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Comparison between R2CHA2DS2-VASc Score and CHA2DS2-VASc Score to Predict Acute Stent Thrombosis in Patients with After Primary Percutaneous Coronary Intervention

Primer Perkütan Koroner Girişim Yapılan Hastalarda Akut Stent Trombozunu Öngörmek İçin R2CHA2DS2-VASc Skoru ile CHA2DS2-VASc Skorlarının Karşılaştırılması

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ABSTRACT

Aim: Acute stent thrombosis (AST) is an important complication resulting from sudden vascular occlusion after stent implantation, especially in patients with ST-segment elevation myocardial infarction (STEMI). It occurs in about 1% of the patients after primary percutaneous coronary intervention. The CHA2DS2-VASc score is easily applied in daily practice and the components of this score are similar to common risk factors of the AST. Chronic renal disease has a hypercoagulable state and this condition is associated with an increased risk of AST in STEMI. Since the CHA2DS2-VASc score is insufficient to assess the risk of AST in patients with renal dysfunction, we aimed to investigate the prognostic significance of the modified score, R2CHA2DS2-VASc score in patients with AST.
Methods: This cross-sectional study retrospectively included 56 patients withAST and 1493 patients without AST after STEMI. The CHA2DS2-VASc and R2CHA2DS2-VASc scores were compared between the two groups.
Results: The median CHA2DS2-VASc and R2CHA2DS2-VASc scores were significantly higher in the AST group (P <0.001, P <0.001, respectively). The R2CHA2DS2-VASc score ≥2 was used as a predictor of the AST with a sensitivity of 65% and specificity of 89%.
Conclusions: The R2CHA2DS2-VASc score is a simple, cheap, and easily accessible score that can predict AST.

Keywords: Acute stent thrombosis, CHA2DS2-VASc score, R2CHA2DS2-VASc score, ST- segment elevation myocardial infarction.

ÖZ

Amaç: Akut stent trombozu (AST), özellikle ST segment yükselmesi olan miyokard infarktüsü (STYMI) hastalarında stent yerleştirildikten sonra ani damar tıkanıklığı sonucu oluşan önemli bir komplikasyondur. Primer perkütan koroner girişim sonrası hastaların yaklaşık% 1'inde ortaya çıkar. CHA2DS2-VASc skoru günlük pratikte kolayca uygulanır ve bu skorun bileşenleri AST'nin risk faktörlerine benzer. Kronik böbrek hastalığında pıhtılaşmaya meyilli bir duruma yol açabilir ve bu durum STYMI' da artmış AST riski ile ilişkilidir. CHA2DS2-VASc skoru renal disfonksiyonlu hastalarda yetersiz olduğundan AST'li hastalarda modifiye skor olan R2CHA2DS2-VASc skorunun prognostik önemini araştırmayı amaçladık.
Yöntem: STYMI sonrası 56 AST' li hasta ve AST'siz 1493 hasta retrospektif olarak bu kesitsel çalışmaya dahil edildi. CHA2DS2-VASc skoru ve R2CHA2DS2-VASc skoru iki grup arasında karşılaştırıldı.
Bulgular: Medyan CHA2DS2-VASc skoru ve medyan R2CHA2DS2-VASc skoru AST grubunda anlamlı olarak daha yüksekti (P <0.001, P <0.001). R2CHA2DS2-VASc skoru ≥2 iken %65 duyarlılık ve % 89 özgüllük ile AST' nin bir prediktörü olarak kullanılabilir.
Sonuç: R2CHA2DS2-VASc skoru, AST' yi tahmin edebilen basit, ucuz ve kolay erişilebilir bir skorlamadır.

Anahtar Kelimeler: Akut stent trombozu, CHA2DS2-VASc skoru, R2CHA2DS2-VASc skoru, ST segment yükselmeli miyokard enfarktüsü.

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INTRODUCTION

Acute stent thrombosis (AST) is a high mortality complication of stent implantation, especially in acute coronary syndrome [1]. Previous studies have shown that AST resulting in acute coronary syndrome has an incidence of up to 1% following coronary stent implantation [2].

Many factors play a role in the pathophysiology of AST, but the exact mechanism is not fully understood. First and foremost of these factors are device-related factors such as stent design, material andsurface coating [3]. Another category includes procedural factors such as stent malposition, undersize stenting, and suboptimal antithrombotic therapy [4]. Another important category relates to a lesion or patient-specific factors such as vessel size, lesion length, acute coronary syndrome, presence of thrombus, plaque features, advanced age, left ventricular ejection fraction, peripheral artery disease, kidney failure, and diabetes mellitus [5].

The CHA2DS2-VASc (congestive heart failure, hypertension, age, diabetes mellitus, stroke, vascular disease, age, sex) score is easily applied in daily practice to predict thromboembolic risk in patients with atrial fibrillation (AF). The components of this score are related to atherosclerosis, vascular spasm and microvascular dysfunction similar to common risk factors of stent thrombosis [6]. Moreover, it has been shown to be a predictor of adverse outcomes after acute coronary syndrome [7]. R2CHA2DS2-VASc (renal failure in addition to CHA2DS2-VASc) is another scoring system that includes 2 points for renal failure (stage 2 or greater) [8].

In this study, we evaluated whether the R2CHA2DS2-VAScscore is useful as a simple tool for predicting the AST among patients with ST-segment elevated myocardial infarction (STEMI) who have undergone primary percutaneous coronary intervention (pPCI).

MATERIAL AND METHODS

Study population

This retrospective analytic,cross-sectional study used the data of 1549 consecutive patients from March 2017 to May 2020 who were admitted to our cardiovascular center with a diagnosis of acute STEMI and underwent pPCI. Acute STEMI was diagnosed when patients had symptoms of acute myocardial infarction and new ST-segment elevation in at least two 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 or new left bundle branch block, later confirmed by increases in troponin levels [9]. Patients with AF, malignancy, no-reflow (postprocedural thrombolysis in myocardial infarction flow grade <3), residual thrombus, stenosis >50% proximal or distal to the culprit lesion left untreated, intraprocedural stent thrombosis, persistent dissection, and stent undersizing and those who underwent coronary bifurcation intervention were excluded. Bedside 12-lead electrocardiography and routine blood tests were obtained from all admitted patients. Bedside echocardiography was also performed for the patients. Data from participants were analyzed retrospectively. Ethics approval was obtained from Gazi Osmanpasa University ethical committee with date: 17.08.2020, number: 20-KAEK-157. All procedures in this study were carried out in accordance with the 1975 Declaration of Helsinki, updated in 2013.

Coronary angiography and pPCI

All patients underwent coronary angiography using a standard technique. First, they were administered 300 mg of acetylsalicylic acid. Ticagrelor of 180 mg was given to patients before undergoing coronary angiography. The patients received 100 IU / kg unfractionated heparin as a bolus.Stenting of the infarct-related artery was successfully completed in all patients immediately after the coronary angiography. Thrombus aspiration was applied in patients with high thrombus burden according to the operator's choice.

Tirofiban was used according to the discretion of the operator. Tirofiban infusion (0.15 mg/kg/min) was given to selected patients with no contraindications or tendency for bleeding. Other necessary medications such as beta-blockers, angiotensin-converting enzyme inhibitors,and statins were given according to relevant European Society of Cardiology guidelines.

Definitions

Stent thrombosis occuring within the first 24 hours after stent implantation was defined as acute stent thrombosis. Academic Research Consortium criteria were used to detect stent thrombosis: presence of a thrombus originating from the instent or 5 mm proximal and distal of the stent, and presence of at least one of following: (a) acute ischemic symptoms at rest, (b) recent ischemic electrocardiographic changes suggestive of acute ischemia, (c) typical rise and fall in cardiac biomarkers [10].

The CHA2DS2-VASc score was calculated for each patient using the data available in the patient files recorded during hospitalization. According to the CHA2DS2-VASc scoring system, patients were given 1 point for congestive heart failure (signs/symptoms of heart failure and ejection fraction<40%), hypertension (taking anti-hypertensive medicine or systolic and diastolic blood pressure ≥140/90 mmHg), diabetes mellitus (defined as a fasting blood glucose level>126 mg/dL or blood glucose level ≥200 mg/dL or using anti-diabetic drugs), history of vascular disease (peripheral artery disease defined as stenosis of at least 50% in noncoronary artery circulation), age 65-74 years, female sex and 2 points for age 75 years or older and previous stroke or transient ischemic attack [11]. Data on race were also collected to determine the estimated glomerular filtration rate (GFR) using the Chronic Kidney Disease Epidemiology (CKD-EPI) creatinine equation [12]. The R2CHA2DS2-VASc score was calculated using the CHA2DS2-VASc scoring system with an additional 2 points assigned for renal failure, which was defined as a calculated GFR less than 60 from the CDK-EPI equation.

Statistical Analysis

Statistics Quantitative variables were defined as mean value ± standard deviation, and qualitative variables were defined as frequency and percentage. The Kolmogorov-Smirnov test was used to evaluate whether the distribution of continuous variables was normal. Categorical and continuous variables were analyzed using the chi-square test and independent-samples t-test, respectively. Multivariate logistic regression analyses were performed to determine the independent predictors. Variables that could be a predictor of stent thrombosis with a significant P value were entered into multivariate analysis. The results of univariate and multivariate regression analyses were presented as odds ratio with a 95% confidence interval (CI). Cutoff values of CHA2DS2-VASc and R2CHA2DS2-VASc scores with the highest sensitivity and specificity were calculated by nonparametric receiver–operating characteristics (ROC) curve analysis. Significance levels were demonstrated by P values. A P value <0.5 was accepted as statistically significant. The statistical analyses were performed with SPSS 18.0 for Windows (SPSS Inc, Chicago, Illinois).

RESULTS

A total of 1549 patients (448 female (28.9%), mean age: 57±11.5 years) of whom 1493 patientswereinthe control group and 56 patients were in the AST group were included in this study. Demographic, clinical and angiographic data of the patients are listed in Table 1. Age, sex, smoking, diabetes mellitus were similar between the groups with AST and without AST. The median CHA2DS2-VASc score was significantly higher in the stent thrombosis group compared to control group (2[3]vs 1[2],P <0.001). Also, more importantly, the median R2CHA2DS2-VASc score was significantly higher in the AST group compared to the control group (3[4]vs1[2],P<0.001). Moreover, all components of the CHA2DS2-VASc score were statistically significantly different between the two groups including LV ejection fraction (%), which was significantly lower in the AST group (39.5 ± 7.2% vs 34.1 ± 7.8%, P<0.001). However, hypertension (41.0 % vs 34.6%, P =0.043), age between 65 and 74 (9.3% vs 5.3%, P<0.001), diabetes mellitus (42.8% vs 36.0%, P=0.114), previous stroke/transient ischemic attack (7.1%vs 1%, P<0.001), vascular disease (25% vs 13.4%, P=0.001), age 75 (14.1% vs 5.7%, P=0 .002), and female gender (28.0% vs 29.0%, P=0.702) were significantly higher in the AST group. Patients with the AST had significantly lower mean GFR (44.1 ± 6.9 mL/min/1.73 m2 vs 64.2 ± 14.2 mL/min/1.73 m2, P <0.001).

There was no significant difference between two cohorts in terms of duration from symptom initiation to pPCI (148.2 [123.4] min vs 148.6 [124.2] min, P=0.286). Regarding angiographic

findings, higher stent length (28 ±15 mm vs. 24 ±10 mm P< 0.001) and lower stent diameter (2.75 ± 0.5 mm vs. 2.75 ± 0.25 mm, P =0.092) were associated with AST.

Table 1: Demographic, Clinical, and Angiographic Features of the Patients.

Variables	Control n=1493	Stent trombosis, n= 56	P value
Age, years, mean	57.5 ±10	56.5 ±13	0.356
Female gender, n (%)	433 (29.0)	15 (28.0)	0.702
Smoking, n (%)	469 (31.4)	17 (30.3)	0.789
Diabetes mellitus, n (%)	537 (36.0)	24 (42.8)	0.114
Hypertension, n (%)	503 (34.6)	23 (41.0)	0.043
History of stroke/TIA, n (%)	15 (1)	4 (7.1)	<0.001
Vascular disease, n (%)	200 (13.4)	14 (25.0)	0.001
Previous MI	148 (9.9)	8 (14.2)	0.496
Peripheral arterial disease	33 (2.2)	7 (12.5)	<0.001
Previous by-pass surgery	30 (2.0)	4 (7.1)	0.001
Total cholesterol, mg/dL	183 ± 41	189 ± 42	0.626
LDL-C, mg/dL	113 ± 31	119 ± 36	0.294
Triglycerides, mg/dL	139 ± 62	152 ± 104	0.282
Killip class >1, n (%)	96 (6.4)	4 (7.1)	0.451
LV ejection fraction, (%)	39.5 ± 7.2	34.1 ± 7.8	<0.001
Serum creatinine, mg/dL	1.06 ± 0.14	1.28 ± 0.72	<0.001
Chronic renal failure, n (%)	131 (8.8)	13 (23.2)	<0.001
GFR, mL/min/1.73 m2	64.2± 14.2	44.1± 6.9	<0.001
CHA2DS2 -VASc score, median	1 [2]	2 [3]	<0.001
R2CHA2DS2-VASc score, median	1 [2]	3 [4]	<0.001
MI type, n(%)			<0.001
Anterior	632 (42.3)	34 (60.7)	
Nonanterior	861 (57.7)	22 (39.3)	
Anemia, n (%)	197 (13.2)	14 (25.0)	0.096
Drugelutingstent, n(%)	1061 (71.1)	40 (71.4)	0.806
StentingwithoutPTCA, n (%)	597 (40.0)	21 (37.5)	0.562
Stent length,(mm) median	24 ± 10	28 ± 15	<0.001
Stent diameter, (mm), median	2.75 ± 0.25	2.75 ± 0.5	0.092
Tirofiban infusion, n (%)	696 (46.6)	37 (66)	<0.001
Thrombus aspiration, n (%)	100 (6.7)	6 (10.7)	0.264
Time to PCI, (min), median	148.2 [123.4]	169.4 [116.8]	0.286
In-hospital mortality, n (%)	20 (0.7)	17 (30.3)	<0.0001

GFR,Glomerular filtration rate; LV, left ventricular; LDL, low density lipoprotein; MI, myocardial infarction; PCI, primary percutaneous intervention; PTCA, percutaneous transluminal coronary angioplasty; TIA, transient ischemic attack.

Variables with a significant P value in the descriptive analysis were entered into univariate and multivariate regression analysis to determine potential risk factors of stent thrombosis. The results of this analysis are illustrated in Table 2. Individual components of the R2CHA2DS2-VASc score as a risk factor of the stent thrombosis were not entered in this analysis to avoid multicollinearity.

Table 2. Univariate and multivariate regression analysis of predictors of stent thrombosis in the study population

Variables	Unadjusted OR(95% CI)	P value	Adjusted OR (95% CI)	P value
CHA2DS2-VASc score	1.72 (1.46-2.01)	<0.001	1.56 (1.41-1.80)	<0.001
R2CHA2DS2-VASc score	2.84(1.96-3.41)	<0.001	3.26 (2.80-4.32)	<0.001
GFR	1.84 (1.21-2.60)	<0.001	2.24 (2.08-3.23)	<0.001
Stent length	1.44 (1.23-1.71)	<0.001	1.41 (1.39-1.72)	<0.001
MI type	1.90 (1.25-2.76)	0.001	1.71 (1.17-2.5)	0.1

CI, confidence interval; GFR, glomerular filtration rate; MI, myocardial infarction; OR, odds ratio.

The results from the multivariate logistic regression analysis showed that GFR (odds ratio [OR]: 2.24, 95% CI: 2.08-3.23, P<0.001), CHA2DS2-VASc score(OR: 1.56, 95% CI:1.41-1.80, P<0.001) and R2CHA2DS2-VASc score (OR:3.26, 95% CI: 2.80-4.32, P<0.001) were significant independent predictors. Then, we performed a ROC analysis as depicted in Figure 1 for evaluating the cutoff values of CHA2DS2-VASc and R2CHA2DS2-VASc scores in predicting the AST. Our study showed that CHA2DS2-VASc score ≥1 could be used as a predictor of the stent thrombosis in patients presenting with STEMI with a sensitivity of 45% and specificity of 75%, area under the curve: 0.654and 95% CI :0.58-0.74 whereas the R2CHA2DS2-VASc score ≥2 could be used as a predictor of the stent thrombosis in patients presenting with STEMI with a sensitivity of 65% and specificity of 89%, area under curve: 0.820 and 95% CI:0.77-0.89.

DISCUSSION

This present study highlighted that in patients with STEMI, renal failure was associated with increased risk of AST. The findings revealed that the R2CHA2DS2-VASc score was a predictor of stent thrombosis after pPCI in patients with

STEMI. Actually both scoring systems were predictive but the sensitivity and specificity of R2CHA2DS2-VASc score was found to be greater in predicting stent thrombosis in patients with STEMI. AST is an abrupt vessel closure. Stent thrombosis is an important complication of stent implantation because it causes acute coronary syndrome. The incidence of AST after pPCI is approximately four times higher than after elective stent implantation [13]. It is known that in patients with AST, the incidence of cardiogenic shock increases and thus mortality also increases, so it has serious consequences. In randomized studies, the incidence of AST ranged from approximately 1.4% to 3.4% [14,15]. Numerous studies of AST formation have demonstrated the involvement of multiple risk factors such as diabetes mellitus, chronic kidney failure, stenting in acute or elective conditions, factors associated with lesions, number of affected vessels, total stent length, and presence of calcification [15-19]. Previous studies have shown various estimators of the stent thrombosis [19]. As confirmed by the findings of this study, lesion length >20 mm, and lower stent diameter were demonstrated to be the predictors of stent thrombosis. Also, GFR could predict AST. However, the need to use to a simple and fast scoring system for stent thrombosis risk classification in STEMI patients who are candidates for pPCI, compels the physician to choose the best treatment strategy. Since the underlying thromboembolic event mechanisms are similar in stent thrombosis and AF, the relationship between CHA2DS2-VASc score, which is a thromboembolic risk marker for AF, and stent thrombosis has been studied in the literature [19]. However, at the same time, patients with chronic renal disease have a hypercoagulable state and this condition is associated with an increased risk of stent thrombosis [18].

Several studies showed that renal dysfunction as an independent predictor of stent thrombosis in STEMI, but these studies did not include the GFR parameter [20]. In this study, GFR was also found to be significantly lower in the stent thrombosis group. Since the CHA2DS2-VASc score was insufficient to indicate the risk of thromboembolism in patients with renal dysfunction, we used the modified R2CHA2DS2-VASc score in this study.

The CHA2DS2-VASc score is a set of risk factors for thromboembolism and stroke, as suggested by the present guidelines for use as a proven predictor of thromboembolic events in patients with AF [21]. Stroke and transient ischemic attack might occur due to nonatherosclerotic vascular pathologies, as well as thromboembolism and atherosclerosis [19]. Abnormal vascular function was recommended as a stroke mediator [22].

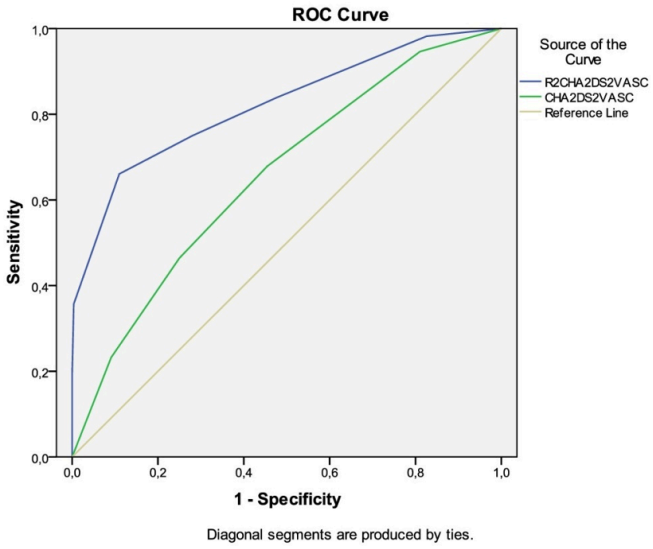

Figure-1: Receiver-operating curve analysis of CHA2DS2-VASc and R2CHA2DS2-VASc scores for predicting acute stent thrombosis

A significant positive correlation existed between the CHA2DS2-VASc and R2CHA2DS2-VASc scores.This should not be a surprise, as the two scoring systems shared many of the same scoring components and were similar to the weights of each component. This indicated the validity of using R2CHA2DS2-VASc score to estimate the risk of stent thrombosis. However, the addition of renal failure may not alter clinical decisions or outcomes because the CHA2DS2-VASc score has already been validated and is currently in use. It is important to try to control modifiable risk factors, such as renal function, because of the high mortality and morbidity associated with thromboembolism. Although most of the risk factors for CKD-EPI, AF and stroke are the same, renal failure may be a separate independent risk factor for thromboembolism. Piccini et al. tried to combine GFR with the CHADS2 score and created the R2CHADS2 score [23]. The GFR was calculated with the Cockcroft–Gault formula. In this study, CKD-EPI equation was used instead of

the Cockcroft–Gault formula for calculating GFR. It was because a previous study showed that the GFR-based scheme, R2CHADS2 , provided a significant improvement in the predictive ability for mortality risk in older patients with AF [24]. Huang et al. enrolled 3,295 patients with coronary artery disease (CAD) and found that R2CHADS2 had a comparable predictability to the Global Acute Coronary Events Registry score [25]. Compared to the CHA2DS2 score ,the R2CHA2DS2 score provided better discrimination for mortality. The results of this study showed that the R2CHA2DS2 score could be used to predict composite events for patients with CAD, and that the area under the curve of R2CHADS2 was statistically greater than the CHA2DS2 score. Decreased renal function was a critical in the prognosis of cardiovascular results in patients with CAD. Several potential mechanisms may explain these findings. Patients with reduced renal function often have consequences such as anemia, excessive volume burden, and oxidative stress that contribute to poor outcomes. In our study, the R2CHA2DS2-VASc score provided better discrimination for stent thrombosis than the CHA2DS2-VASc score.

Although the CHA2DS2-VASc score has already been tested in a previous study, the prognostic role of the modified R2CHA2DS2-VASc score in AST in patients with STEMI has not been addressed before. This study suggested that the R2CHA2DS2-VASc scoremight predict the risk of AST with reasonable efficacy for patients with STEMI better compared to the CHA2DS2-VASc score.

Conclusion

The R2CHA2DS2-VASc score is an easily calculated and efficient index that can be considered a powerful and independent predictor of stent thrombosis in STEMI patients.This study suggested that,it could be a useful adjunct to standard tests in the diagnosis of stent thrombosis.

Limitations

Our study has several limitations. It was an observational, retrospective, single-center study with a relatively small number of patients. In this study, patients with non-STelevation myocardial infarction and unstable coronary artery disease were not included. In addition, patients with procedural complications that might cause AST were excluded from the study by careful examination of angiographic images, but intravascular imaging techniques such as intravascular ultrasound were not used. Therefore, future studies should include the aforementioned conditions and validate the findings of this study.

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