Association of the CHA₂DS₂VASc Score with Acute Stent Thrombosis in Patients with an ST Elevation Myocardial Infarction Who Underwent a Primary Percutaneous Coronary Intervention

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Significance of the Study

- Acute stent thrombosis is a rare life-threatening complication of primary percutaneous coronary interventions (pPCIs). The CHA₂DS₂VASc score is a simple risk scoring system that can be calculated on admission before pPCI. Our findings provided evidence that the CHA₂DS₂VASc score may be used to identify high-risk patients with STEMI following a pPCI for acute stent thrombosis.

Keywords

CHA₂DS₂VASc score · ST elevation myocardial infarction · Acute stent thrombosis · Primary percutaneous coronary intervention

Abstract

Objective: In this study, we aimed to determine the predictive value of the CHA₂DS₂VASc score for acute stent thrombosis in patients with an ST elevation myocardial infarction treated with a primary percutaneous coronary intervention (pPCI). **Methods:** This was a retrospective study conducted among 3,460 consecutive patients with STEMI who under-

went a pPCI. The stent thrombosis was considered a definite or confirmed event in the presence of symptoms suggestive of acute coronary syndrome and angiographic confirmation of stent thrombosis based on the diagnostic guidelines of the Academic Research Consortium. The stent thrombosis was classified as acute if it developed within 24 h. **Results:** The mean CHA₂DS₂VASc score was 3.29 ± 1.73 in the stent thrombosis group, whereas it was 2.06 ± 1.14 in the control group ($p < 0.001$). In multivariable logistic regression analysis, CHA₂DS₂VASc scores ≥ 4 were independently associated with acute stent thrombosis (OR = 1.64; 95% CI 1.54–1.71, $p < 0.001$). In a receiver operating characteristic curve analysis, the best cut-off value for the CHA₂DS₂VASc score was

≥4, with 60% sensitivity and 73% specificity. Of note, patients with a CHA₂DS₂VASc score of 4 had a 4.3 times higher risk of acute stent thrombosis compared to those with a CHA₂DS₂VASc score of 1. **Conclusions:** The CHA₂DS₂VASc score may be a significant independent predictor of acute stent thrombosis in patients with STEMI treated with a pPCI. Therefore, the CHA₂DS₂VASc score may be used to assess the risk of acute stent thrombosis in patients with STEMI following a pPCI.

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Introduction

Acute stent thrombosis is a rare life-threatening complication of percutaneous coronary interventions (PCI), with an estimated incidence of 0.5–2% in elective procedures [1]. The incidence of stent thrombosis is much higher in patients with an ST elevation myocardial infarction (STEMI) treated with a primary PCI (pPCI) [2]. Several previous studies have shown that acute stent thrombosis is associated with elevated mortality rates and adverse cardiovascular outcomes, particularly among patients who have undergone a pPCI [3, 4]. Thus, there is a need for a specific risk scoring system to predict this fatal pPCI-related complication.

At present, there are no guideline-based risk scoring systems for predicting the risk of acute stent thrombosis in STEMI patients who have been treated with a pPCI. The CHA₂DS₂VASc score is a guideline-based risk calculator that has been used to estimate the risk of thromboembolism in patients with nonvalvular atrial fibrillation [5]. The score is calculated by assigning 1 point for each of the following: congestive heart failure (an ejection fraction of 40% or less), hypertension, age between 65 and 74 years, diabetes mellitus, vascular diseases (myocardial infarctions or peripheral arterial diseases), and female sex [6]. Two points are then assigned for a history of strokes or transient ischemic attacks and age >75 years [6]. A previous study reported that the CHA₂DS₂VASc score was an independent predictor of in-hospital and long-term mortality in patients with acute coronary syndrome [7]. In addition, a recent study found an association between the CHA₂DS₂VASc score and acute stent thrombosis in patients with stable coronary artery disease [8]. In light of these data, the aim of the present study was to examine the potential utility of admission CHA₂DS₂VASc scores in predicting acute stent thrombosis in STEMI patients who have undergone a pPCI.

Patients and Methods

Patient Population

In total, 3,503 patients who were diagnosed with STEMI and underwent a pPCI between February 2009 and December 2016 were retrospectively identified. Patients with atrial fibrillation on admission and those who developed atrial fibrillation during the course of their hospital stay were excluded, in addition to patients who used any oral anticoagulation agents and presented with more than 12 h since the onset of symptoms. Patients who developed stent thrombosis after 24 h were also excluded. Finally, 3,460 patients were enrolled into the study. The demographic characteristics of the patients, and related clinical information, were obtained from the hospital's electronic database. The CHA₂DS₂VASc score of each patient was calculated. As all of the patients underwent a pPCI, each patient had a CHA₂DS₂VASc score of at least 1. The study protocol was approved by the local ethics committee, and the study was carried out according to the principles of the Declaration of Helsinki. The need for informed consent was waived due to the retrospective design of this study.

Laboratory Data and Echocardiographic Examination

Venous blood samples were obtained from all of the subjects on admission before the pPCI. An automated complete blood count device (Coulter LH 780 Hematology Analyzer; Beckman Coulter Ireland Inc., Galway, Ireland) was used to measure hematologic parameters. Transthoracic echocardiography was performed in all of the patients within 24 h using a GE Vivid 7 system echocardiography machine (GE Healthcare, Piscataway, NJ, USA). The left ventricular ejection fraction of each patient was calculated using Simpson's method with a 2.5–3.5-MHz phased-array transducer. Systolic dysfunction was defined as a left ventricular ejection fraction <40%.

PCI and Medications

All of the patients underwent coronary angiography via the femoral artery after admission and received 300 mg of acetylsalicylic acid and a 300- to 600-mg oral loading dose of clopidogrel on admission. A standard intravenous bolus of unfractionated heparin (70–100 U/kg) and additional doses as needed were given to achieve an activating clotting time of >250 s before the coronary intervention. Stenting of the infarct-related artery, with or without balloon angioplasty, was successfully completed immediately after the coronary angiography. In accordance with the hospital's protocol, thrombus aspiration was not mandatory in all patients with a high thrombus burden, and it was applied at the discretion of the interventional cardiologist. In addition, as per our institutional protocol, use of the glycoprotein IIb/IIIa inhibitor tirofiban (Ag-grastat; DSM Pharmaceuticals, Greenville, NC, USA) at a dose of 12.5 mg/50 mL was left to the judgment of the cardiologist. Two independent operators who were blinded to the patients' clinical data evaluated all the coronary angiograms for stent thrombosis and thrombosis in myocardial infarction (TIMI) flow, before and after the procedure.

Definitions

The stent thrombosis was defined as a definite or confirmed event in the presence of symptoms suggestive of acute coronary syndrome and angiographic confirmation of stent thrombosis in accordance with the guidelines of the Academic Research Consor-

tium [9]. In addition, based on the elapsed time since stent implantation, stent thrombosis was classified as acute if it developed within 24 h. All of the patients who developed acute stent thrombosis underwent a reintervention after the diagnosis. STEMI was defined as (1) at least 2 contiguous leads with ST segment elevations >2.5 mm in men aged <40 years and >2 mm in men aged >40 years or >1.5 mm in women in leads V2 to V3 and/or >1 mm in the other leads in the absence of left ventricular hypertrophy or left bundle branch block), (2) prolonged (> 30 min) typical chest pain at rest, and (3) an increase in serum biomarkers of myocardial damage [10]. For patients diagnosed before 2012, in accordance with the previous universal definition of a myocardial infarction, the following cut-off points were used to define persistent ST elevations: >0.1 mV in all leads other than leads V2 to V3, where the following cut-off points applied: >0.2 mV in men and >0.15 mV in women or new-onset left bundle branch block [11]. Hypertension was defined as receiving antihypertensive treatment or systolic pressure >140 mm Hg and/or diastolic pressure >90 mm Hg on at least 2 separate measurements during hospitalization [12]. Diabetes mellitus was defined as taking oral antidiabetic agents or insulin or follow-up fasting blood glucose levels ≥ 126 mg/dL in accordance with the criteria of the American Diabetes Association [13]. Hyperlipidemia was defined as taking lipid-lowering medications upon presentation [14]. Chronic kidney disease was considered in the presence of an estimated glomerular filtration rate <60 mL/min/1.73 m² for >3 months, with or without kidney damage [15]. Congestive heart failure was defined based on a previous diagnosis of heart failure. All clinical evaluations were conducted according to the Killip classification.

Statistical Analysis

All continuous variables were expressed as means $\pm$ SD. The Kolmogorov-Smirnov test was used to test the normality of the data. Continuous variables with normal distributions were compared using an independent samples *t* test. Continuous variables with skewed distributions were compared using the Mann-Whitney U test. Categorical variables were expressed as numbers and percentages, and Pearson's χ^2 or Fisher's exact tests were used to evaluate the differences. Hierarchical logistic regression analysis was used for the multivariable analysis. Parameters with *p* values < 0.05 in the univariable analysis were incorporated into the multivariable logistic regression analysis. The logistic regression analysis was made on all clinically relevant parameters found to be significant in the multivariable analysis. In the multivariable model, confounders in the multivariable analysis were considered predictors of acute stent thrombosis. The OR indicated the relative risk of acute stent thrombosis in the groups.

In the multivariable analysis, a forward hierarchical logistic regression model was used. The OR indicated the relative risk of acute stent thrombosis in each CHA₂DS₂VASc subgroup as compared with that in the lowest-risk subgroup (CHA₂DS₂VASc score = 1). In the multivariable models, confounders in a bivariate analysis as predictors of acute stent thrombosis were considered. Two models were generated to indicate the impact of potential confounders on the association between the CHA₂DS₂VASc score and acute stent thrombosis. One model was unadjusted, whereas the other was adjusted for all confounders, including demographics (age and sex), smoking, comorbidities (hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease, peripheral arterial disease, and strokes), Killip class, anterior myocardial infarction,

stent diameter, stent length, and no reflow. The goodness of fit and calibration of the CHA₂DS₂VASc score were assessed and found to be appropriate. The Hosmer-Lemeshow statistic of the logistic model was 0.30. Two-tailed *p* < 0.05 was considered statistically significant, and 95% CI are presented for all OR. All analyses were performed using the Statistical Package for Social Sciences software, version 20.0 (SPSS; IBM, Armonk, NY, USA).

Results

The study population was composed of 3,460 patients with STEMI who underwent pPCI. In the study, 556 (16.1%) patients were female. The study population was divided into 2 groups, i.e., a stent thrombosis group and a control group. In total, 136 (3.9%) patients developed acute stent thrombosis within 24 h. The baseline characteristics and laboratory findings, including the angiographic features and interventional outcomes of the patients with and without stent thrombosis, are presented in Table 1. Patients with acute stent thrombosis tended to be older and male compared to those without acute stent thrombosis (*p* < 0.05 for all). The frequencies of diabetes mellitus, hypertension, hyperlipidemia, smoking, chronic kidney disease, cerebrovascular incidents, and a previous stent implantation were higher in the stent thrombosis group (*p* < 0.05 for all). On admission, an anterior myocardial infarction was more common in patients with stent thrombosis than in non-stent thrombosis patients (*p* = 0.031). The laboratory findings revealed that the patients with stent thrombosis had higher levels of creatinine and lower glomerular filtration rates compared to the non-stent thrombosis patients (*p* < 0.001 and *p* < 0.001, respectively). After the intervention, the TIMI blood flow was lower in the patients with stent thrombosis compared to those without stent thrombosis, and tirofiban was commonly used in the patients with stent thrombosis (*p* = 0.026 and *p* < 0.001, respectively). There were no between-group differences in terms of implantation rates of bare metal or drug-eluting stents. In addition, the mean stent diameters and lengths were similar in both groups (*p* > 0.05 for all). In the acute stent thrombosis group, the mean CHA₂DS₂VASc score was 3.29 $\pm$ 1.73, whereas the mean score in the control group was 2.06 $\pm$ 1.14 (*p* < 0.001). Of note, there was a high frequency of elevated CHA₂DS₂VASc scores in the stent thrombosis group.

Table 2 presents the results of the univariable and multivariable analyses. In the univariable regression analysis, the following factors were predictors of acute stent thrombosis: age, female sex, smoking, diabetes mellitus, hyper-

Table 1. Baseline characteristics, clinical and angiographic features, and outcomes of all of the patients

	Control group (n = 3,324)	Acute stent thrombosis (n = 136)	p value
Age, years	56±12	61±13	0.002
Male, gender	2,794 (84.1)	104 (76.5)	0.018
BMI	28.1±3.8	27.7±3.6	0.719
<i>History</i>			
Hypertension	1,020 (30.7)	60 (44.1)	0.001
Diabetes mellitus	702 (21.1)	64 (47.1)	<0.001
Hyperlipidemia	964 (29.0)	53 (39.0)	0.012
Current smoking status	1,458 (43.9)	82 (60.3)	0.015
Percutaneous coronary intervention	308 (9.3)	28 (20.6)	<0.001
Coronary artery bypass graft surgery	80 (2.4)	2 (1.5)	0.482
Chronic kidney disease	42 (1.3)	11 (8.1)	<0.001
Stroke	48 (1.4)	5 (3.7)	0.038
Peripheral artery disease	84 (2.5)	9 (6.6)	0.004
CHA ₂ DS ₂ -VASc score	2.06±1.14	3.29±1.73	<0.001
Median CHA ₂ DS ₂ -VASc score (25–75 percentile)	2.0 (1.0–3.0)	3.0 (2.0–4.0)	<0.001
<i>CHA₂DS₂-VASc score</i>			
1	1,370 (41.2)	22 (16.2)	<0.001
2	947 (28.5)	32 (23.5)	0.208
3	575 (17.3)	23 (16.9)	0.907
4	327 (9.8)	27 (19.9)	<0.001
5	96 (2.9)	16 (11.8)	<0.001
6	5 (0.2)	7 (5.1)	<0.001
7	4 (0.1)	9 (6.6)	<0.001
<i>At admission</i>			
Systolic blood pressure, mm Hg	129±27	126±29	0.484
Killip class ≤2	3,089 (92.9)	123 (90.4)	0.270
Killip class 4	76 (2.3)	6 (4.4)	0.110
Left ventricular ejection fraction, %	44±13	46±14	0.146
Chest pain period, h	4.3±4.7	4.6±5.0	0.661
Door-to-balloon time, min	20.0±9.9	19.3±9.2	0.589
Anterior myocardial infarction, %	1,448 (43.6)	72 (52.9)	0.031
<i>Admission laboratory variables</i>			
Creatine kinase-MB, ng/mL			
Admission	95±78	98±75	0.228
Peak	161±135	167±123	0.106
Troponin I, ng/dL			
Admission	16±19	18±18	0.231
Peak	33±18	35±19	0.344
Creatinine, mg/dL	0.9±0.2	1.2±0.3	<0.001
Glomerular filtration rate (CKD-EPI)	92±24	81±22	<0.001
White blood cell count, cells/μL	12.0±4.4	12.8±4.0	0.243
Hematocrit, %	40.7±4.8	39.6±5.1	0.616
Platelet count, cells/μL	238±68	255±78	0.098
<i>Vessel stenosis (>50%)</i>			
1 vessel	1,712 (51.5)	74 (54.4)	0.506
2 vessels	810 (24.4)	24 (17.6)	0.072
3 vessels	802 (24.1)	38 (27.9)	0.309
<i>TIMI blood flow before the intervention</i>			
0	1,828 (55.0)	66 (48.5)	0.138
I	178 (5.4)	10 (7.4)	0.314
II	347 (10.3)	17 (12.5)	0.443
III	971 (29.2)	43 (31.6)	0.546

Table 1 (continued)

	Control group (n = 3,324)	Acute stent thrombosis (n = 136)	p value
<i>TIMI blood flow after the intervention</i>			
0	196 (5.9)	6 (4.4)	0.469
I	500 (15.0)	30 (22.1)	0.026
II	518 (15.6)	22 (16.2)	0.852
III	2,110 (63.5)	78 (57.4)	0.147
<i>Intervention type</i>			
PTCA and stenting	2,872 (86.4)	121 (89.0)	0.390
Direct stenting	452 (13.6)	15 (11.0)	0.390
Manual thrombectomy	176 (5.3)	12 (8.8)	0.075
<i>Stent type</i>			
Drug-eluting stent	3,050 (91.8)	124 (91.2)	0.810
Bare metal stent	295 (8.9)	18 (13.2)	0.082
Total stent length, mm	20.9±6.2	21.6±6.2	0.104
Length >28 mm	378 (11.4)	16 (11.8)	0.888
Minimal stent diameter, mm	3.2±1.0	3.0±0.7	0.365
Diameter >3 mm	377 (11.3)	11 (8.1)	0.239
<i>Treatment</i>			
ACEI or ARB	3,110 (93.6)	128 (94.1)	0.795
Tirofiban	1,568 (47.2)	114 (83.8)	<0.001
β-Blockers	2,882 (86.7)	116 (85.3)	0.636
Statins	2,948 (88.7)	126 (92.6)	0.151
Diuretics	334 (10.0)	20 (14.7)	0.079
Insulin treatment	1,048 (31.5)	52 (38.2)	0.100
Oral antihyperglycemic agents	1,276 (38.4)	66 (48.5)	0.017
In-hospital mortality	126 (3.8)	10 (7.4)	0.036

Continuous variables are presented as means ± SD, and nominal variables are presented as numbers (%). PTCA, percutaneous transluminal coronary angioplasty; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Table 2. Univariate analysis and multivariate model for acute stent thrombosis

Univariate analysis	p value	OR (95% CI)	Multivariate analysis	p value	OR (95% CI)
Age	<0.001	1.09 (1.08–1.13)	Age	0.062	1.00 (1.00–1.01)
Female gender	<0.001	1.32 (1.28–1.38)	Female gender	0.114	1.02 (0.97–1.04)
Smoking	<0.001	1.79 (1.71–1.88)	Smoking	0.007	1.20 (1.12–1.29)
Chronic kidney disease	<0.001	1.94 (1.87–2.08)	Chronic kidney disease	<0.001	1.57 (1.51–1.64)
Hypertension	<0.001	1.63 (1.56–1.70)	Hypertension	0.207	1.04 (0.96–1.19)
Hyperlipidemia	0.003	1.29 (1.25–1.32)	Hyperlipidemia	0.004	1.07 (1.00–1.37)
Diabetes mellitus	<0.001	3.12 (3.08–3.21)	Diabetes mellitus	<0.001	1.75 (1.36–1.96)
Peripheral artery disease	0.007	1.28 (1.21–1.34)	Peripheral artery disease	0.128	1.02 (1.01–1.21)
Stroke	0.045	1.23 (1.20–1.29)	Stroke	0.053	1.28 (1.21–1.33)
Stent diameter (1-mm increase)	0.003	0.62 (0.45–0.85)	Stent diameter (1-mm increase)	0.007	0.65 (0.51–0.77)
Stent length (1-mm increase)	<0.001	1.12 (1.02–1.24)	Stent length (1-mm increase)	<0.001	1.08 (1.03–1.16)
Killip class >1 on admission	<0.001	2.56 (2.21–3.03)	Killip class >1 on admission	0.001	1.78 (1.65–1.91)
Anterior myocardial infarction	0.004	1.76 (1.38–2.14)	Anterior myocardial infarction	0.014	1.41 (1.32–1.79)
CHA ₂ DS ₂ -VASc score 4	<0.001	1.87 (1.74–2.11)	CHA ₂ DS ₂ -VASc score 4	<0.001	1.64 (1.54–1.71)
No reflow	0.147	1.29 (0.91–1.82)	No reflow	0.176	1.23 (0.89–1.74)

All clinically relevant parameters were included in the model.

Table 3. In-hospital event rates and logistic regression models for mortality and acute stent thrombosis by CHA₂DS₂-VAsC score

	CHA ₂ DS ₂ -VAsC score						
	1 (n = 1,392)	2 (n = 979)	3 (n = 598)	4 (n = 352)	5 (n = 112)	6 (n = 12)	7 (n = 13)
In-hospital mortality, n (%)	10 (0.7)	22 (2.2)	47 (7.9)	34 (9.7)	17 (15.2)	2 (16.7)	4 (30.8)
Mortality							
Model 1: unadjusted	1 (reference)	3.1 (1.4–6.7)	11.7 (5.9–23.4)	14.7 (7.2–30.2)	24.7 (11.0–55.4)	27.6 (5.3–142)	61.4 (16.2–232)
Model 2: adjusted for all covariates ^a	1 (reference)	1.6 (0.6–4.2)	2.3 (1.8–8.3)	2.8 (1.9–9.3)	4.3 (2.6–10.4)	6.2 (4.6–21.6)	39.2 (13.2–116)
Acute stent thrombosis events, n (%)	22 (1.6)	32 (3.3)	23 (3.8)	27 (7.6)	16 (14.3)	7 (58.8)	9 (69.3)
Events							
Model 1: unadjusted	1 (reference)	2.1 (1.2–3.6)	2.4 (1.3–4.5)	5.1 (2.8–9.1)	10.3 (5.2–20.4)	87.1 (25.5–296)	140 (40.1–489)
Model 2: adjusted for all covariates ^a	1 (reference)	1.8 (1.1–4.1)	2.0 (1.5–5.8)	4.3 (2.4–7.7)	8.3 (4.1–14.6)	36.2 (12.4–136)	96.3 (29.4–236)

Values are presented as OR (95% CI) unless otherwise stated. ^a Includes demographics (age and sex), smoking, comorbidities (hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease, peripheral arterial disease, and stroke), Killip class, anterior myocardial infarction, stent diameter, stent length and no-reflow.

tension, chronic kidney disease, hyperlipidemia, peripheral artery disease, cerebrovascular incidents, Killip class, stent diameters and lengths, anterior myocardial infarctions, and CHA₂DS₂VAsC scores ≥ 4 . In the multivariable regression analysis, using a model adjusted for the aforementioned parameters, smoking (OR = 1.20; 95% CI 1.12–1.29, $p = 0.007$), chronic kidney disease (OR = 1.57; 95% CI 1.51–1.64, $p < 0.001$), hyperlipidemia (OR = 1.07; 95% CI 1.0–1.37, $p = 0.004$), diabetes mellitus (OR = 1.75; 95% CI 1.36–1.96, $p < 0.001$), stent diameters (OR = 0.65; 95% CI 0.51–0.77, $p = 0.007$), stent lengths (OR = 1.08; 95% CI 1.03–1.16, $p < 0.001$), Killip class > 1 on admission (OR = 1.78; 95% CI 1.65–1.91, $p = 0.001$), anterior myocardial infarctions (OR = 1.41, 95% CI 1.32–1.79, $p = 0.014$), and CHA₂DS₂VAsC scores of ≥ 4 (OR = 1.64; 95% CI 1.54–1.71, $p < 0.001$) were independently associated with acute stent thrombosis.

In-hospital mortality and the occurrence of acute stent thrombosis in accordance with the CHA₂DS₂VAsC score are shown in Table 3. After adjusting for relevant confounders, including demographics (age and sex), smoking, comorbidities (hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease, peripheral arterial disease, and strokes), Killip class, anterior myocardial infarctions, stent diameters, stent lengths, and no reflow, patients with CHA₂DS₂VAsC scores of 2, 3, 4, 5, 6, and 7 had a 1.8 (95% CI 1.1–4.1), 2.0 (95% CI 1.5–5.8), 4.3 (95% CI 2.4–7.7), 8.3 (95% CI 4.1–14.6), 36.2 (95% CI 12.4–136), and 96.3 (95% CI 29.4–236, respectively) times higher risk of developing acute stent thrombosis. Notably, the occurrence of stent thrombosis and in-hospital mortality increased with every 1 point increase in the CHA₂DS₂VAsC score (Fig. 1).

A receiver ROC curve was drawn to establish the predictive accuracy of the CHA₂DS₂VAsC score, and the area under the ROC curve of the CHA₂DS₂VAsC score was calculated (Fig. 2). In terms of the development of acute stent thrombosis after the pPCI, the CHA₂DS₂VAsC score had an area under the curve of 0.720 (95% CI 0.67–0.77, $p < 0.001$) on the ROC curve. The ROC analysis showed that the best cut-off value of the CHA₂DS₂VAsC score to predict acute stent thrombosis was ≥ 4 , with 60% sensitivity and 73% specificity.

Discussion

The present study showed that the CHA₂DS₂VAsC score was a strong and independent predictor of acute stent thrombosis in patients with STEMI who underwent pPCI and that every 1-point increase in the CHA₂DS₂VAsC score increased the risk of acute stent thrombosis.

Acute stent thrombosis, which is also known as an abrupt vessel closure, is classified according to the time elapsed since stent implantation [9]. In a previous study, when compared with PCI in elective stenting, the incidence of acute stent thrombosis following pPCI was nearly 4-fold higher [2]. Previous studies [2, 4] have also reported elevated mortality rates and an increased incidence of cardiogenic shock in patients with acute stent thrombosis, thereby demonstrating its serious consequences. Randomized trials also demonstrated variability in the incidence of acute stent thrombosis, with the incidence of acute stent thrombosis varying from approximately 1.4% to as high as 3.4% [1, 2, 4]. In the present study, the inci-

Fig. 1. Absolute risk of acute stent thrombosis and in-hospital mortality events by CHA₂DS₂VASc score.

Fig. 2. ROC curve of the CHA₂DS₂VASc score. The best cut-off value of the CHA₂DS₂VASc score for the prediction of acute stent thrombosis was ≥ 4 with 60% sensitivity and 73% specificity.

dence of acute stent thrombosis was 3.9%, which was slightly higher than that found in the Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) trial [16] and How Effective Are Antithrombotic Therapies in Primary Percutaneous Coronary Intervention (HEAT-PPCI) study [17]. Multiple risk factors, such as diabetes mellitus, chronic renal failure, stenting in the acute setting or the elective setting, lesion-related factors, the number of affected vessels, the total stent length, and the presence of calcifications, have been implicated in the occurrence of acute stent thrombosis [18–23]. Data from the HORIZONS-AMI trial [16] showed that current smoking was more common in patients with acute stent thrombosis. In agreement with the findings of these studies, diabetes mellitus, smoking, stent lengths, anterior myocardial infarctions, and chronic renal failure were independent predictors of acute stent thrombosis in the multivariable logistic regression analysis in the present study.

The CHA₂DS₂VASc risk score was developed and validated mainly to estimate the risk of thromboembolisms in patients with nonvalvular atrial fibrillation [24]. However, previous studies have investigated the clinical application and importance of this score in various clinical settings. One study demonstrated that the CHA₂DS₂VASc risk score might be an independent predictor of no reflow in STEMI patients [25]. Other studies that evaluated the potential value of the CHA₂DS₂VASc score in predicting the risk of adverse cardiovascular outcomes among acute coronary syndrome patients showed that elevated CHA₂DS₂VASc scores were independently associated with increased in-hospital and long-term mortality [26–28]. Similarly, in our cohort, elevated CHA₂DS₂VASc scores were associated with an increased incidence of in-hospital mortality. In a recent study on the association between CHA₂DS₂VASc scores and acute stent thrombosis in patients with stable coronary artery disease and acute coronary syndrome, a score of 3 or more had an

independent predictive value for acute stent thrombosis [8]. We found similar results in our study with a larger cohort of only STEMI patients.

Although acute stent thrombosis is associated with an elevated risk of mortality, especially among STEMI patients treated with a pPCI, there are no guideline-based risk scoring systems available to predict the risk of acute stent thrombosis in STEMI patients following pPCI treatment. The CHA₂DS₂VASc score is a simple, inexpensive, and non-laboratory-dependent risk score model. As demonstrated in earlier studies, various components of the CHA₂DS₂VASc score, i.e., diabetes mellitus, age, and congestive heart failure, are risk factors for the development of acute stent thrombosis. Thus, given that these clinical entities are risk factors for the development of acute stent thrombosis, the CHA₂DS₂VASc score may predict the risk of acute stent thrombosis. As shown in the present study, the CHA₂DS₂VASc score may be a useful risk index for estimation of the risk of acute stent thrombosis in patients with STEMI following a pPCI. Notably, the occurrence of stent thrombosis increased with every 1-point increment in the CHA₂DS₂VASc score. The findings point to a potentially strong association between elevated CHA₂DS₂VASc scores and the occurrence of acute stent thrombosis.

In terms of the applicability of the CHA₂DS₂VASc score in daily clinical practice for acute stent thrombosis in STEMI patients, the data presented here may help health professionals to optimize dual antiplatelet therapy according to the patient's CHA₂DS₂VASc score. The use of high-potency P2Y₁₂ inhibitors, such as ticagrelor or prasugrel, in the acute setting rather than clopidogrel, which takes up to 6 h to become active, may be considered in STEMI patients with higher CHA₂DS₂VASc scores. A recent study reported that patients treated with cangrelor appeared to have a decreased risk of acute stent thrombosis compared to those treated with clopidogrel [29]. Thus, cangrelor may be administered to bring about acute platelet inhibition in STEMI patients with a high CHA₂DS₂VASc score. Further studies similar to HORIZONS-AMI and HEAT-PPCI are needed to determine

the optimum strategies to reduce stent thrombosis while managing the bleeding risk. Moreover, this study highlights the need for further work to assess whether the treatment benefit or risk with a high-potency dual antiplatelet therapy in terms of acute stent thrombosis differs depending on the CHA₂DS₂-VASc score.

Limitations of This Study

Our study had some limitations. First, as this was an observational, single-center, retrospective study, the results are not applicable to other populations. However, the study cohort was relatively large, and it represented daily practice in a real clinical setting. Second, the study might have some selection bias, although we included consecutive patients. Third, despite the use of a multivariable analysis, some residual unmeasured confounders of acute stent thrombosis may not have been evaluated. Fourth, we did not perform a comparative analysis between other well-known risk scores, such as the TIMI risk score, and the CHA₂DS₂VASc score.

Conclusion

The present study provided evidence that the CHA₂DS₂VASc risk score appeared to be an independent predictor of the risk of acute stent thrombosis in patients with STEMI treated with a pPCI. The results suggest that follow-up of patients with a CHA₂DS₂VASc risk score ≥ 4 should be performed more cautiously, as the risk of acute stent thrombosis among this patient group is high. However, as this was a retrospective study, definitive conclusions cannot be drawn about the value of the CHA₂DS₂VASc risk score based on the present findings. Further prospective, multicenter, and larger studies are needed to confirm our findings.

Disclosure Statement

All authors declare that they do not have any conflicts of interests.

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