Predictive Accuracy of CHA_2DS_2-VASc Score in Determining Infarct-Related Artery Patency in Patients with ST-Elevation Myocardial Infarction

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ABSTRACT

Introduction: Infarct related artery patency before percutaneous coronary intervention is associated with better clinical outcomes in ST elevation myocardial infarction patients. Infarction area is smaller and left ventricular functions are better preserved in patients with spontaneous reperfusion before primary percutaneous coronary intervention, which is associated with less cardiogenic shock and significantly lower mortality. CHA_2DS_2-VASc score is a tool used in predicting the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation, although in recent years the focus has been on predictive value of CHA_2DS_2-VASc score in a wide spectrum of cardiovascular diseases regardless of the presence of atrial fibrillation. The objective of this study was to evaluate the predictive accuracy of CHA_2DS_2-VASc score in determining infarct related artery patency in ST elevation myocardial infarction patients.

Patients and Methods: A total of 723 patients who presented to our hospital with chest pain and underwent primary percutaneous coronary intervention with the diagnosis of ST elevation myocardial infarction were retrospectively analyzed. CHA_2DS_2-VASc score was calculated separately for all patients. Study population was divided into two groups as the occluded infarct related artery group (TIMI 0, 1, 2) and patent infarct related artery group (TIMI 3). A multivariate logistic regression analysis was performed in order to determine predictive value of CHA_2DS_2-VASc score.

Results: There were TIMI 0, 1 or 2 flow (occluded infarct related artery group) in 568 (78.6%) patients and TIMI 3 flow (patent infarct related artery group) in 155 (21.4%) patients. Patients in the occluded infarct related artery group had a significantly higher CHA_2DS_2-VASc score compared to the patent infarct related artery group (2 ± 1 vs. 1 ± 1, $p < 0.001$). The result of Receiver Operating Characteristic (ROC) curve analysis carried out to predict infarct related artery patency was 0.74. We found that a CHA_2DS_2-VASc score < 2 predicted infarct related artery patency with a sensitivity of 70.9% and a specificity of 44.5% (AUC: 0.735, 95% CI: 0.691-0.779, $p < 0.001$).

Conclusion: The CHA_2DS_2-VASc score can be used as a simple and reliable tool to predict infarct related artery patency in ST elevation myocardial infarction patients undergoing primary percutaneous coronary intervention.

Key Words: CHA_2DS_2-VASc score; ST-elevation myocardial infarction; infarct related artery patency.

ST Yükselmeli Miyokart Enfarktüsü Geçiren Hastalarda Enfarkt ile İlişkili Arter Açıklığının Belirlenmesinde CHA_2DS_2-VASc Skorunun Prediktif Doğruluğu

ÖZ

Giriş: Perkütan koroner girişim öncesi enfark ilişkili arter açıklığı, ST yükselmeli miyokart enfarktüsü hastalarında daha iyi klinik sonuçlarla ilişkilidir. Birincil perkütan koroner girişimden önce spontan reperfüzyon meydana gelen hastalarda enfarkt alanı daha küçük olup bu hastalarda sol ventrikül fonksiyonları daha iyi korunur ve bu durum daha az kardiyojenik şok ve belirgin olarak daha düşük mortaliteyle ilişkilidir. CHA_2DS_2-VASc skoru non-valvüler atriyal fibrilasyon hastalarında iskemik inme ve sistemik emboli riskini öngörmek için kullanılan bir araç olmakla beraber son yıllarda atriyal fibrilasyonun varlığına bakılmaksızın çok çeşitli kardiyovasküler hastalıklarda CHA_2DS_2-VASc skorunun prediktif değerine odaklanılmıştır. Bu çalışmanın amacı, ST yükselmeli miyokart enfarktüsü hastalarında enfarkt ilişkili arter açıklığının belirlenmesinde CHA_2DS_2-VASc skorunun prediktif doğruluğunu değerlendirmektir.

Hastalar ve Yöntem: Çalışmamızda hastanemize göğüs ağrısıyla başvurup ST yükselmeli miyokart enfarktüsü tanısıyla birincil perkütan koroner girişim uygulanan 723 hastanın retrospektif analizi yapıldı. Tüm hastalar için ayrı ayrı CHA_2DS_2-VASc skoru hesaplandı. Çalışma popülasyonu enfark ilişkili arter tıkalı grup (TIMI 0, 1, 2) ve enfarkt ilişkili arter açık grup (TIMI 3) olmak üzere iki ayrı gruba ayrıldı. CHA_2DS_2-VASc skorunun prediktif değerini belirlemek için multivaryate lojistik regresyon analizi yapıldı.

Bulgular: Toplam 568 (%78.6) hastada TIMI 0, 1 veya 2 akım (tıkalı enfarkt ilişkili arter grubu) ve 155 (%21.4) hastada TIMI 3 akım (patent enfarkt ilişkili arter grubu) vardı. Enfarkt ilişkili arter tıkalı gruptaki hastalar, enfarkt ilişkili arter açık grubuna göre daha yüksek CHA_2DS_2-VASc skoruna (2 ± 1'ye karşılık 1 ± 1,

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p< 0.001) sahipti. Enfarkt ilişkili arter açıklığını tahmin etmek için yapılan "Receiver Operating Characteristic (ROC)" curve analizinin sonucu 0.74 idi ve CHA_2DS_2-VASc skorunun < 2 olmasının enfarkt ilişkili arter açıklığını %70.9 duyarlılık ve %44.5 özgüllükle öngördüğü saptanmıştır (AUC: 0.735, %95 CI: 0.691-0.779, p< 0.001).

Sonuç: CHA_2DS_2-VASc skoru, birincil perkütan koroner girişim uygulanan ST yükselmeli miyokart enfarktüsü hastalarında enfarkt ilişkili arter açıklığını tahmin etmek için basit ve güvenilir bir araç olarak kullanılabilir.

Anahtar Kelimeler: CHA_2DS_2-VASc skoru; ST yükselmeli miyokart enfarktüsü; enfarkt ilişkili arter açıklığı.

INTRODUCTION

Ischemic heart disease is the most common cause of deaths worldwide. In recent years, owing to the developments in reperfusion therapy, modern antithrombotic treatment and primary protection, the incidence, short- and long-term morbidity and mortality of ST-elevation myocardial infarction (STEMI) have been significantly decreased[1]. Several studies have shown that primary percutaneous coronary intervention (PPCI) improves clinical outcomes in STEMI patients[2]. A rapid and successful revascularization of infarct-related artery (IRA) has been proven to be the most effective treatment option in STEMI patients[3,4]. The thrombolysis in myocardial infarction (TIMI) flow score is a current scoring method used to evaluate coronary blood flow[5]. IRA patency before PCI (percutaneous coronary intervention) is an important determinant of TIMI 3 flow after PCI, which is associated with better clinical outcomes in STEMI patients[6]. Infarction area is smaller and left ventricular functions are better preserved in patients with spontaneous reperfusion before PPCI, which is associated with less cardiogenic shock and significantly lower mortality[7]. Therefore, factors related to IRA patency before PCI provides additional prognostic information about the clinical course of STEMI. Different biochemical and clinical parameters were evaluated to predict pre-PCI IRA patency in STEMI patients. In a study by Acet et al. platelet-to-lymphocyte ratio (PLR), uric acid (UA), and neutrophil-to-lymphocyte ratio (NLR) were evaluated in estimating IRA patency in STEMI patients and PLR and UA were shown to predict IRA patency in STEMI patients[8]. CHA_2DS_2-VASc risk score [congestive heart failure, hypertension (HT), age > 75 years, diabetes mellitus (DM), a history of stroke or TIA, vascular disease, age of 65-74 years, sexual category] is a tool used to predict the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation (AF)[9]. The components of CHA_2DS_2-VASc score are known to be associated also with negative clinical outcomes for cardiovascular diseases. Various studies have shown that CHA_2DS_2-VASc score is a predictor of a high thrombus burden, no-reflow, short- and long-term mortality in STEMI patients[10-12]. In recent years, the focus has been on the predictive value of CHA_2DS_2-VASc score in a wide spectrum of cardiovascular diseases regardless of the presence of AF. There is no study investigating the relationship between CHA_2DS_2-VASc score and IRA patency in STEMI patients. The objective of this study was to evaluate the predictive role of CHA_2DS_2-VASc score in determining IRA patency in STEMI patients undergoing PPCI.

PATIENTS and METHODS

In this study, a total of 1055 patients who presented to the emergency department of our hospital with a complaint of chest pain and were diagnosed with STEMI between February 2019 and May 2020 were retrospectively examined. A total of 723 patients were included in the study. The inclusion and exclusion criteria of the study are shown in Figure 1. The study design was presented to the local ethics committee of our hospital and the necessary approval was obtained. Patients' clinical, demographic and angiographic features, and laboratory outcomes at the time of admission were obtained from the hospital files and computer recordings and recorded for the analysis. STEMI was diagnosed based on ischemic symptoms with new ST-segment elevation in at least 2 contiguous leads of > 0.2 mV in men or > 0.15 mV in women in leads V2 to V3 and/or of > 1 mm (0.1 mV) in other contiguous leads, a new left bundle branch block, and elevated troponin levels[13]. HT was defined as a resting blood pressure measured as > 140/90 mmHg or current use of antihypertensive medications. DM was defined as a fasting blood glucose value measured as > 126 mg/dL or current use of oral antidiabetics or insulin. Lastly, hyperlipidemia was defined based on the current guidelines. Transthoracic echocardiography (TTE) (Vivid 7; GE Medical System, Horten, Norway) was performed in all patients at the time of presentation before angiography, and left ventricular ejection fraction (LVEF) was calculated using the Simpson method. CHA_2DS_2-VASc risk score was computed for each patient based on the definition proposed by Lip et al.[14]. When CHA_2DS_2-VASc score was calculated, congestive heart failure (CHF), HT, 65-74 age range, DM, vascular disease and female gender receive each 1 point, while age ≥ 75 years and previous stroke or transient ischemic attack each 2 points. Coronary angiographic images of all patients were evaluated by two independent invasive cardiologists. The cases that were evaluated differently by the observers were decided according to a common consensus. The anatomic severity of coronary

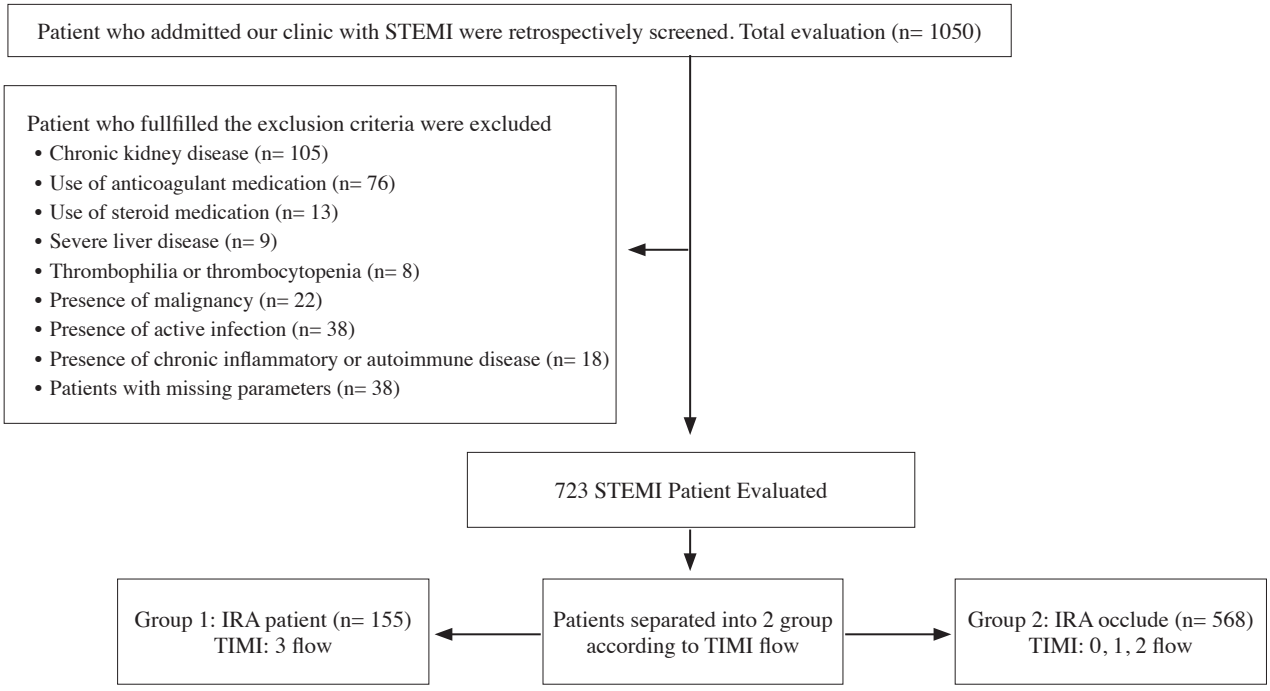


Figure 1. Flow chart for study population.

stenosis was quantitatively evaluated with the anatomical SYNTAX score (SS) using the original SS website (www.syntaxscore.com). In the coronary angiographic imaging, infarct-related blood flow was graded according to the TIMI classification as follows: TIMI flow grade 0: absence of any antegrade flow; TIMI flow grade 1: partial opaque flow beyond the occlusion, with incomplete distal filling; TIMI flow grade 2: opaque filling up to the distal of the epicardial artery, but delayed antegrade flow; TIMI flow grade 3: normal opaque filling of the epicardial artery[15]. The patients were divided into two groups according to the TIMI scale. The occluded IRA group was defined as the patients with TIMI grades 0, 1 and 2 flows, while the patent IRA group was defined as the patients with TIMI grade 3 flow.

Statistical Analysis

Statistical analysis was performed with R statistics for Windows R version 4.02 (Vienna, Austria) software. All numeric variables were expressed as median and interquartile range, and nominal variables as number and percentage. Comparison of the continuous variables between two groups was made with Mann-Whitney U test, while categorical data were compared using Chi-square or Fisher-Exact test. Multivariate regression analyses were performed using the logistic regression model in order to evaluate the effects of factors that have been shown to be significant in previous studies, on IRA patency. $p< 0.05$ values were considered statistically significant. Receiver Operating Characteristic (ROC) curve analysis was used to determine the optimum cut-off value of CHA_2DS_2-VASc, which predicts IRA patency. In addition, a relative importance plot was used to show the importance of the parameters in the regression model.

RESULTS

A total of 723 STEMI patients treated with PPCI were included in the study. Demographic, clinic, and angiographic features of the patients included in the study are shown in Table 1. No significant difference was found between both groups in terms of age, gender, HT, DM, smoking status, hyperlipidemia, systolic blood pressure (SBP) and heart rate. In the angiographic examination, the IRA was LAD in 290 (40%), CX in 96 (13%), RCA in 334 (46%) and greft in 3 (0.4%) patients. A total of 568 (78.6%) patients had TIMI 0, 1 or 2 flow grade (occluded IRA group) 155 (21.4%) had TIMI 3 flow grade (patent IRA group). In the echocardiographic examination, LVEF was significantly higher in the patent IRA group (60 ± 5 vs. 50 ± 5, $p< 0.001$). The mean CHA_2DS_2-VASc score was significantly higher in the occluded IRA group compared to the patent IRA group (2 ± 1 vs. 1 ± 1, $p< 0.001$). In univariate regression analysis, CHA_2DS_2-VASc score, SS, LVEF, serum creatinine level and SBP were higher in the study population. When applying these parameters to multivariate logistic regression analysis, CHA_2DS_2-VASc score (OR= 2.56, 95% CI= 1.49-4.39, $p< 0.001$), SS (OR= 2.01,

Table 1. Demographic, clinical, and angiographic characteristics of the patients

Parameters	Infarct related artery patient group (n= 155)	Infarct related artery occluded group (n= 568)	p value
Clinical variables			
Age, years	53.1 (49.5-60.3)	51.3 (45-60.2)	0.61
Male, n (%)	118 (76.1)	371 (65.3)	0.01
Diabetes mellitus, n (%)	33 (21.3)	197 (34.7)	0.002
Hypertension, n (%)	60 (38.7)	253 (44.5)	0.19
Smoking, n (%)	80 (51.6)	291 (51.2)	0.93
Systolic blood pressure (mmHg)	120 (109-138)	121 (110-140)	0.25
Heart rate (bpm)	82 (70-94)	88 (58-118)	0.07
Serum creatinine (mg/dL)	0.80 (0.78-1.009	0.92 (0.70-1.07)	0.03
Serum albumin (mg/dL)	38 (37-41)	37 (34-41)	< 0.001
Serum total bilirubine (mg/dL)	0.50 (0.34-0.78)	0.64 (0.41-0.86)	0.02
White blood cell ($10^3/mm^3$)	5700 (5500-7000)	58 00 (4400-6900)	0.01
Lymphocyte ($10^3/mm^3$)	2300 (1800-3150)	1900 (1600-3300)	0.64
Hemoglobin (g/dL)	12 (10.7-13.9)	12.3 (10.9-13.7)	0.33
Serum glucose (mg/dL)	108 (95.5-157)	109 (93-144)	0.32
LDL-cholesterol (mg/dL)	131 (109-154)	129 (99-147)	0.11
HDL-cholesterol (mg/dL)	41 (38-51)	40 (32-47)	< 0.001
Triglyceride (mg/dL)	133 (106-186)	118 (87-155)	< 0.001
Total cholesterol (mg/dL)	210 (168-230)	201 (164-228)	0.04
Platelet ($10^3/mm^3$)	223 (203-305)	229 (176-252)	0.01
Admission LVEF [mean ± SD (%)]	60 (55-65)	50 (45-55)	< 0.001
CHA_2DS_2-VASc score	1 (0-2)	2 (1-3)	< 0.001
CRP (mg/L)	3.5 (3-4)	4 (4-5)	0.15
Infarct-related artery, n (%)			
LAD	40 (39)	250 (40)	0.88
CX	14 (14)	82 (13)	
RCA	47 (46)	287 (45)	
GRAFT	1 (0.9)	2 (0.3)	

CX: Circumflex artery, IRA: Infarct-related artery, LVEF: Left ventricular ejection fraction, LAD: Left anterior descending artery, RCA: Right coronary artery, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, CRP: C-reactive protein, CHA2DS2-VASc: Congestive heart failure or left ventricular systolic dysfunction, hypertension, age 75 years (2 points), diabetes mellitus, previous stroke (2 points), vascular disease, age between 65 and 74 years, female gender.

95% CI= 1.49-2.72, p< 0.001), and LVEF (OR= 0.35, 95% CI= 0.29-0.46, p< 0.001 were found to be independent risk factors for IRA patency (Table 2). In ROC analysis, a CHA_2DS_2-VASc score of < 2 predicted IRA patency with a sensitivity of 70.9% and a specificity of 44.5% (AUC= 0.735, 95% CI= 0.691-0.779, p< 0.001; Figure 2). Relative importance of the variables are shown in Figure 3. Adjusted variable plot of the CHA_2DS_2-VASc score presented in Figure 4. As is seen in the figure, after adjusting age, SBP, creatinine, CRP, LDL, SS, and total cholesterol; odds-ratio increases as the CHA_2DS_2-VASc score increases.

Table 2. Preoperative and postoperative echocardiography values

		Univariate			Multivariate	
Variables	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Age, years (from 45 to 60)	0.87	0.49-1.55	0.40			
Systolic blood pressure, mmHg (from 110 to 140)	0.14	0.06-0.30	< 0.001	1.14	0.85-1.56	0.34
Serum creatinine, mg/dL (from 0.71 to 1.07)	1.12	0.60-2.11	< 0.001	1.35	0.83-2.17	0.22
CRP, mg/L (from 4 to 5)	0.78	0.57-1.07	0.10	1.21	1.001-1.44	0.02
Ldl (from 103 to 150)	1.28	0.71-2.34	0.11	0.74	0.46-1.18	0.21
LVEF (from 45 to 65)	0.36	0.30-0.45	< 0.001	0.35	0.29-0.46	< 0.001
Syntax score (from 8 to 14)	3.12	1.86-5.23	< 0.001	2.01	1.49-2.72	< 0.001
CHA_2DS_2-VASc score (from 1 to 3)	1.78	1.34-2.31	< 0.002	2.56	1.49-4.39	< 0.001

MAC: Mitral annular calcification, EF: Ejection fraction, LVESD: Left ventricular end-systolic diameter, LVEDD: Left ventricular end-diastolic diameter, TR: Tricuspid regurgitation, PABs: Pulmonary arterial pressure, IVS: Interventricular septum, LA: Left atrium, MR: Mitral regurgitation, MV: Mitral valve, PVL: Paravalvular leakage.

Figure 2. ROC curves of CHA2DS2-VASc in predicting the IRA patency. The area under the curve (AUC) is 0.735 (95% confidence interval 0.691-0.779, p< 0.001).

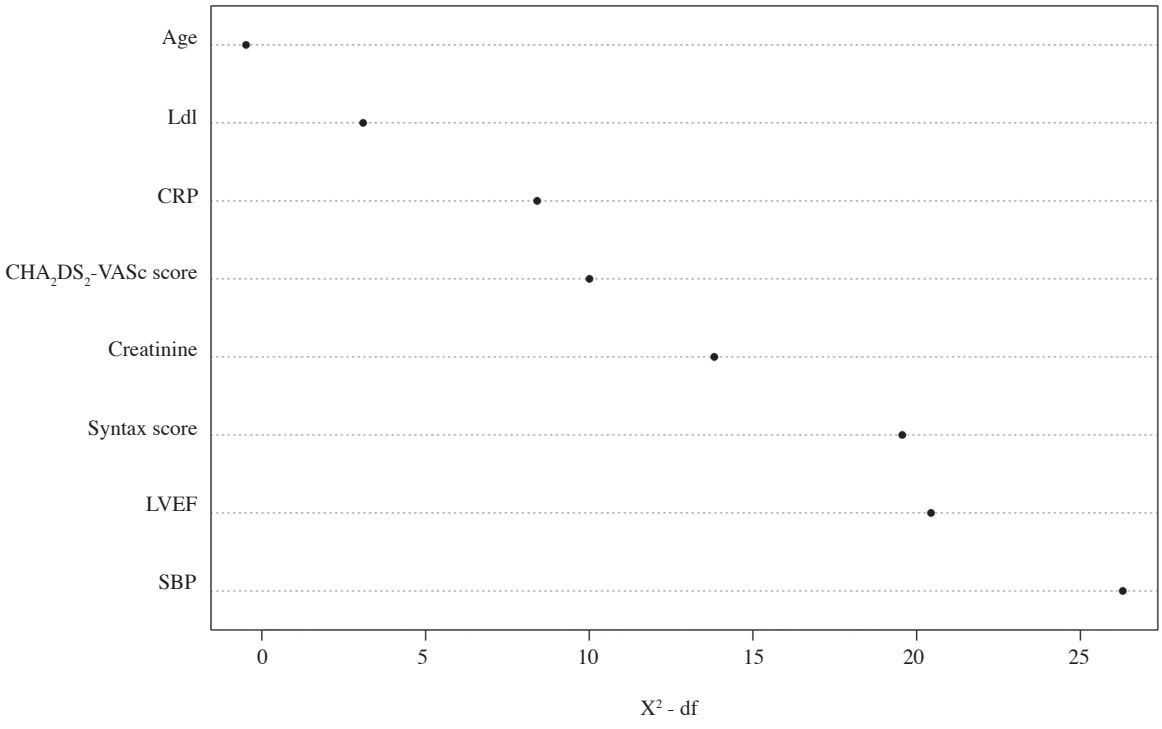
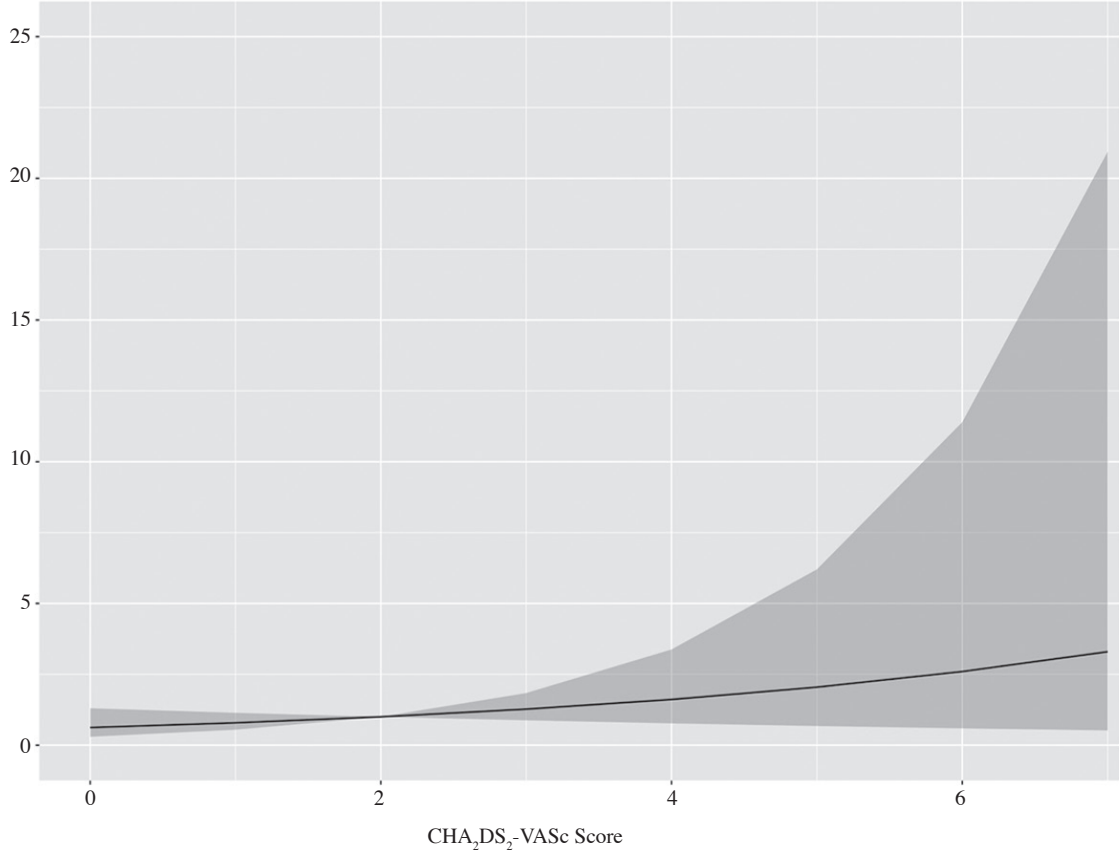


Figure 3. Relative importance of the variables.



Adjusted to Age= 51.3, SBP= 120, Creatinine= 0.85, CRP= 4, LDL= 131, Syntax score= 13, Total cholesterol= 205

Figure 4. Adjusted variable plot of the CHA_2DS_2-VASc score.

DISCUSSION

In the present study, we investigated the relationship between CHA_2DS_2-VASc score calculated at the time of admission and IRA patency in patients undergoing PPCI due to STEMI. Our results indicated that CHA_2DS_2-VASc score was significantly higher in STEMI patients with an occluded IRA, and in addition we found that CHA_2DS_2-VASc score was an independent predictor of IRA patency in STEMI patients.

PPCI is the most effective reperfusion strategy currently implemented for STEMI. A rapid and effective reperfusion of the occluded coronary artery is associated with lower in-hospital and long-term mortality and a better clinical outcome. Although the prognosis is excellent following a successful PPCI, it is obvious that the prognosis is much better in patients with spontaneous TIMI-3 flow provided before PPCI. Although STEMI patients have similar clinical presentations, it is observed during angiography that the IRA is occluded in some of these patients, while it is patent in others. Patency status of the IRA after coronary occlusion in STEMI patients is associated with lysis of intracoronary thrombi that is developed spontaneously or induced by drugs used before PCI. Spontaneous TIMI 3 flow is determined by the balances among fibrinolysis, coagulation, inflammation, thrombosis, and atherosclerosis that are different for each patient. In a study by Stone et al. spontaneously developing TIMI-3 flow before PCI was proved to be a strong and independent predictor of in-hospital and late-term survival following mechanical reperfusion[16]. In the PAMI study, initial TIMI 3 flow obtained by spontaneous reperfusion (SR) was found to be associated with better left ventricular systolic functions, less adverse cardiovascular events and lower short- and long-term mortality, independently from a successful PPCI[16]. This means that SR can provide additional benefit in protection of myocardial functions in STEMI patients before PPCI. In a combined database analysis of CADILLAC and HORIZONS-AMI trials, Brener et al. proposed that pre-PCI SR can decrease 1-year mortality by 39% in STEMI[17]. Therefore, the authors reported that SR can provide extra mortality benefit in STEMI patients independently from PPCI. It was shown in the recently conducted TOTAL study that pre-procedure upstream anticoagulation in STEMI patients was associated with a better flow before PCI, lower thrombus burden and less need for thrombectomy during PCI[18]. However, no significant difference was found in terms of 1-year mortality, repeating infarction and heart failure. It was demonstrated in the ATLANTIC study that pretreatment with ticagrelor in the ambulance did not improve TIMI flow grade before the procedure and did not affect regression of ST elevation, but decreased stent thrombosis ATLANTIC study had two major limitations; there was a short time between two strategies (only 31 minutes) and the selected population consisted of relatively low-risk STEMI patients (symptoms that presented for < 6 hours were included and patients with cardiogenic shock, hemodynamic stability and high-degree atrioventricular block were excluded)[19]. Although in both studies early initiation of anticoagulant and antiaggregant treatments did not show a positive effect on mortality, different results could be obtained in selected high-risk patients.

CHA_2DS_2-VASc score is a risk index used to predict stroke and embolic events and to decide in which AF patient's anticoagulation therapy for stroke prophylaxis would be beneficial. Recent studies have shown that CHA_2DS_2-VASc score is associated with the severity of coronary artery disease, in-hospital, 12-month and long-term mortality of STEMI patients and 1-year all-cause mortality in patients with acute coronary syndrome (ACS), regardless of the presence of AF[20-22]. In the current study we found that a high CHA_2DS_2-VASc score was a negative predictor of IRA patency in STEMI patients treated with PPCI and the cut-off value of CHA_2DS_2-VASc score predicting IRA pattency was < 2. In the light of the above mentioned information, we believe that SR can be estimated in STEMI patients with CHA_2DS_2-VASc score, which is a practical bedside test that can be applied during the first pre-hospital medical contact and thus, options such as faster transferring patients with high CHA_2DS_2-VASc scores to centers with PCI, giving priority to these patients in centers with high volume procedures and prehospital administration of antiaggregant and anticoagulant treatment in these patients as early as possible would provide additional mortality benefit.

Our study has some limitations. First, our study was a retrospective and single-center study. Since the study design was retrospective and cross-sections, there were no short- and long-term data regarding cardiovascular outcome points such as mortality, arrhythmias, repeating acute coronary events and re-hospitalization. Some patients might have undiagnosed peripheral artery disease during angiography, which might have affected CHA_2DS_2-VASc score. Because of these limitations, the current study should be accepted as a hypothesis maker trial and these findings should be confirmed in a sufficiently robust prospective cohort study.

Ethics Committee Approval: This study was approved by Kartal Kosuyolu High Specialization Training and Research Hospital Ethics Committee (2021/3/476, Date: 09.02.2021).

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - ZŞ, RZ; Analysis/Interpretation - ZŞ, RZ; Data Collection - ZŞ, RZ; Writing - ZŞ, EA; Critical Revision - EÇ, EA; Final Approval - ZŞ; Statistical Analysis - EÇ, RZ; Overall Responsibility - ZŞ.

Conflict of Interest: The authors have no conflicts of interest to declare.

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