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Predictors of Complex Aortic Plaques in Patients Undergoing Transoesophageal Echocardiography

Transözefajiyal Ekokardiyografik İnceleme Yapılan Hastalarda Kompleks Aort Plaklarının Öngördürücüleri

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ABSTRACT

Introduction: Atrial fibrillation (AF) is one of the most important causes of ischaemic stroke according to the TOAST classification. The CHA_2DS_2-VASc score is a widely used scoring system for estimating systemic thromboembolism in patients with non-valvular AF. TOAST classification indicates that an ischaemic stroke may also be due to large artery atherosclerosis. Since some of the atherosclerotic risk factors also occur in the CHA_2DS_2-VASc scoring system, we hypothesised that this scoring system can also predict the presence of complex aortic plaques and their stroke risk.

Methods: We retrospectively investigated 551 patients who underwent transthoracic echocardiography and subsequent transoesophageal echocardiography (TEE). Baseline characteristics of the patients were recorded, and the CHA_2DS_2-VASc score was calculated before the TEE examination. Aortic plaques are classified as complex when they are protruding more than 4 mm, mobile or have irregular boundaries.

Results: Among 551 patients, 110 complex aortic plaques (CAPs) were detected. Considering all the patients, higher CHA_2DS_2-VASc score [odds ratio (OR): 2.905], increasing age (OR: 1.056), and male (OR: 3.008) were significantly associated with CAP. CHA_2DS_2-VASc score was even more significantly associated with CAP in patients with a previous stroke [p<0.001, OR: 16.754 (4.196-66.894), confidence interval (CI): 95%]. After excluding complicated aortic plaques from the calculation, higher CHA_2DS_2-VASc score in patients with AF was also associated with the presence of CAPs (p<0.001, OR: 3.379 1.848-6.179, CI: 95%).

Conclusion: Although the CHA_2DS_2-VASc score has been validated to estimate thromboembolic risk in patients with non-valvular AF, the results of this study show that a high CHA_2DS_2-VASc score may also indicate an increased risk for CAP in patients with both sinus and non-valvular-AF rhythm.

Keywords: Complex aortic plaques, CHA_2DS_2-VASc score, ischaemic stroke

ÖZ

Amaç: Atriyal fibrilasyon (AF) TOAST sınıflamasına göre iskemik inmenin önemli bir nedenidir. CHA_2DS_2-VASc skor non-valvüler AF'li hastalarda iskemik stroke ve tromboemboli riskini belirlemek için sıklıkla kullanılan bir skorlama sistemidir. Bunun yanı sıra TOAST sınıflamasında, büyük arter aterosklerozu kardiyoembolizm gibi iskemik inmenin ayrı bir sınıfıdır. Biz bu çalışmamızda CHA_2DS_2-VASc skorunun kompleks aortik plaklar (KAP) ile olan ilişkisini incelemeyi amaçladık.

Yöntemler: Retrospektif olarak transtorasik ve sonrasında transözefajiyal ekokardiyografi (TÖE) uygulanmış 551 hasta analiz edildi. Hastaların demografik ve klinik özellikleri kaydedildi. CHA_2DS_2-VASc skoru TÖE incelemesi öncesinde hesaplandı. 4 mm'den büyük, hareket eden veya düzensiz sınırları olan plaklar KAP olarak kabul edildi.

Bulgular: Beş yüz elli bir hasta dahil edildi ve 110 KAP saptandı. Tüm hastalar göz önüne alındığında CHA_2DS_2-VASc skoru [olasılık oranı (OR): 2,905], yaş (OR: 1,056) ve ve erkek cinsiyet (OR: 3,008) anlamlı bir şekilde KAP ile ilişkili saptandı. Buna ek olarak daha önce iskemik inme geçiren [p<0,001, OR: 16,754 (4,196-66,894), güven aralığı (GA) %95] veya AF'li hastalarda da (p<0,001, OR: 3,379 1,848-6,179, GA: %95) KAP CHA_2DS_2-VASc skoru ile ilişkili saptandı.

Sonuç: Her ne kadar CHA2DS2-VASc skoru non-valvüler AF hastalarında tromboembolik riski hesaplamak için geliştirilmiş olsa da, bu çalışmanın sonucu CHA2DS2-VASc skorunun hem sinüs hem de AF ritmindeki hastalarda artmış KAP riskine işaret edeceğini de göstermiştir.

Anahtar Kelimeler: Kompleks aort plakları, CHA_2DS_2-VASc skoru, iskemik inme

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Introduction

Ischaemic stroke is one of the leading causes of mortality and morbidity worldwide and it is related to multiple underlying aetiologies. Although the trial of ORG 10172 in acute stroke treatment (TOAST) ischaemic stroke classification has divided ischaemic strokes into five subgroups according to the underlying aetiology, the underlying aetiologies cannot be definitely diagnosed in the majority of the cases (1).

Cardioembolism is assumed to be the underlying cause in 30% of ischaemic strokes. Previous studies have demonstrated that the CHA_2DS_2-VASc score predicts cardioembolic stroke particularly in patients with non-valvular atrial fibrillation (NV-AF). Moreover, some studies suggested that it might also predict stroke risk even in patients with sinus rhythm (2-4). Current literature suggests that an increment in the CHA_2DS_2-VASc score is related to a higher stroke risk due to left atrial (LA) abnormalities, which create a favourable milieu for thrombus formation (5). Most of the risk factors that make up the CHA_2DS_2-VASc score are also traditional risk factors for atherosclerosis; therefore, an increased CHA_2DS_2-VASc score may also imply a higher atherosclerotic burden. Overwhelming evidence in the literature suggests that the presence of aortic atheroma plaques predicts future ischaemic stroke, especially when the thickness exceeds 4 mm. Sugioka et al. (6) have demonstrated a significant relationship between $CHADS_2$ score and complex aortic plaques (CAP). Since the CHA_2DS_2-VASc score predicts ischaemic stroke modestly better than the CHADS score (1), regardless of the underlying rhythm, we aimed to investigate the relationship between the CHA_2DS_2-VASc score and CAP.

Methods

Study Population

We retrospectively analysed 651 patients who underwent transoesophageal echocardiography (TEE) between January 2016 and January 2018 in our university clinic. Twenty-one patients were excluded due to the lack of prior transthoracic echocardiographic (TTE) data and 79 patients were excluded due to the absence of clinical variables. Finally, 551 patients (267 men and 284 women) were included in the analysis. The study protocol was approved by the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Ethics Committee (decision no: 51436, date: 07.02.2018) and patients were included after their informed consent was obtained.

Patients' demographic characteristics such as age, sex and medical history including diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD), peripheral arterial disease, ischaemic stroke and AF were recorded.

CHA_2DS_2-VASc score was calculated according to the recommendations of the current guidelines. In brief, one point was given for the history of heart failure, presence of diabetes, HT, age between 65 and 75 years, female sex, vascular disease and two points for age >75 years and history of previous stroke. History of myocardial infarction, symptomatic peripheral arterial disease and the presence of CAPs were considered to be vascular diseases as recommended.

Echocardiographic Data

TTE was performed prior to the TEE examination of each patient in accordance with the American Society of Echocardiography and European Association of Cardiovascular Imaging guidelines. TEE was performed for various clinical indications such as infective endocarditis, assessment of valvular diseases or identification of the aetiology of an ischaemic stroke. TTE and TEE findings that were suggested as potential sources of cardioembolism according to the TOAST classification were collected. In the TOAST trial, cardiac abnormalities, which are prone to be the source of embolism, were divided into two groups: high risk and medium risk.

TEE was performed to all the patients using a commercially available ultrasound imaging system with a 3-D matrix array transoesophageal transducer (Philips Medical systems, IE33, Andover, MA, USA and probe X7-2t). The thoracic aorta was screened when the probe was withdrawn gradually from the descending aorta after the routine assessment of the cardiac structures. Aortic plaques were considered complex if the plaque protruded more than 4 mm from intima to the lumen in the horizontal plane and perpendicular to the arterial wall. We also considered plaques as complex if the plaque had a mobile component or an ulceration. Plaque ulceration was defined as a 2 mm indentation of the plaque surface towards the arterial wall.

Statistical Analyses

SPSS version 20 (SPSS Inc., Chicago, IL, USA) was used for the data analysis. MedCalc Statistical Software version 18 (MedCalc Software bvba, Ostend, Belgium) was used for building the graphics. Data are presented as (i) mean ± standard deviation for continuous variables and (ii) counts with percentages for categorical variables. Normality of distribution for continuous variables was analysed using the Shapiro-Wilk test. Depending on the distribution pattern, independent samples t-test or Mann-Whitney U test was used for group comparisons of the continuous variables. Chi-square test or Fischer's Exact test was performed for the group comparisons of categorical variables as appropriate. Univariate and multivariate logistic regression analyses were used to assess the possible association among demographic, clinical, imaging findings, CHA_2DS_2-VASc scores and the presence of CAPs. Variables with $p<0.05$ in the univariate logistic regression were included in the multivariate logistic regression. Age, sex, HT, stroke, DM and CAD were included in the multivariate analysis regardless of their statistical significance in the univariate analysis. The statistical significance threshold in the multivariate analyses was adjusted using Bonferroni correction. Cochran-Armitage test was performed to test the trend between CHA_2DS_2-VASc scores and the prevalence of CAP. Unless otherwise stated, $p<0.05$ indicated statistical significance.

Results

Patients Demographics

The characteristics of all the 551 patients are shown in Table 1. Mean age was 55±18 years, and 49.1% of the patients were men. The prevalence of AF was high (33.4%). A total of 167 (30.3%) patients had a recent or previous ischaemic stroke. Echocardiographic findings that were supposed to be a potential source of cardioembolism according to TOAST classification are also shown in Table 1.

Potential Cardiac Source of Embolism

Fifty-two patients had LA/left atrial appendage (LAA) thrombi, three had left ventricular (LV) thrombi, 28 had a LV akinetic segment, three had an atrial myxoma, 97 had a diagnosis of dilated cardiomyopathy and 46 patients had a mitral stenosis with respect to the high risk for cardioembolism according to the TOAST classification. In addition, 184 patients had AF, of which 36 patients possessed a CHA_2DS_2-VASc score of 2, and CAP was detected in three of these 36 patients with AF. Therefore, the patients were deemed to have a high risk for future thromboembolism.

Table 1. Demographic and echocardiographic characteristics of all patients

	Value (n=551)
Age	55±18
Gender	
Female	284 (51.5%)
Male	267 (48.5%)
HT	266 (48.3%)
Stroke	167 (30.3%)
DM	114 (20.7%)
CAD	106 (19.2%)
Atrial fibrillation	184 (33.4%)
LVEF	54±8
LA diameter	41±8
LAA thrombus	47 (8.5%)
LAA SEC	92 (16.7%)
LAA velocity	60±24
CAP	74 (18.3%)
PFO	93 (16.9%)
ASD	38 (6.9%)
ASA	34 (6.2%)
LV thrombus	3 (0.5%)
Dilated CM	97 (17.6%)
Akinetic segment presence	28 (5.1%)
LA thrombus	5 (0.9%)
Myxoma	2 (0.4%)
IE	28 (5.1%)
MR	443 (80.4%)
MR grade	
Mild	200 (36.3%)
Moderate	166 (30.1%)
Moderate to severe	39 (7.1%)
Severe	38 (6.9%)
MS	46 (8.3%)
MS grade	
Mild	27 (4.9%)
Moderate	16 (2.9%)
Severe	3 (0.5%)
MVP	19 (3.4%)
MAC	7 (1.3%)
CHA_2DS_2-VASc score	2±2

HT: Hypertension, DM: diabetes mellitus, CAD: coronary artery disease, LVEF: left ventricular ejection fraction, LA: left atrial, LAA: left atrial appendage, SEC: spontaneous echo contrast, CAP: complex aortic plaque, PFO: patent foramen ovale, ASD: atrial septal defect, ASA: atrial septal aneurysm, LV: left ventricle, CM: cardiomyopathy, IE: infective endocarditis, MR: mitral regurgitation, MS: mitral stenosis, MVP: mitral valve prolapse, MAC: mitral annular calcification

Complex Aortic Plaques

Patients were divided into two groups according to the presence or absence of CAP. CAP were detected in a total of 110 patients*. In univariate analyses, there was a statistically significant difference between the groups with respect to age ($p<0.001$), HT ($p<0.001$), CAD ($p<0.001$), DM ($p=0.003$) and AF ($p<0.001$). Mean CHA_2DS_2-VASc score was significantly higher in patients with CAP (2±1 in patients without CAP and 4±1 in patients with CAP, $p<0.001$). After multivariate analyses, male sex ($p<0.001$) and age ($p=0.001$) were independently associated with the presence of CAP. As expected, CHA_2DS_2-VASc score was also independently associated with the presence of CAP [$p<0.001$, odds ratio (OR): 2.905 (1.906-4.428), confidence interval (CI): 95%] (Table 2). Trend analyses of CHA_2DS_2-VASc score and presence of CAP demonstrated a significant linear relationship, which is depicted in Figures 1, 2 and 3.

The Relationship Between Cardiac Rhythm and Complex Aortic Plaques

Among the 551 patients, 184 patients had AF and AF patients had a higher percentage of CAP (28.1% vs 54.5%). Although there was a significant difference in the univariate analyses ($p<0.001$), AF was not independently associated with the presence of CAP in the multivariate analyses ($p=0.307$). CHA_2DS_2-VASc score was also significantly associated with CAP both in the univariate and multivariate analyses [$p<0.001$ and OR: 3.379 (1.848-6.179), CI: 95%]. Among the cases with sinus rhythm, 50 of them had CAPs. Although age, HT, DM, CAD, LV ejection fraction and CHA_2DS_2-VASc score were significant in the univariate analysis, only CHA_2DS_2-VASc score was independently associated with the presence of CAP after the multivariate analysis [$p<0.001$, 3.021 (1.620-5.623), CI: 95%] (Table 3).

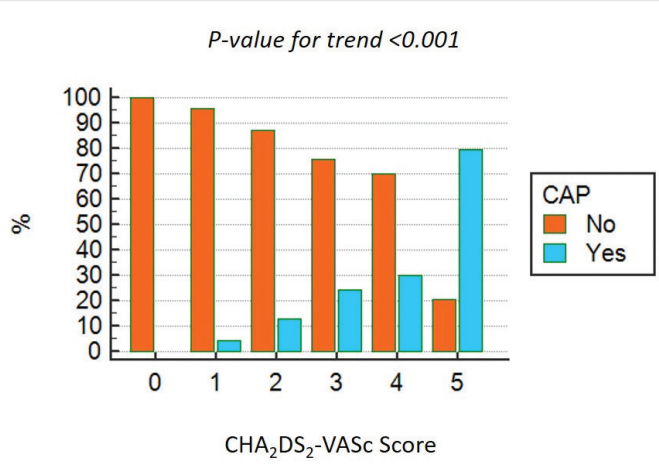


Figure 1. Trend analysis for CHA_2DS_2-VASc-VASc score and CAP in all patients
CAP: complex aortic plaque

Table 2. Group comparisons along with univariate and multivariate logistic regression analyses in all patients with or without complex aortic plaque

	Group comparisons			Univariate logistic regression		Multivariate logistic regression	
	CAP- (n=441)	CAP+ (n=110)	p	OR (95% CI)	p	OR (95% CI)	p
Age	51±17	71±10	<0.001	1.117 (1.091-1.144)	<0.001	1.056 (1.023-1.090)	0.001
Male	209 (47.4%)	58 (57.2%)	0.338	1.238 (0.815-1.881)	0.317	3.008 (1.526-5.391)	0.001
HT	180 (40.8%)	86 (78.2%)	<0.001	5.196 (3.181-8.487)	<0.001	0.609 (0.279-1.331)	0.214
Stroke	131 (29.7%)	36 (32.7%)	0.563	1.151 (0.736-1.801)	0.537	0.425 (0.188-0.960)	0.039
DM	76 (17.2%)	32 (34.5%)	<0.001	2.535 (1.593-4.032)	<0.001	0.533 (0.260-1.094)	0.086
CAD	65 (14.7%)	41 (37.3%)	<0.001	3.437 (2.153-5.487)	<0.001	0.409 (0.193-0.869)	0.020
AF	124 (28.1%)	60 (54.5%)	<0.001	3.068 (1.998-4.711)	<0.001	0.697 (0.348-1.394)	0.307
LVEF	55±7	51±10	<0.001	0.946 (0.924-0.968)	<0.001	1.015 (0.972-1.059)	0.506
LA diameter	40±8	43±6	<0.001	1.041 (1.015-1.068)	0.002	0.952 (0.909-0.997)	0.038
LAA thrombus	28 (6.3%)	19 (17.3%)	<0.001	3.080 (1.648-5.755)	<0.001	2-202 (0.881-5.503)	0.091
LAA spontaneous echo contrast	48 (14.5%)	27 (36.5%)	<0.001	2.775 (1.698-4.536)	<0.001	0.968 (0.454-2.066)	0.934
LAA velocity	63±23	50±23	<0.001	0.976 (0.966-0.986)	<0.001	0.991 (0.977-1.006)	0.231
PFO	81 (18.4%)	12 (10.9%)	0.065	0.544 (0.285-1.038)	0.065	-	-
ASD	32 (7.3%)	6 (5.5%)	0.674	0.737(0.300-1.810)	0.506	-	-
ASA	30 (6.8%)	4 (3.6%)	0.272	0.517 (0.178-1.500)	0.225	-	-
LV thrombus	2 (0.5%)	1 (0.9%)	0.488	2.014 (0.181-22.412)	0.569	-	-
Dilated CM	68 (15.4%)	29 (26.4%)	0.011	1.964 (1.195–3.227)	0.008	2.003 (0.835-4.803)	0.120
Akinetic segment	10 (3.0%)	5 (6.8%)	0.125	1.161 (0.979-1.375)	0.136	-	-
Akinetic segment number	4±2	5±3	0.561	1.192 (0.716-1.983)	0.500	-	-
LA thrombus	4 (0.9%)	1 (0.9%)	0.998	1.002 (0.111-9.058)	0.998	-	-
LA SEC	59 (13.4%)	33 (30%)	<0.001				
Myxoma	2 (0.5%)	0	0.479	-	0.999	-	-
IE	24 (5.4%)	4 (3.6%)	0.627	0.254 (0.223-1.980)	<0.001	1.308(0.482-3.555)	0.598
MR	342 (77.6%)	101 (91.8%)	<0.001	3.249 (1.585-6.658)	-	-	-
MS	37 (8.4%)	9 (8.9 %)	0.944	0.973 (0.455-2.081)	0.944	-	-
MVP	18 (4.1%)	1 (0.9%)	0.103	0.216 (0.028-1.633)	0.137	-	-
MAC	5 (1.1%)	2 (1.8%)	0.566	1.615 (0.309-8.436)	0.570	-	-
CHA_2DS_2-VASc score	2±1	4±1	<0.001	2.537 (2.114-3.046)	<0.001	2.905 (1.906-4.428)	<0.001

HT: Hypertension, DM: diabetes mellitus, CAD: coronary artery disease, AF: atrial fibrillation, LVEF: left ventricular ejection fraction, LA: left atrium, LAA: left atrial appendage, CAP: complex aortic plaque, PFO: patent foramen ovale, ASD: atrial septal defect, ASA: atrial septal aneurysm, LV: left ventricle, CM: cardiomyopathy, IE: infective endocarditis, MR: mitral regurgitation; MS: mitral stenosis, MVP: mitral valve prolapse, MAC: mitral annular calcification, OR: odds ratio , CI: confidence interval, LA SEC: left atrial spontaneous echo contrast

When the stroke patients were analysed according to presence of CAP, AF was found to be significantly more frequent in CAPs (+) patients.

Discussion

Our study demonstrated that the CHA_2DS_2-VASc score is strongly correlated with the presence of CAPs regardless of the underlying rhythm and that as the CHA_2DS_2-VASc score increased, the possibility of CAP detection also increased. After adjustment for atherosclerotic risk factors, LA abnormalities and cardiac rhythm, CHA_2DS_2-VASc score was still independently and significantly associated with the presence of CAPs. Moreover, trend analyses between CHA_2DS_2-VASc score and CAPs revealed that every 1 point increase in CHA_2DS_2-VASc score was significantly associated with an increased risk of the presence of CAPs. Although the CHA_2DS_2-VASc score was primarily developed to estimate the stroke risk in patients with NV-AF, current studies suggest that these scores might also predict the future stroke risk even in patients without AF. This may be explained by the fact that most of the parameters included in the CHA_2DS_2-VASc scoring system are also the risk factors for stroke (7). Therefore, concomitance of a high CHA_2DS_2-VASc score, CAPs and stroke should be expected and the findings of our study provide evidence for this concomitance.

Although the aetiology and treatment modalities of ischaemic stroke are well defined in the literature, the precise cause of the ischaemic event in a particular patient cannot be established in most stroke cases (8). The TOAST classification system divides strokes into five subgroups according to the cause: cardioembolism, large artery atherosclerosis, small-vessel occlusion, stroke of other determined aetiology and stroke of undetermined aetiology. Strokes have an undetermined aetiology

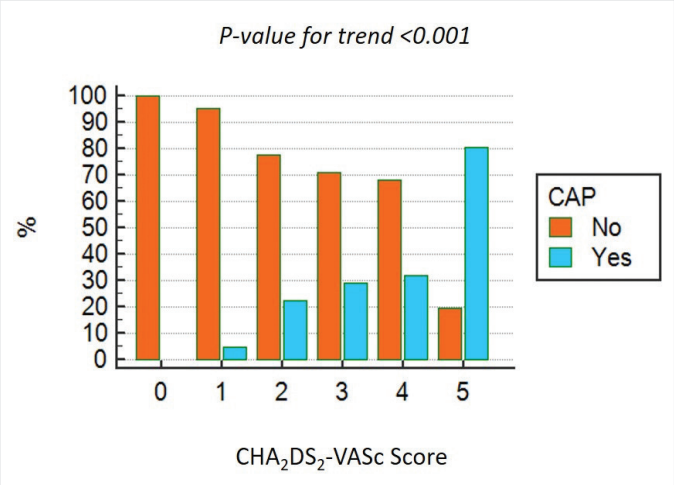


Figure 2. Trend analysis for CHA_2DS_2-VASc score and CAP in patients with atrial fibrillation

CAP: complex aortic plaque

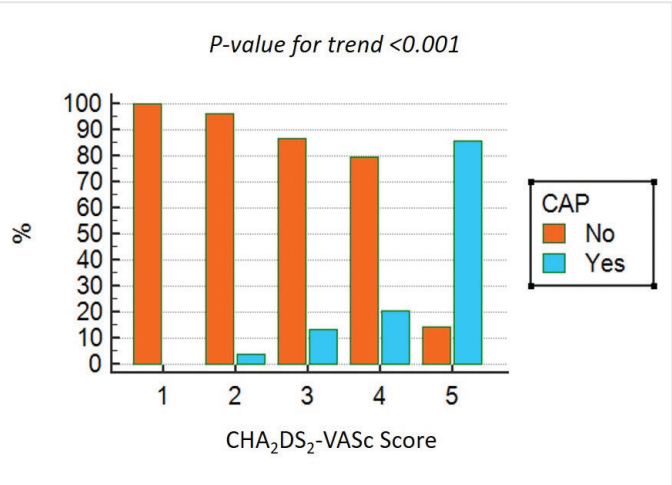


Figure 3. Trend analysis for CHA_2DS_2-VASc-VASc score and CAP patients with stroke

CAP: Complex aortic plaque

Table 3. Group comparisons along with univariate and multivariate logistic regression analyses in patients with atrial fibrillation

	Group comparisons			Univariate logistic regression		Multivariate logistic regression	
	AF+ & CAP- (n=124)	**AF+ & CAP+ (n=60)**	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
Age	61±11	75±8	<0.001	1.147 (1.094-1.202)	<0.001	1.032 (0.995-1.070)	0.089
Male	65 (52.4%)	33 (55.0%)	0.755	1.109 (0.598-2.060)	0.742	3.655 (1.453-9.199)	0.006
HT	80 (64.5%)	51 (85.0%)	0.005	3.117 (1.403-6.925)	0.005	0.530 (0184-1.521)	0.238
Stroke	24 (19.4%)	14 (23.3%)	0.299	1.268 (0.601-2.674)	0.553	0.112 (0.016-0.787)	0.028
DM	35 (28.3%)	20 (33.3%)	0.496	1.271 (0.654-2.470)	0.478	0.548 (0.188-0.1596)	0.270
CAD	36 (29.0%)	28 (46.7%)	0.021	2.139 (1.130-4.050)	0.020	0.518 (0.181-1.484)	0.221
LVEF	52±9	48±10	0.016	0.985 (0.955-1.015)	0.327	-	-
LA diameter	47±10	46±7	0.806	0.990 (0.952-1.029)	0.599	-	-
LAA thrombus	23 (18.5%)	16 (26.7%)	0.249	1.597 (0.770-3.313)	0.209	-	-
LAA SEC	43 (34.7%)	28 (46.7%)	0.109	1.648 (0.880-3.088)	0.119	-	-
LAA velocity	52±23	42±21	0.013	0.982 (0.967-0.998)	0.025	0.996 (0.979–1.013)	0.659
PFO	20 (16.1%)	4 (6.7%)	0.101	0.371 (0.121-1.140)	0.084	-	-
ASD	5 (4%)	1 (1.7%)	0.397	0.403 (0.046-3.532)	0.412	-	-
ASA	6 (4.8%)	1 (1.7%)	0.292	0.333 (0.039-2.833)	0.314	-	-
LV thrombus	2 (1.6%)	0	1.000	-	-	-	-
Dilated CM	39 (31.5%)	19 (31.7%)	0.326	1.010 (0.520-1.960)	0.977	-	-
Akinetic segment	7 (7.4%)	4 (8.9%)	0.747	0.968 (0.777-1.204)	0.767	-	-
Akinetic segment diameter	4±2	5±3	1.000	1.046 (0.596-1.834)	0.876	-	-
LA thrombus	1 (0.8%)	1 (1.7%)	0.598	2.085 (0.128-33.912)	0.606	-	-
Myxoma	1 (0.8%)	0	1.000	-	-	-	-
IE	0	0	-	-	-	-	-
MR	115 (92.7%)	57 (95.0%)	0.754	1.487 (0.388-5.705)	0.563	-	-
MS	10 (8.1%)	6 (10.0%)	0.781	1.267 (0.438-3.666)	0.463	-	-
MVP	1(0.8%)	1 (1.7%)	0.598	2.085 (0.128-33.912)	0.606	-	-
MAC	1 (0.8%)	1 (1.7%)	0.598	2.085 (0.128-33.912)	0.606	-	-
CHA_2DS_2-VASc score	3±1	5±1	<0.001	2.192 (1.662-2.892)	<0.001	3.379 (1.848-6.179)	<0.001

HT: Hypertension, DM: diabetes mellitus, CAD: coronary artery disease, AF: atrial fibrillation, LVEF: left ventricular ejection fraction, LA: left atrium, LAA: left atrial appendage, SEC: spontaneous echo contrast, CAP: complex aortic plaque, PFO: patent foramen ovale, ASD: atrial septal defect, ASA: atrial septal aneurysm, LV: left ventricle, CM: cardiomyopathy, IE: infective endocarditis, MS: mitral stenosis, MR: mitral regurgitation, MVP: mitral valve prolapse, MAC: mitral annular calcification, OR: odds ratio , CI: confidence interval

when the underlying cause cannot be established or more than one possible aetiologies are detected (1). In our study, we demonstrated that 39% of patients had at least two possible sources of embolism. Since the suggested strategy of treatment differs between TOAST groups, it is essential to precisely decide on the aetiology of the stroke. This scope of view is also valuable in patients with AF. Both the American College of Cardiology/American Heart Association and European Society of Cardiology (ESC) (9,10) guidelines on the treatment of AF strongly recommend anticoagulation in patients with a higher stroke risk; however, it has been demonstrated in previous studies that statin is more beneficial than anticoagulation in patients with stroke due to the CAPs. Di Tullio et al. (11) compared acetylsalicylic acid therapy with anticoagulation in patients with a previous stroke and aortic arch atherosclerosis. There was no difference between the groups in terms of recurrent stroke and death; however, in that study, although statin therapy was not given routinely to all patients, statin treatment was associated with improved outcomes with respect to recurrent stroke and death. In the light of these previous studies and ours, it would be fairly reasonable to administer statin therapy in patients with stroke and CAP regardless of antithrombotic therapies.

Sugioka et al. (6) demonstrated that the CHADS score is associated with the presence of CAPs, which is concordant with our findings. Although the CHADS score was used to estimate the stroke risk, current guidelines recommend the use of the CHA_2DS_2-VASc score, which has a modestly higher predictive ability for stroke. Sugioka had also shown a higher prevalence of CAPs in patients with AF. Although in our study, the univariate analysis suggested the same in our study, after adjustment for possible confounders, multivariate analyses have revealed that there is no independent association between CAPs and cardiac rhythm. Since most of the risk factors of AF and atherosclerosis are overlapping, one can expect the co-occurrence of AF and CAPs. However, there is no evidence in the literature regarding the accelerated atherosclerosis in AF patients, which is the case in our study as well.

Yang et al. (12) have also demonstrated a significant relationship between CHA_2DS_2-VASc score and CAPs. In that study, they concluded that the concomitance of AF and CAP may increase the risk of stroke by different mechanisms. In our study, 60 out of 184 AF patients had CAPs (32.6%), which eventually increased each patient's CHA_2DS_2-VASc score. There were 19 patients with a CHA_2DS_2-VASc score of 2. Among these patients, the score of two patients was 1 before the TEE examination and 1 point added as a result of the presence of CAPs, and consequently anticoagulation was indicated. Contrariwise to Yang et al. (12), there was a higher number of patients with CAP in our study (8.2% vs 19.9%). This may be explained by the higher CHA_2DS_2-VASc scores of the patients in our study (1.75±1.61 vs 2±2). Beside the CHA_2DS_2-VASc score, ESC considers the Turkish population as a very high-risk population for atherosclerosis (13). This may also explain the higher prevalence of CAP in our study.

Impact on the Treatment Strategy

In our study, 36 patients had AF with a CHA_2DS_2-VASc score of 2. Among these, three patients were considered as having an intermediate risk for stroke before the TEE examination; eventually, the presence of CAP increased their CHA_2DS_2-VASc score and anticoagulant therapy was finally indicated. Among those with a previous stroke, 38 patients had AF (22.7%). If AF was considered as the primary underlying aetiology, anticoagulant therapy could be sufficient. However, 14 of 38 patients had CAP, which could well also be the obscure underlying aetiology. In conclusion, 14/167 (8.38%) patients with stroke were detected to possess multiple sources of embolism, which requires both anticoagulant and statin therapies.

The major limitation of our study is its retrospective design. We included patients who underwent TEE examinations within the last 16 months; therefore, it did not reflect the effect of treatment on any patient. Another limitation of our study is that it as a single centre study, which is the reason for the relatively small number of patients with AF or stroke. Furthermore, we did not make mention of the clinical consequences of CAPs in our study population.

Since it was previously well defined in the literature that CAPs were associated with ischaemic stroke, patients with AF and high CHA_2DS_2-VASc scores need to be treated with statins in addition to the anticoagulant therapy. Future studies are needed to evaluate the value of statin therapy in patients with a high ischaemic stroke risk.

Conclusion

Although the CHA_2DS_2-VASc score predicts ischaemic stroke in patients with NV-AF, it is also useful for the prediction of CAPs, which are related to the ischaemic stroke in the literature.

Ethics

Ethics Committee Approval: The study was approved by the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Ethics Committee (decision no: 51436, date: 07.02.2018).

Informed Consent: Patients were included after their informed consent was obtained.

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