Medical Principles and Practice

DOI: 10.1159/000495526
Received: 12/19/2017
Accepted: 11/18/2018
Published(online): 11/18/2018

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ISSN: 1011-7571 (Print), eISSN: 1423-0151 (Online)
https://www.karger.com/MPP
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The Association of the CHA_2DS_2VASc Score with Acute Stent Thrombosis in Patients with an ST Elevation Myocardial Infarction Who Underwent a Primary Percutaneous Coronary Intervention

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Keywords: CHA_2DS_2VASc score · ST elevation myocardial infarction · Acute stent thrombosis · Primary percutaneous coronary intervention

Short title: CHA_2DS_2VASc Score for Acute Stent Thrombosis

Significance of the Study

Acute stent thrombosis (ST) is a rare life-threatening complication of primary percutaneous coronary interventions (pPCIs). The CHA_2DS_2VASc score is a simple risk scoring system that can be calculated on admission before pPCI. Our findings provided evidence that the CHA_2DS_2VASc score may be used to identify high-risk patients with STEMI following a pPCI for acute ST.

Abstract

Objective: In this study, we aimed to determine the predictive value of the CHA_2DS_2VASc score for acute stent thrombosis (ST) in patients with an ST elevation myocardial infarction (STEMI) treated with a primary percutaneous coronary intervention (pPCI). ***Methods:*** This was a retrospective study conducted among 3,460 consecutive patients with STEMI patients who underwent pPCIs. Acute ST was considered as a definite or confirmed event in the presence of symptoms suggestive of acute coronary syndrome and angiographic confirmation of ST based on the diagnostic guidelines of the Academic Research Consortium. The ST was classified as acute if it developed within 24 h. ***Results:*** The mean CHA_2DS_2VASc score was 3.29 ± 1.73 in the ST group, whereas it was 2.06 ± 1.14 in the control group ($p < 0.001$). In multivariable logistic regression analysis, the CHA_2DS_2VASc score ≥ 4 was independently associated with acute ST (odds ratio [OR]: 1.64, 95% confidence interval [CI]: 1.54-1.71, $p < 0.001$). In a receiver operating characteristic curve analysis, the best cut-off value for the CHA_2DS_2VASc score was ≥ 4, with 60% sensitivity and 73% specificity. Of note, patients with a CHA_2DS_2VASc score of 4 had a 4.3 times higher risk of acute ST compared to those with CHA_2DS_2VASc score of 1. ***Conclusions:*** The CHA_2DS_2VASc score may be a significant independent predictor of acute ST in patients with STEMI treated with a pPCI. Therefore, the CHA_2DS_2VASc score may be used to assess the risk of acute ST in patients with STEMI following a pPCI.

Introduction

Acute stent thrombosis (ST) is a rare life-threatening complication of percutaneous coronary interventions (PCIs), with an estimated incidence of 0.5–2% in elective procedures [1]. The incidence of ST is much higher in patients with an ST elevation myocardial infarction (STEMI) treated with a primary PCI (pPCI) [2]. Several previous studies showed that acute ST was associated with elevated mortality rates and adverse cardiovascular outcomes, particularly among patients who underwent 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 ST in STEMI patients who were treated with a pPCI. The CHA_2DS_2VASc score is a guideline-based risk calculator that has been used to estimate the risk of thromboembolism in patients with non-valvular 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 CHA_2DS_2VASc 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 CHA_2DS_2VASc score and acute ST 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 CHA_2DS_2VASc scores in predicting acute ST in STEMI patients who underwent 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 onset of symptoms more than 12 h. Patients who developed acute ST after 24 h were also excluded. Finally, 3,460 patients were enrolled in the study. The demographic characteristics of patients, and related clinical information were obtained from the hospital's electronic database. The CHA_2DS_2VASc score of each patient was calculated. As all the patients underwent a pPCI, each patient had a CHA_2DS_2VASc 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 the study.

Laboratory Data and Echocardiographic Examination

Venous blood samples were obtained from all 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 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 the patients underwent coronary angiography via the femoral artery after admission and received 300 mg of acetylsalicylic acid and a 300–600 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 sec 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, the use of the glycoprotein IIb-IIIa inhibitor tirofiban (Aggrastat; 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 acute ST and thrombosis in myocardial infarction (TIMI) flow, before and after the procedure.

Definitions

Acute ST was defined as a definite or confirmed event in the presence of symptoms suggestive of acute coronary syndrome and angiographic confirmation of ST in accordance with the guidelines of the Academic Research Consortium [9]. In addition, based on the elapsed time since stent implantation, ST was classified as acute if it developed within 24 h. All patients who developed acute ST underwent a re-intervention after the diagnosis. STEMI was defined as i) at least two 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–V3 and/or >1 mm in the other leads in the absence of left ventricular hypertrophy or left bundle branch block); ii) prolonged (> 30 min) typical chest pain at rest; and iii) 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 mmHg and/or diastolic pressure > 90 mmHg on at least two separate measurements during hospitalization [12]. Diabetes mellitus was defined as taking oral anti-diabetic 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 taking lipid-lowering medications upon presentation [14]. Chronic kidney disease was considered an estimated glomerular filtration rate< 60 mL/min/1.73 m^2 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 mean ± standard deviation. The Kolmogorov–Smirnov test was conducted to test for normality of data. Continuous variables with normal distributions were compared using an independent sample *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 chi-square 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 ST. The odds ratio (OR) indicated the relative risk of acute ST in the groups.

In the multivariable analysis, a forward hierarchical logistic regression model was used. The OR indicated the relative risk of acute ST in each CHA_2DS_2VASc subgroup as compared with that in the lowest-risk subgroup (CHA_2DS_2VASc score = 1). In the multivariable models, confounders in a bivariate analysis as predictors of acute ST were considered. Two models were generated to indicate the impact of potential confounders on the association between the CHA_2DS_2VASc score and acute ST. One model was unadjusted, whereas the other was adjusted for all confounders, including demographics (age and sex), smoking, co-morbidities (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 CHA_2DS_2VASc score were assessed and found to be appropriate. The Hosmer–Lemeshow statistic of the logistic model was 0.30. A two-tailed *p* value of < 0.05 was considered to be statistically significant, and 95% confidence intervals (CIs) are presented for all ORs. 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 two groups: an ST group and a control group. In total, 136 (3.9%) patients developed acute ST within 24 h. The baseline characteristics and laboratory findings, including the angiographic features and interventional outcomes of the patients with and without ST, are presented in Table 1. Patients with acute ST tended to be older and male as compared with those without acute ST ($p < 0.05$ for all). The frequencies of diabetes mellitus, hypertension, hyperlipidemia, smoking, chronic kidney disease, cerebrovascular incidents, and previous stent implantation were higher in the ST group ($p < 0.05$ for all). On admission, an anterior myocardial infarction was more common in patients with ST than in non-ST patients ($p = 0.031$). The laboratory findings revealed that the patients with ST had higher levels of creatinine and lower glomerular filtration rates as compared with those of the non-ST patients

(p < 0.001 and p < 0.001, respectively). After the intervention, the TIMI blood flow was lower in the patients with ST as compared to those without ST, and tirofiban was commonly used in the patients with ST (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 ST group, the mean CHA_2DS_2VASc score was 3.29 ± 1.73, whereas the mean score in the control group was 2.06 ± 1.14 (p < 0.001). Of note, there was a high frequency of elevated CHA_2DS_2VASc scores in the ST group.

Table 2 presents the results of the univariable and multivariable analyses. In the univariable regression analysis, the following factors were predictors of acute ST: age, female sex, smoking, diabetes mellitus, hypertension, chronic kidney disease, hyperlipidemia, peripheral artery disease, cerebrovascular incidents, Killip class, stent diameters and lengths, anterior myocardial infarctions, and CHA_2DS_2VASc score of ≥ 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 CHA_2DS_2VASc scores of ≥4 (OR: 1.64, 95% CI: 1.54-1.71, p < 0.001) were independently associated with acute ST.

In-hospital mortality and the occurrence of acute ST in accordance with the CHA_2DS_2VASc score are shown in Table 3. After adjusting for relevant confounders, including demographics (age and sex), smoking, co-morbidities (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 CHA_2DS_2VASc scores of 2, 3, 4, 5, 6, and 7 had an 1.8 times higher risk (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), of the development of acute ST. Notably, the occurrence of ST and in-hospital mortality increased with every 1 point increase in the CHA_2DS_2VASc score (Fig. 1).

A receiver operating characteristic (ROC) curve was drawn to establish the predictive accuracy of the CHA_2DS_2VASc score, and the area under the ROC curve of the CHA_2DS_2VASc score was calculated (Fig. 2). In terms of the development of acute ST after the pPCI, the CHA_2DS_2VASc score had an area under the curve value 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 CHA_2DS_2VASc score to predict acute ST was ≥ 4, with 60% sensitivity and 73% specificity.

Discussion

The present study showed that the CHA_2DS_2VASc score was a strong and independent predictor of acute ST in patients with STEMI who underwent pPCI, and that every 1-point increase in the CHA_2DS_2VASc score increased the risk of acute ST.

Acute ST, 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 PCIs in elective stenting, the incidence of acute ST following pPCIs was nearly four-fold higher [2]. Previous studies [2, 4] also reported elevated mortality rates and an increased incidence of cardiogenic shock in patients with acute ST, thereby demonstrating its serious consequences. Randomized trials also demonstrated variability in the incidence of acute ST, with the incidence of acute ST varying from approximately 1.4% to as high as 3.4% [1, 2, 4]. In the present study, the incidence of acute ST 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 stetting or elective setting, lesion-related factors, number of affected vessels, total stent length, and the presence of calcifications, have been implicated in the occurrence of acute ST [18-23]. Data from the HORIZONS-AMI trial [16] showed that current smoking was more common in patients with acute ST. In common with the findings of these studies, diabetes mellitus, smoking, stent lengths, anterior myocardial infarctions, and chronic renal failure were independent predictors of acute ST in the multivariable logistic regression analysis in the present study.

The CHA_2DS_2VASc risk score was developed and validated mainly to estimate the risk of thromboembolisms in patients with non-valvular 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 CHA_2DS_2VASc risk score might be an independent predictor of no-reflow in STEMI patients [25]. Other studies that evaluated the potential value of the CHA_2DS_2VASc score in predicting the risk of adverse cardiovascular outcomes among acute coronary syndrome patients showed that elevated CHA_2DS_2VASc scores were independently associated with increased in-hospital and long-term mortality [26-28]. Similarly, in our cohort, elevated CHA_2DS_2VASc scores were associated with an increased incidence of in-hospital mortality. In a recent study on the association between CHA_2DS_2VASc scores and acute ST in patients with stable coronary artery disease and acute coronary syndrome, a score of 3 or more had independent predictive value for acute ST [8]. We found similar results in our study with a larger cohort of only STEMI patients.

Although acute ST 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 ST in STEMI patients following pPCI treatment. The CHA_2DS_2VASc score is a simple, inexpensive, and non-laboratory-dependent risk score model. As demonstrated in earlier studies, various components of the CHA_2DS_2VASc score, namely diabetes mellitus, age, and congestive heart failure, are risk factors for the development of acute ST. Thus, given that these clinical entities are risk factors for the development of acute ST, the CHA_2DS_2VASc score may predict the risk of acute ST. As shown in the present study, the CHA_2DS_2VASc score may be a useful risk index for estimation of the risk of acute ST in patients with STEMI following a pPCI. Notably, the occurrence of ST increased with every 1-point increment in the CHA_2DS_2VASc score. The findings point to a potentially strong association between elevated CHA_2DS_2VASc scores and the occurrence of acute ST.

In terms of the applicability of the CHA_2DS_2VASc score in daily clinical practice for acute ST in STEMI patients, the data presented here may help health professionals to optimize dual anti-platelet therapy according to a patient's CHA_2DS_2VASc 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 CHA_2DS_2VASc scores. A recent study reported that patients treated with cangrelor appeared to have a decreased risk of acute ST as compared with those treated with clopidogrel [29]. Thus, cangrelor may be administered to bring about acute platelet inhibition in STEMI patients with a high CHA_2DS_2VASc score. Further studies similar to HORIZONS-AMI and HEAT-PPCI are needed to determine the optimum strategies to reduce ST while managing 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 ST differs depending on the CHA_2DS_2-VASc score.

Limitations of the Study

Our study had some limitations. First, as it was an observational, single-center, and 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 ST 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 CHA_2DS_2VASc score.

Conclusion

The present study provided evidence that the CHA_2DS_2VASc risk score appeared to be an independent predictor of the risk of acute ST in patients with STEMI treated with a pPCI. The results suggest that follow-up of patients with a CHA_2DS_2VASc risk score ≥ 4 should be performed more cautiously, as the risk of acute ST among this patient group is high. However, as this was a retrospective study, definitive conclusions cannot be drawn about the value of the CHA_2DS_2VAScrisk score based on the present findings. Further prospective, multicenter, and larger studies are needed to confirm our findings.

Conflict of Interest

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

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

	Control group, n : 3324	Acute stent thrombosis, n: 136	p value
Age	56 ± 12	61 ± 13	0.002
Male, gender	2794 (84.1)	104 (76.5)	0.018
Body mass index	28.1 ± 3.8	27.7 ± 3.6	0.719
History			
Hypertension	1020 (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	1458 (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_2DS_2-VASc score (mean ± SD)	2.06 ± 1.14	3.29 ± 1.73	<0.001
CHA_2DS_2-VASc score (median, 25-75 percentile)	2.0 (1.0 – 3.0)	3.0 (2.0 – 4.0)	<0.001
CHA_2DS_2-VASc score=1	1370 (41.2)	22 (16.2)	<0.001
CHA_2DS_2-VASc score=2	947 (28.5)	32 (23.5)	0.208
CHA_2DS_2-VASc score=3	575 (17.3)	23 (16.9)	0.907
CHA_2DS_2-VASc score=4	327 (9.8)	27 (19.9)	<0.001
CHA_2DS_2-VASc score=5	96 (2.9)	16 (11.8)	<0.001
CHA_2DS_2-VASc score=6	5 (0.2)	7 (5.1)	<0.001
CHA_2DS_2-VASc score=7	4 (0.1)	9 (6.6)	<0.001
At admission			
Systolic blood pressure (mm Hg)	129 ± 27	126 ± 29	0.484
Killip class ≤2	3089 (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, hours	4.3 ± 4.7	4.6 ± 5.0	0.661
Door to balloon time, minutes	20.0 ± 9.9	19.3 ± 9.2	0.589
Anterior myocardial infarction (%)	1448 (43.6)	72 (52.9)	0.031
Admission laboratory variables			
Admission creatine kinase-MB (ng/mL)	95 ± 78	98 ± 75	0.228
Peak creatine kinase-MB (ng/mL)	161 ± 135	167 ± 123	0.106
Admission troponin I (ng/dL)	16 ± 19	18 ± 18	0.231
Peak troponin I (ng/dL)	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
Vessel stenosis (>50%)			
1 vessel	1712 (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
TIMI blood flow before intervention			
TIMI 0	1828 (55.0)	66 (48.5)	0.138
TIMI I	178 (5.4)	10 (7.4)	0.314
TIMI II	347 (10.3)	17 (12.5)	0.443
TIMI III	971 (29.2)	43 (31.6)	0.546
TIMI blood flow after intervention			

TIMI 0	196 (5.9)	6 (4.4)	0.469
TIMI I	500 (15.0)	30 (22.1)	0.026
TIMI II	518 (15.6)	22 (16.2)	0.852
TIMI III	2110 (63.5)	78 (57.4)	0.147
Intervention type			
PTCA and stenting	2872 (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
Stent type			
Drug eluting stent	3050 (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
>28 mm	378 (11.4)	16 (11.8)	0.888
Minimal stent diameter (mm)	3.2 ± 1.0	3.0 ± 0.7	0.365
> 3 mm	377 (11.3)	11 (8.1)	0.239
Treatment			
ACEI or ARB	3110 (93.6)	128 (94.1)	0.795
Tirofiban	1568 (47.2)	114 (83.8)	<0.001
Beta blockers	2882 (86.7)	116 (85.3)	0.636
Statins	2948 (88.7)	126 (92.6)	0.151
Diuretics	334 (10.0)	20 (14.7)	0.079
Insulin treatment	1048 (31.5)	52 (38.2)	0.100
Oral antihyperglycemic agents	1276 (38.4)	66 (48.5)	0.017
In-hospital mortality	126 (3.8)	10 (7.4)	0.036

Abbreviations: PTCA, percutaneous transluminal coronary angioplasty; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker. Continuous variables are presented as mean±SD; nominal variables presented as frequency

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_2DS_2-VASc score ≥ 4	<0.001	1.87 (1.74 – 2.11)	CHA_2DS_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. OR, Odds ratio; CI, confidence interval.

Table 3 In-hospital events rate and logistic regression models for mortality and acute stent thrombosis according to CHA_2DS_2-VASc score

	CHA_2DS_2-VASc						
	1 (n=1392)	2 (n=979)	3 (n=598)	4 (n=352)	5 (n=112)	6 (n=12)	7 (n=13)
In-hospital mortality, number of deaths	10	22	47	34	17	2	4
Mortality, %	0.7	2.2	7.9	9.7	15.2	16.7	30.8
Mortality, OR (%95CI) 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, number of events	22	32	23	27	16	7	9
Event rate ,%	1.6	3.3	3.8	7.6	14.3	58.3	69.3
Events, OR (%95CI) 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)

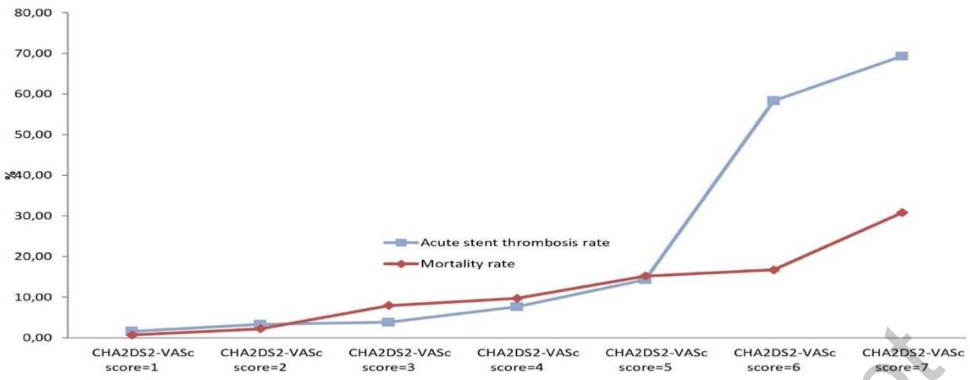
[a] Includes demographics (age, sex), smoking, comorbidities (hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease, peripheral arterial disease, stroke); Killip class, anterior myocardial infarction, stent diameter, stent length and no-reflow

Figure Legend

Figure 1: The absolute risk of acute stent thrombosis (ST) and in-hospital mortality events according to CHA_2DS_2VASc score.

Figure 2: The receiver operating characteristic curve (ROC) curve of the CHA_2DS_2VASc score. The best cut-off value of the CHA_2DS_2VASc score to predict the acute stent thrombosis (ST) was ≥ 4 with 60% sensitivity and 73% specificity.

Abbreviations: ST; stent thrombosis, ROC; receiver operating characteristic curve



80,00
70,00
60,00
50,00
%
40,00
30,00
20,00
10,00
0,00
Acute stent thrombosis rate
Mortality rate
CHA2DS2-VASc score=1
CHA2DS2-VASc score=2
CHA2DS2-VASc score=3
CHA2DS2-VASc score=4
CHA2DS2-VASc score=5
CHA2DS2-VASc score=6
CHA2DS2-VASc score=7

Fig. 1

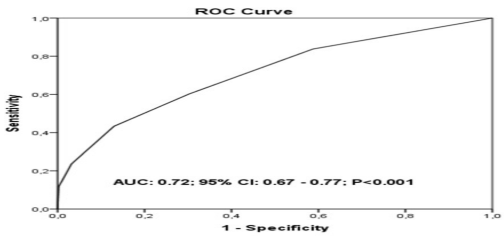

ROC Curve
1,0
0,8
0,6
0,4
0,2
0,0
Sensitivity
AUC: 0.72; 95% CI: 0.67 - 0.77; P<0.001
0,0
0,2
0,4
0,6
0,8
1,0
1 - Specificity

Fig. 2