the CHA2DS2-VASc score is not sufficiently known in patients with PAE.
In this study we analyzed the CHA2DS2-VASc score of patients with and without AF suffering from acute PAE

Materials and Methods

This study retrospectively evaluated the data registries of patients who hospitalized due to PAE between January 2011 and December 2016. The diagnosis of PAE was confirmed by the presence of the symptoms and findings of acute ischemia with an onset five days before hospital admission, observation of a short occlusion in arterial bifurcation and trifurcation line consistent with a thrombus formation using doppler ultrasonography and angiographic methods (intraarterial digital subtraction angiography, computed tomography (CT), magnetic resonance (MR) angiography), and detection of an embolus with defined margins during surgery. Acute embolism affecting visceral organs was diagnosed by the presence of acute onset of symptoms and demonstration of embolic occlusion using imaging methods such as CT and MRI.
Patients with valvular AF, intraventricular thrombus, atrial myxoma, infective

endocarditis, prosthetic valve, history of critical leg ischemia, graft occlusion, and vascular aneurysm and iatrogenic causes of embolism were excluded. Accordingly 150 patients with PAE were included in the study. Patients were divided in two groups regarding AF. The two groups were compared with respect to age, demographic risk factors, previous use of anti-platelet and anticoagulant drugs, CHA2DS2-VASc score and mortality. CHA2DS2-VASc score, anti-platelet and anticoagulant use, hospitalization procedure and mortality rate were compared between the patients according to the localization of PAE. This study was approved by local ethical committee.

Statistical analysis

Statistical analysis was performed using the SPSS (version 15.0, SPSS Inc., Chicago, Illinois) software package. Continuous variables were expressed as mean ± standard deviation (mean ± SD), and categorical variables were expressed as percentage (%). The Kolmogorov-Smirnov test was performed to test whether variables were normally distributed. Inter-group differences were evaluated using Student's t-test for normally distributed continuous variables and using Mann-Whitney U-test for variables that did not show normal distribution. Chi-square test was used for the comparison of categorical variables. A two-tailed p value of <0.05 was considered statistically significant.

Results

Demographic and clinical characteristics of patients were shown in Table 1. Atrial fibrillation was present 59% of patients. Patients with AF were older, more often female, with a history of hypertension, heart failure, hyperlipidemia, prior stroke and transient ischemic attack (TIA) (p<0.05). The history of diabetes mellitus, coronary heart disease and chronic renal failure was similar among groups (p>0.05).

AF patients had higher vitamin K antagonist (warfarin) and novel oral anticoagulation use comparing to the patients without AF (p<0,05). However anti-platelet use similar among groups. 80% of patients in two group underwent operation. In-Hospital mortality was similar between groups (p<0.05).

The number of embolization sites including upper and lower extremity and other system embolization was similar between AF and non–AF groups. However all mesenteric embolization was occurred in AF patients. (Figure 1).

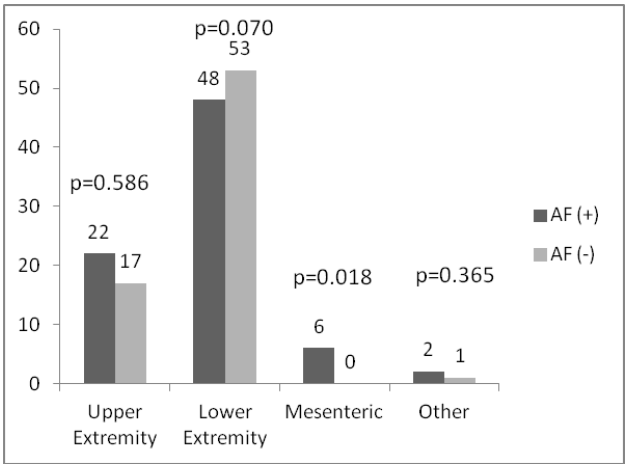

Figure 1.Number of embolic event between AF and non-AF based on anatomic distribution

Values were demonstrated as number

AF: Atrial Fibrillation

P<0.05 accepted significant

AF patients had higher CHA2DS2-VASc score comparing to those without AF (mean±sd; 5.1±1.7; vs 3.5±1.8, median (min-max) 5(1-8) vs 4 (0-7) p<0.001). CHA2DS2-VASc score was higher in AF groups in terms of emboli localization including upper (4.9±1.9 vs 3.2±1.7 p=0.005) and lower extremity (5.1±1.6 vs 3.6±1.7 p<0.001). CHA2DS2-VASc score is not different between lower and upper extremity in both AF (5,1±1,6 vs 4,9±1,9 p=0.701) and non-AF groups (3.6±1.7 vs

Table 1. Clinical characteristics of patients

	Atrial Fibrillation (+) N:79	Atrial Fibrillation (-) N:71	p
Age, year mean±sd	73.9±12.4	67.7±15.2	0.006
Female, gender n (%)	42 (53%)	19 (27%)	0.001
CHA2DS2-VASc score mean±sd median (min-max)	5.1±1.7; 5(1-8)	3.5±1.8; 4 (0-7)	<0.001
CHA2DS2-VASc score of upper extremity mean±sd	4.9±1.9	3.2±1.7	0.005
CHA2DS2-VASc score of lower extremity mean±sd	5.1±1.6	3.6±1.7	<0.001
Hypertension n (%)	61 (77%)	40 (56%)	0.006
Diabetes Mellitus n (%)	33 (42%)	31 (44%)	0.815
Coronary Artery Disease n (%)	34 (43%)	24 (34%)	0.246
Peripheral Artery Disease n (%)	36 (46%)	23 (32%)	0.099
Heart Failure n (%)	24 (30%)	6 (8%)	0.001
Hyperlipidemia n (%)	41 (52%)	24 (34%)	0.026
Chronic Renal Failure n (%)	12 (15%)	15 (21%)	0.345
Stroke n (%)	31 (39%)	17 (24%)	0.045
Number of Total Stroke median (min-max)	1(0-2)	1 (1-3)	0.573
Transient Ischemic Attack n (%)	21 (27%)	8 (11%)	0.018
Number of Transient Ischemic Attack median(min-max)	1 (1-3)	1 (1-2)	0.079
Prior peripheral arterial embolism n (%)	17 (21%)	7(10%)	0.052
VKA use n (%)	41 (52%)	0 (0%)	<0.001
NOAC use n (%)	11 (14%)	4 (6%)	0.091
Antiplatelet use n (%)	45 (57%)	34 (48%)	0.266
Operation n (%)	63 (80%)	57 (80%)	0.935
In-hospital mortality n (%)	11 (14%)	5 (7%)	0.235

NOAC: Novel Oral Anticoagulants, VKA: Vitamin K Antagonists CHA_2DS_2-VASc score [congestive heart failure / left ventricular dysfunction, hypertension, age≥75 years (doubled), diabetes, stroke (doubled) – vascular disease, 65–74 years of age, and sex category (female)],
Min:minimum Max: Maximum N:number sd: standart deviation

3.2±1.7 p=0.392) respectively. .
Figure 2 demonstrated the distribution of patients regarding three CHA2DS2-VASc score group (CHA2DS2-VASc score 1-3, 4-6, and 7-9 respectively). As seen in figure 2 the number of AF patients with CHA2DS2-VASc score (7-9) was higher than those without AF (22 (28%) vs 4 (6%) p<0.001). However the number of AF patients with CHA2DS2-VASc score (1-3) was lower than those without AF (18 (23%) vs 9 (41%) p=0.017). The percentage and number of two groups with CHA2DS2-VASc score 4-6 was similar between groups (38 (49%) vs 35 (49%) p=0.993).

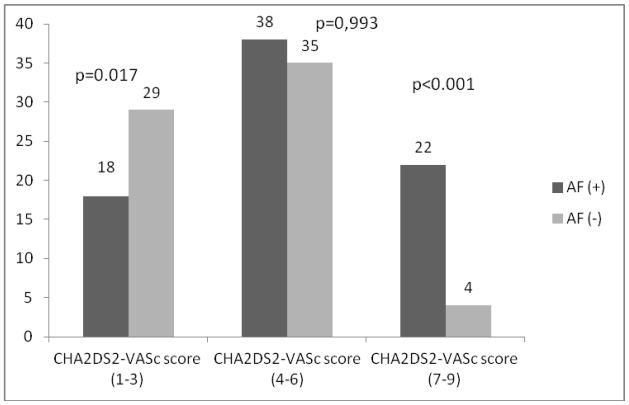

Figure 2: Number of patients according to the CHA2DS2-VASc groups (1-3,4-6 and 7-9). AF and non-AF patients
AF: Atrial Fibrillation
CHA2DS2-VASc [congestive heart failure / left ventricular dysfunction, hypertension, age≥75 years (doubled), diabetes, stroke (doubled) – vascular disease, 65–74 years of age, and female sex]

Discussion

In this study we compared the thromboembolic risk level based on CHA2DS2-VASc score of the patients with and without AF suffering from PAE. We found that patients with AF had higher CHA2DS2-VASc score than those without AF.
Atrial fibrillation related cerebral embolism accounts for 10-15% of strokes approximately 25% of strokes in people older than 80 years (5). Although AF related PAE occur rarely than cerebral embolism. The rate of AF history in PAE is higher than that in cerebral embolism. Previous trials reported that AF was present in 60–95% of patients operated because of PAE (6-7). In a Turkish registry Karapolat et al reported that AF was the responsible for 59% of peripheral embolism, followed by valvular heart and other cardiac diseases. Our findings regarding AF rate identical to that of Karapolat et al. However we excluded valvular and any other cardiac disease that may cause non-AF related peripheral embolism.
Emboli are most frequently observed in the lower extremities, and in the upper extremities in AF and non-AF groups which is consistent with the previous trials. However the rate of other embolic localization sites were lower (8-10). Causes of the different localization of PAE in the course of AF are not clearly known. Thromboembolic risk level based on CHA2DS2-VASc score doesn't affect thromboemboli localization because of the CHA2DS2-VASc score was not different regarding emboli localization. Less branching of peripheral arteries may have an effect on the emboli localization. Beside this, the rate of left and right side limb embolus localization is also different. Based on this finding anatomical arrangement has a considerable effect on the location of an embolism (11).In this study, mesenteric embolism rate was lower comparing to previous studies (6-9) and almost all patients suffering mesenteric embolism had AF, However mesenteric embolism was not detected in non-AF group. There are several reasons why AF patients had significantly higher mesenteric embolism. First, It is clearly known that AF is one of the most common causes of mesenteric embolism (12,13). Based

on this data AF patients have higher mesenteric embolism than those without AF. Second, visceral embolism including mesenteric embolism might have been underestimated for being difficult to remember this condition in the diagnosis, frequently remaining overlooked or misdiagnosed in both groups. On the other hand, it was suggested that splenic embolisms result in insignificant clinical consequences and renal embolisms become symptomatic and manifest clinical signs in late periods and this explains why such visceral embolisms are underreported (14,15)

In this study we found that mean CHA2DS2-VASc score of patients with AF was higher than those without AF. Also percentage of high risky patients in terms of thromboembolism was accumulated in AF group. One of the explanation is that age, the rate of hypertension, heart failure, stroke and TIA which were the clinical variables including in CHA2DS2-VASc score was higher in AF groups. An interesting finding is that prior PAE rate was similar between AF and non-AF groups despite higher thromboembolic risk level and stroke rate of AF patients. Warfarin use rate was significantly higher in AF group. Bekwelem et al reported that use of anticoagulation was related with a 30% greater reduction in PAE incidence compared to stroke (9). Although statistically insignificant, AF patients had higher use of NOAC which might have protective effect for PAE.

Almost all the patients (96%) in non- AF group had one or more point of CHA2DS2-VASc score. None of them received vitamin K antagonist and very low percentage of patients (6%) treated with NOACs before index event. Hsu PC et al reported that the rate of peripheral arterial occlusive disease increased from among the patients with CHADS score 0 to among those with CHADS score 5-6 and a high a CHADS score remained a significant predictor of new-onset peripheral arterial occlusive disease (16). Although current guidelines don't recommend anticoagulation treatment in non-AF patients with higher thromboembolic risk level. Treatment options including anti-platelet or anticoagulants should be evaluated in prospective randomized controlled trials

Study limitations

Since the data of the present study are based on retrospective review of hospital records, some data may be missing or inaccurately recorded. Low rate of visceral embolism due to misdiagnosed or undiagnosed patients associated with difficulties in diagnosing mesenteric, renal and splenic embolism might have biased the study findings. On the other hand, some patients with PAE may have remained asymptomatic due to small size of the embolism, and this may have caused that some patients with PAE may have not examined objectively. Besides we don't have data whether non-AF patients had silent AF episodes. Therefore these patients might be mistakenly included in non- AF group.

Conclusion

Patients with AF suffering from PAE have higher thromboembolic risk level based on CHA2DS2-VASc score comparing to those without AF. Concordantly patients with AF have higher rate of stroke and transient ischemic attack history. However prior PAE rate was similar between AF and non-AF groups. Therefore we suggest a prospective clinical trial to test the predictive value of CHA2DS2-VASc score for PAE.

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