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Mohamed Abd El-Kader
MD, Department of Cardiology, Faculty of Medicine, Benha University, Benha, Egypt

Ahmed Mostafa Bahgat Hamed
MSc, Department of Cardiology, Faculty of Medicine, Benha University, Benha, Egypt

Hesham Khaled Rasheed
MD, Department of Cardiology, Faculty of Medicine, Benha University, Benha, Egypt

Shereen Ibrahim Farag
MD, Department of Cardiology, Faculty of Medicine, Benha University, Benha, Egypt

Corresponding Author:
Ahmed Mostafa Bahgat Hamed
MSc, Department of Cardiology, Faculty of Medicine, Benha University, Benha, Egypt

Prediction of angiographic (TIMI GRADE) blood flow using the novel CHA2DS2-VASC-HSF score in patients with STEMI

Mohamed Abd El-Kader, Ahmed Mostafa Bahgat Hamed, Hesham Khaled Rasheed and Shereen Ibrahim Farag

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Abstract
Background: The CHA2DS2-VASc-HSF score, a novel risk stratification tool, has been proposed to predict angiographic outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PPCI). This study aimed to evaluate the predictive value of the CHA2DS2-VASc-HSF score in relation to the angiographic Thrombolysis in Myocardial Infarction (TIMI) blood flow grade.
Methods: This cross-sectional study included 100 patients with acute STEMI admitted to the Cardiology Department at Benha University Hospitals and Health Insurance Hospitals from November 2022 to November 2023. All patients underwent PPCI within 12 hours of symptom onset. The CHA2DS2-VASc-HSF score was calculated for each patient. Angiographic TIMI flow grades were assessed post-PPCI, and the association between CHA2DS2-VASc-HSF scores and TIMI grades was analyzed.
Results: Among the 100 STEMI patients, 16 experienced the no-reflow phenomenon, while 84 maintained normal or slow coronary blood flow. The CHA2DS2-VASc-HSF score was significantly higher in the no-reflow group compared to the normal/slow flow group (4.44±1.82 vs. 2.44±1.57, $p < 0.001$). The CHA2DS2-VASc-HSF score demonstrated the highest predictive accuracy for no-reflow with an area under the curve (AUC) of 0.868, sensitivity of 93.75%, and specificity of 66.67% at a cutoff value >2. Multivariate logistic regression analysis identified CK-MB levels, Killip classification, multivessel disease, stent length, and tirofiban infusion as independent predictors of no-reflow.
Conclusion: The CHA2DS2-VASc-HSF score is a robust predictor of the no-reflow phenomenon in STEMI patients undergoing PPCI. Its high sensitivity and moderate specificity suggest its potential utility in clinical practice to identify high-risk patients and tailor therapeutic strategies accordingly.

Keywords: STEMI, CHA2DS2-VASc-HSF score, no-reflow, TIMI flow grade, primary PCI

Introduction
ST-segment elevation myocardial infarction (STEMI) represents a prevalent and severe manifestation of coronary artery disease, wherein primary percutaneous coronary intervention (PPCI) is now the dominant therapeutic approach. Despite this, the occurrence of compromised microvascular function immediately post-PPCI, as determined by the IMR, exhibits a significant correlation with peak creatine kinase (CK) levels at initial presentation, subsequent left ventricular performance at a 3-month interval, and the extent of functional recuperation over the same period, as measured by wall motion scoring and myocardial salvage metrics [1].
Mitigating the mortality associated with myocardial infarction is predominantly contingent upon prompt diagnosis and the implementation of efficacious treatment modalities. A critical component of myocardial infarction management is the swift and proactive initiation of effective coronary reperfusion therapy. STEMI, recognized as the most severe manifestation of acute coronary syndrome, underscores the urgency of such interventions [2].
The TIMI (Thrombolysis in Myocardial Infarction) Coronary Flow Grading Scale was formulated to provide a standardized and consistent approach to documenting epicardial perfusion observed during coronary angiography, ensuring a uniform methodology in the assessment of coronary blood flow.

TIMI flow grade classification scheme has been widely used to assess coronary blood flow in acute coronary syndromes [3].

In certain instances, even when the culprit lesion is successfully reopened, the ischemic myocardium fails to achieve adequate perfusion, a condition termed the NRP. This phenomenon serves as an independent prognosticator of both long- and short-term mortality and morbidity, thereby substantially reducing the efficacy of PPCI in STEMI patients. The absence of a well-defined risk assessment protocol leads to the occurrence of NRP in up to 60% of STEMI cases. Consequently, there is a critical need to develop a straightforward and efficient risk stratification method for predicting NRP [4].

The CHA2DS2-VASc scoring system, which represents an advancement of the original CHADS2 score, has been extensively utilized as a predictive tool for thromboembolic risk stratification in individuals with non-valvular atrial fibrillation. This score plays a critical role in informing clinical decisions concerning the initiation of anticoagulant or antiplatelet therapy. The elements constituting these scores are intricately linked to atherosclerosis, vascular spasm, and microvascular dysfunction-factors that coincide with the risk determinants of the NRP. The CHA2DS2-VASc score is calculated by assigning a single point for the presence of congestive heart failure, hypertension, diabetes mellitus, age between 65 and 74 years, female gender, and vascular conditions such as a history of myocardial infarction, peripheral artery disease, or complex aortic plaques. Furthermore, individuals aged 75 years or older, as well as those with a prior history of transient ischemic attack or stroke, are allocated two points each within this scoring framework [5].

A recently developed scoring system, known as the CHA2DS2-VASc-HSF score, introduces an innovative approach by integrating three additional parameters into the pre-existing CHA2DS2-VASc framework: smoking status (S), hyperlipidemia (H), and a family history of coronary artery disease (F). This enhancement aims to provide a more comprehensive assessment by including these supplementary risk factors. Moreover, the gender component has been revised, substituting male sex for the previously included female sex [6].

The purpose of this study was to investigate the use of CHA2DS2- VASc-HSF score to predict Angiographic TIMI grade blood flow in patients with STEMI treated by PPCI.

Patients and Methods

This cross-sectional study utilized data from 100 patients admitted to the Cardiology Department of Benha University Hospitals and Health Insurance Hospitals, spanning from November 2022 to November 2023. These patients were diagnosed with acute STEMI and underwent primary PCI within 12 hours of symptom onset.

Informed written consent was secured from each patient after providing a detailed explanation of the study's purpose. Each participant was assigned a confidential code number to ensure anonymity. The study was conducted following approval from the Research Ethics Committee of the Faculty of Medicine at Benha University.

Based on the American College of Cardiology and European Society of Cardiology guidelines for the diagnosis of STEMI, the inclusion criteria were established. The criteria for inclusion in this study were as follows: the presence of characteristic angina that persisted for more than 30 minutes and was not entirely alleviated by nitroglycerin, new ST-segment elevation in at least two contiguous leads (Defined as ≥0.2 mV in men or ≥0.15 mV in women for leads V2 to V3, or ≥1 mm (0.1 mV) in other leads), or the presence of a new left bundle branch block. In addition, it was imperative to have elevated myocardial injury markers, such as troponin or CK-MB, that exceeded the normal upper limit within 12 hours of the onset of symptoms [21].

Exclusion criteria

Patients' refusal, non-STEMIs, spontaneous coronary artery dissection, significant arrhythmias, hemodynamic instability.

The following evaluations and procedures were administered to all patients:

Patient History

A detailed patient history was taken. We also recorded routine laboratory investigations, kidney function testes, cardiac enzymes as CKMB, CK dephosphorylates creatine phosphate to creatine. The laboratory data encompassed several parameters: hyperlipidemia, defined by a total cholesterol (TC) level exceeding 200 mg/dL or a LDL-C level above 160 mg/dL; hemoglobin levels, with reference ranges of 130–172 g/L for men and 110–150 g/L for women; creatinine concentrations, ranging from 59–104 μmol/L in men and 45–84 μmol/L in women; eGFR between 90–120 ml/min/1.73m²; HbA1c within 4.8–6.0%; cTnI levels from 0.01–0.23 ng/L; CK-MB levels spanning 2.0–7.2 ng/L; and LVEF ranging from 50–70% [4].

Full clinical Examination

Encompassing an assessment of vital signs, including heart rate, where sinus tachycardia was identified as a heart rate exceeding 100 bpm. Patients often reported a newfound perception of their heartbeat that had not been previously experienced. Additionally, diastolic and systolic blood pressure measurements, as well as oxygen saturation levels, were meticulously recorded.

Investigations

A 12-lead ECG was recorded upon arrival, immediately following angioplasty, and at subsequent intervals of 3, 6, 12, 24, and 48 hours. The electrocardiogram was evaluated for rate, rhythm, and conduction abnormalities. To evaluate the coronary arteries, coronary angiography was executed, and quantitative analysis was subsequently performed using the Philips Inturis Suite R2.2 software, meticulously managed by the supervising radiographer. At the time of STEMI diagnosis in the emergency department, all patients were administered 300 mg of aspirin and 600 mg of clopidogrel. Subsequent coronary angiography was conducted, with PPCI predominantly executed through the radial artery, which served as the preferred access route. Heparin was promptly administered at a dose of 80–100 units per kilogram of body weight.

CHA2DS2-VASc Score Calculation

The CHA2DS2-VASc score was calculated by aggregating the numerical values assigned to each pertinent risk factor. These factors encompass congestive heart failure (1 point), hypertension (1 point), age 75 years or older (2 points), diabetes mellitus (1 point), a prior history of stroke,

transient ischemic attack, or thromboembolism (2 points), vascular disease (including antecedent myocardial infarction, peripheral arterial disease, or the presence of complex aortic plaques) (1 point), age between 65 and 74 years (1 point), and female sex (1 point). Congestive heart failure was determined based on a documented history of heart failure [7]. Hypertension was deemed present if the patient had a documented history of the condition or was currently undergoing antihypertensive treatment [8]. Diabetes mellitus was recognized based on either a prior diagnosis or the administration of insulin or oral hypoglycemic agents at the time of admission [9]. In the formulation of the CHA2DS2-VASc score, thromboembolic events were exclusively accounted for, with a prior history of stroke or transient ischemic attack meticulously corroborated through the patient's documented clinical history. PAD was stringently defined by the presence of a stenosis measuring 50% or more within non-coronary arterial vessels [10].

CHA2DS2-VASc-HSF score

The CHA2DS2-VASc-HSF score for each patient was meticulously calculated by allocating one point to each of the following clinical parameters: age ranging from 65 to 74 years, male gender, hypertension, congestive heart failure, diabetes mellitus, and vascular pathologies (Encompassing a history of myocardial infarction, complex aortic plaque formation, or peripheral arterial disease). Two points were allocated for patients aged 75 years or older and for those with a history of stroke or transient ischemic attack. Additional points were given for smoking, hyperlipidemia, and a family history of coronary artery disease [4].

Killip Grades

Class I consisted of patients who exhibited no clinical indications of HF. Class II included individuals with mild to moderate HF, which was evidenced by the presence of wet rales affecting less than half of the total area of both pulmonary fields. In Class III, patients exhibited manifestations of advanced HF, characterized by extensive wet rales occupying more than 50% of both lung fields, thereby heightening the risk for acute pulmonary edema. Class IV was reserved for patients in a state of cardiogenic shock [11].

TIMI Flow Grade

Blood flow was assessed using the TIMI flow grading system, categorized as follows: Grade 0 indicates an absence of antegrade blood flow through the occluded vessel (No perfusion); Grade 1 reflects minimal passage of contrast agent through the stenosis, insufficient to fill the distal coronary bed (Penetration without perfusion); Grade 2 is characterized by the contrast agent filling the distal coronary bed, albeit at a reduced rate (Partial perfusion); and Grade 3 denotes rapid and complete filling of the distal coronary bed by the contrast agent (Complete perfusion) [12]. The sensitivity, specificity and correlation between the CHA2DS2- VASc-HSF scores and Angiographic blood flow according to TIMI score was established.

Sample Size Calculation

This investigation draws upon the study by Mahfouz *et al.*, 2021, utilizing Epi Info STATCALC for sample size determination under specific statistical assumptions: a two-sided 95% confidence interval, an 80% statistical power, and a 5% margin of error. The calculated odds ratio was 1.115. Consequently, the final maximum sample size, as derived from the Epi Info output, was set at 100 subjects.

Statistical analysis

Statistical evaluations were carried out using SPSS v28 (IBM©, Armonk, NY, USA). For quantitative parametric measures, values were expressed as the mean and SD and examined via the unpaired Student t-test. Quantitative non-parametric measures were depicted as median and IQR and subjected to analysis with the Mann-Whitney U test. Qualitative variables were displayed as frequency and percentage and scrutinized using either the Chi-square test or Fisher's exact test, as deemed appropriate. Logistic regression was also used to estimate the relationship between a dependent variable and one (Univariate) or more independent variables (Multivariate). The precision of odds ratios (OR) was estimated using a 95% CI, with a p-value considered significant if <0.05 at a 95% confidence level.

Results

The present investigation encompassed a cohort of 100 patients diagnosed with STEMI, who were subsequently stratified into two distinct groups based on the occurrence of no-reflow phenomena: the no-reflow group (n=16) and the normal/slow flow group (n=84).

The no-reflow group exhibited significantly elevated values for age, weight, and BMI when compared to the normal/slow flow group (p<0.05). In contrast, variables such as sex, height, and family history showed no statistically significant differences between the two groups. Regarding the medical history, hypertension, diabetes mellitus, history of heart failure, history of TIA or stroke, vascular disease and hyperlipidemia were significantly higher in no-reflow group compared to the normal/slow flow group (p<0.05), whereas there was an insignificant difference between the studied groups regarding smoking. There were insignificant differences between the studied groups regarding the vital signs examinations (SBP, DBP and HR). Table 1

Table 1: Baseline characteristics, Medical history and Vital signs of the studied groups

	Total (n=100)	No-reflow group (n=16)	Normal/slow flow group (n=84)	P value
Age (Years)	56.02±11.5	72.8±5.1	52.8±9.45	<0.001*
Sex	63 (63%)	9 (56.25%)	54 (64.29%)	0.743
Weight (Kg)	63.6±4.48	66.2±5.33	63.1±4.14	0.010*
Height (m)	1.6±0.04	1.63±0.04	1.6±0.04	0.669
BMI (Kg/m^2)	23.9±2.11	25.1±2.69	23.7±1.92	0.017*
Family history	18 (18%)	5 (31.25%)	13 (15.48%)	0.250
Medical history				
Hypertension	41 (41%)	12 (75%)	29 (34.52%)	0.004*
Diabetes mellitus	27 (27%)	9 (56.25%)	18 (21.43%)	0.010*

History of heart failure	4 (4%)	3 (18.75%)	1 (1.19%)	0.012*
History of stroke/ TIA	6 (6%)	4 (25%)	2 (2.38%)	0.006*
Vascular disease	17 (17%)	7 (43.75%)	10 (11.9%)	0.006*
Hyperlipidemia	31 (31%)	9 (56.25%)	22 (26.19%)	0.037*
Smoking	47 (47%)	9 (56.25%)	38 (45.24%)	0.592
Vital signs				
SBP (mmHg)	124.4±9.9	126.9±11.9	123.9±9.44	0.276
DBP (mmHg)	75.3±9.26	78.1±9.11	74.8±9.25	0.184
HR (beats/min)	85.04±9.34	86.4±7.7	84.8±9.63	0.516

BMI: body mass index, TIA: transient ischemic attack, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate*: statistically significant as P value <0.05.

Regarding the laboratory investigations, serum creatinine and eGFR were significantly worse in no reflow group compared to the normal group (<0.001, 0.001). Other laboratory findings (Hb, PLT, WBCs, glucose, HbA1C, ALT and AST) were insignificantly different between both groups and there were insignificant differences between the studied groups regarding the findings of their lipid profile (total cholesterol, triglycerides, HDL, and LDL). Table 2

Table 2: Laboratory examinations and Lipid profile of the studied groups

		Total (n=100)	No-reflow group (n=16)	Normal/slow flow group (n=84)	P value
Hb (g/dL)	Mean ±SD	12.7±1.21	12.9±1.19	12.6±1.22	0.278
	Range	10.5 - 14.5	10.6 - 14.5	10.5 - 14.5	
PLT (*10^9/L)	Mean ±SD	300.9±85.7	316.8±85.3	298±86.01	0.425
	Range	150 - 448	166 - 448	150 - 448	
WBCs (*10^9/L)	Mean ±SD	7.4±1.79	7.9±2.04	7.3±1.73	0.157
	Range	4.5 - 10.4	4.6 - 10.4	4.5 - 10.3	
Glucose (mg/dL)	Mean ±SD	94.7±15.72	95.6±14.3	94.5±16.05	0.804
	Range	70 - 120	74 - 116	70 - 120	
HbA1C (%)	Mean ±SD	5.5±0.64	5.7±0.6	5.5±0.64	0.221
	Range	4.5 - 6.5	4.7 - 6.5	4.5 - 6.5	
Serum creatinine (mg/dL)	Mean ±SD	0.79±0.19	0.97±0.39	0.76±0.09	<0.001*
	Range	0.32 - 1.7	0.32 - 1.7	0.6 - 0.89	
eGFR (ml/min/1.73 m^2)	Mean ±SD	70.1±6.98	75.4±8.73	69.1±6.17	0.001*
	Range	60 - 89	63 - 89	60 - 80	
ALT (U/L)	Mean ±SD	32.98±8.01	29.8±7.52	33.6±8.0	0.084
	Range	20 - 45	21 - 45	20 - 45	
AST (U/L)	Mean ±SD	27.1±7.75	27.0±8.2	27.1±7.71	0.964
	Range	15 - 40	15 - 40	15 - 40	
Lipid profile					
Total cholesterol (mg/dL)	Mean ±SD	143.9±14.9	142.0±14.2	144.3±15.1	0.569
	Range	120 - 169	121 - 164	120 - 169	
Triglycerides (mg/dL)	Mean ±SD	160.0±11.1	156.8±11.7	160.6±10.88	0.198
	Range	140 - 180	141 - 179	140 - 180	
HDL (mg/dL)	Mean ±SD	51.7±6.8	49.4±6.14	52.2±6.86	0.131
	Range	40 - 65	40 - 60	40 - 65	
LDL (mg/dL)	Mean ±SD	77.9±18.41	73.8±15.53	78.7±18.89	0.324
	Range	50 - 110	51 - 94	50 - 110	

Hb: hemoglobin, PLT: platelets, WBCs: white blood cells, HbA1C: glycosylated hemoglobin, eGFR: estimated glomerular filtration rate, ALT: alanine aminotransferase, AST: aspartate aminotransferase, HDL: high-density lipoprotein, LDL: low density lipoprotein *: statistically significant as P value <0.05.

Cardiac biomarkers, specifically Troponin I and CK-MB, exhibited a statistically significant elevation in the no-reflow cohort as compared to the normal/slow flow cohort (P=0.001, 0.005, and <0.001, respectively). The EF demonstrated a pronounced reduction within the no-reflow group relative to the normal/slow flow group (P=0.001). Furthermore, a significant variance in Killip class distribution was observed between the groups; Class 1 occurrence was notably diminished in the no-reflow group versus the normal/slow flow group (25% vs. 67.86%), whereas the prevalence of Class >1 was substantially higher in the no-reflow group (75% vs. 32.14%) (p<0.001). Additionally, the interval from the onset of pain to balloon inflation was significantly protracted in the no-reflow group compared to the normal/slow flow group (P=0.004). Table 3

Table 3: Cardiac biomarkers Ejection fraction and Killip class and Pain-to-balloon time of the studied groups

		Total (n=100)	No-reflow group (n=16)	Normal/slow flow group (n=84)	P value
Troponin I (ng/L)	Mean ±SD	0.06±0.05	0.13±0.08	0.05±0.03	0.001*
	Range	0 - 0.29	0.01 - 0.29	0 - 0.2	
	Median (IQR)	0.05 (0.03-0.08)	0.13 (0.05-0.18)	0.05 (0.03-0.07)	
CK-MB (ng/L)	Mean ±SD	4.96±1.34	5.81±1.51	4.8±1.25	0.005*
	Range	2.7 - 8	4 - 8	2.7 - 7	

EF (%)	Mean ±SD	56.6±4.93	52.81±3.41	57.32±4.86	0.001*
	Range	48 - 65	48 - 59	50 - 65	
Killip class	1	61 (61%)	4 (25%)	57 (67.86%)	< 0.001*
	>1	39 (39%)	12 (75%)	27 (32.14%)	
Pain-to-balloon time (hr.)	Mean ±SD	4.05±1.54	5.06±1.95	3.86±1.38	0.004*
	Range	2 - 8	2 - 8	2 - 6	

IQR: interquartile range, CK-MB: creatine kinase-myocardial band, NT-pro BNP: NT-pro brain natriuretic peptide, *: statistically significant as P value <0.05. EF: ejection fraction

In contrast to the normal or slow flow groups, the no-reflow cohort demonstrated significantly higher CHADS2, CHA2DS2-VASc, and CHA2DS2-VASc-HSF scores, with the differences reaching statistical significance (P=0.001, <0.001, and 0.001, respectively). Table 4

Table 4: Clinical scores of the studied groups

		Total (n=100)	No-reflow group (n=16)	Normal/slow flow group (n=84)	P value
$CHADS_2$ score	Mean ±SD	1.61±0.58	2.06±0.77	1.52±0.5	0.001*
	Range	1 - 3	1 - 3	1 - 2	
CHA_2DS_2-VASc score	Mean ±SD	1.57±0.9	2.56±1.46	1.38±0.6	<0.001*
	Range	1 - 5	1 - 5	1 - 3	
CHA_2DS_2-VASc-HSF score	Mean ±SD	2.76±1.76	4.44±1.82	2.44±1.57	<0.001*

*: statistically significant as P value <0.05.

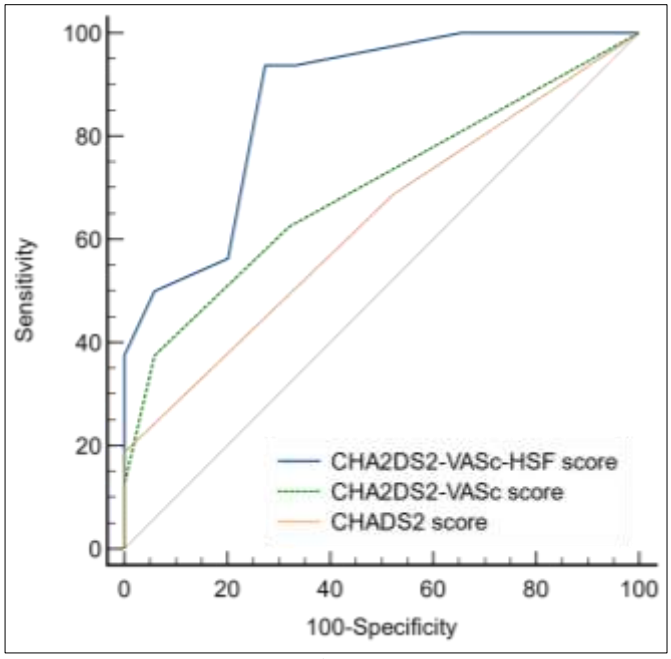
No significant differences were observed between the groups under study in relation to the angiographic data (Culprit vessel, multivessel disease, initial TIMI flow grade, stent length, tirofiban infusion, and thrombus aspiration). Table 5

Table 5: Angiographic data of the studied groups

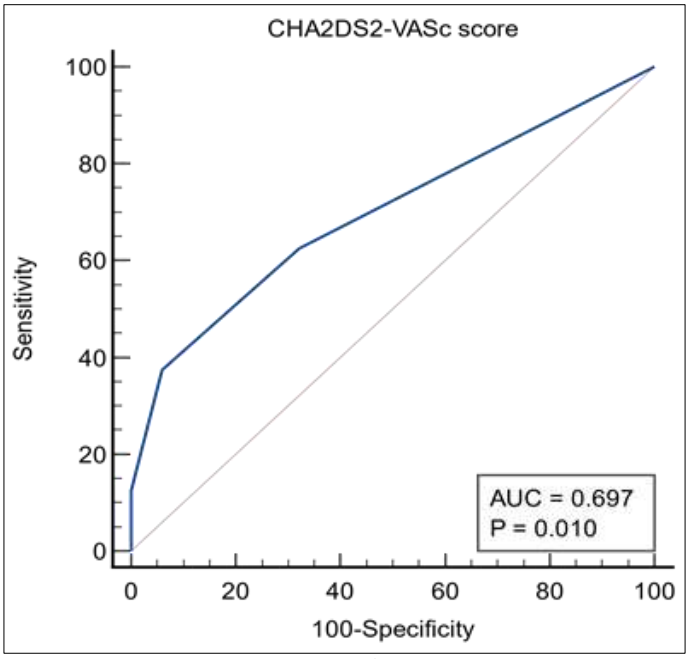
		Total (n=100)	No-reflow group (n=16)	Normal/slow flow group (n=84)	P value
Culprit vessel	LM	4 (4%)	1 (6.25%)	3 (3.57%)	0.947
	LAD	54 (54%)	9 (56.25%)	45 (53.57%)	
	RCA	27 (27%)	4 (25%)	23 (27.38%)	
	LCX	15 (15%)	2 (12.5%)	13 (15.48%)	
Multivessel disease		34 (34%)	6 (37.5%)	28 (33.33%)	0.972
Initial TIMI flow grade	0-1	56 (56%)	8 (50%)	48 (57.14%)	0.800
	≥2	44 (44%)	8 (50%)	36 (42.86%)	
Stent length (mm)	Mean±SD	2.48±0.6	2.44±0.51	2.49±0.62	0.758
	Range	1.5 - 3.5	2 - 3	1.5 - 3.5	
Tirofiban infusion		29 (29%)	7 (43.75%)	22 (26.19%)	0.263
Thrombus aspiration		5 (5%)	2 (12.5%)	3 (3.57%)	0.180

LM: left main, LAD: left anterior descending, LCX: left circumflex, RCA: right coronary artery, TIMI: thrombolysis in myocardial infarction, *: statistically significant as P value <0.05.

CHADS2 score can significantly predict the incidence of no reflow with AUC of 0.651, P value of 0.038, and at cutoff value >2 with 81.25% sensitivity, 35.71% specificity, 19.4% PPV and 90.9% NPV. CHA2DS2-VASc score can significantly predict the incidence of no reflow with AUC of 0.697, P value of 0.010, and at cutoff value >2 with 62.5% sensitivity, 67.86% specificity, 27% PPV and 90.5% NPV. CHA2DS2-VASc-HSF score was the best score as it can significantly predict the incidence of no reflow with AUC of 0.868, P value <0.001, and at cutoff value >2 with 93.75% sensitivity, 66.67% specificity, 34.9% PPV and 98.2% NPV. Figure 1



A)



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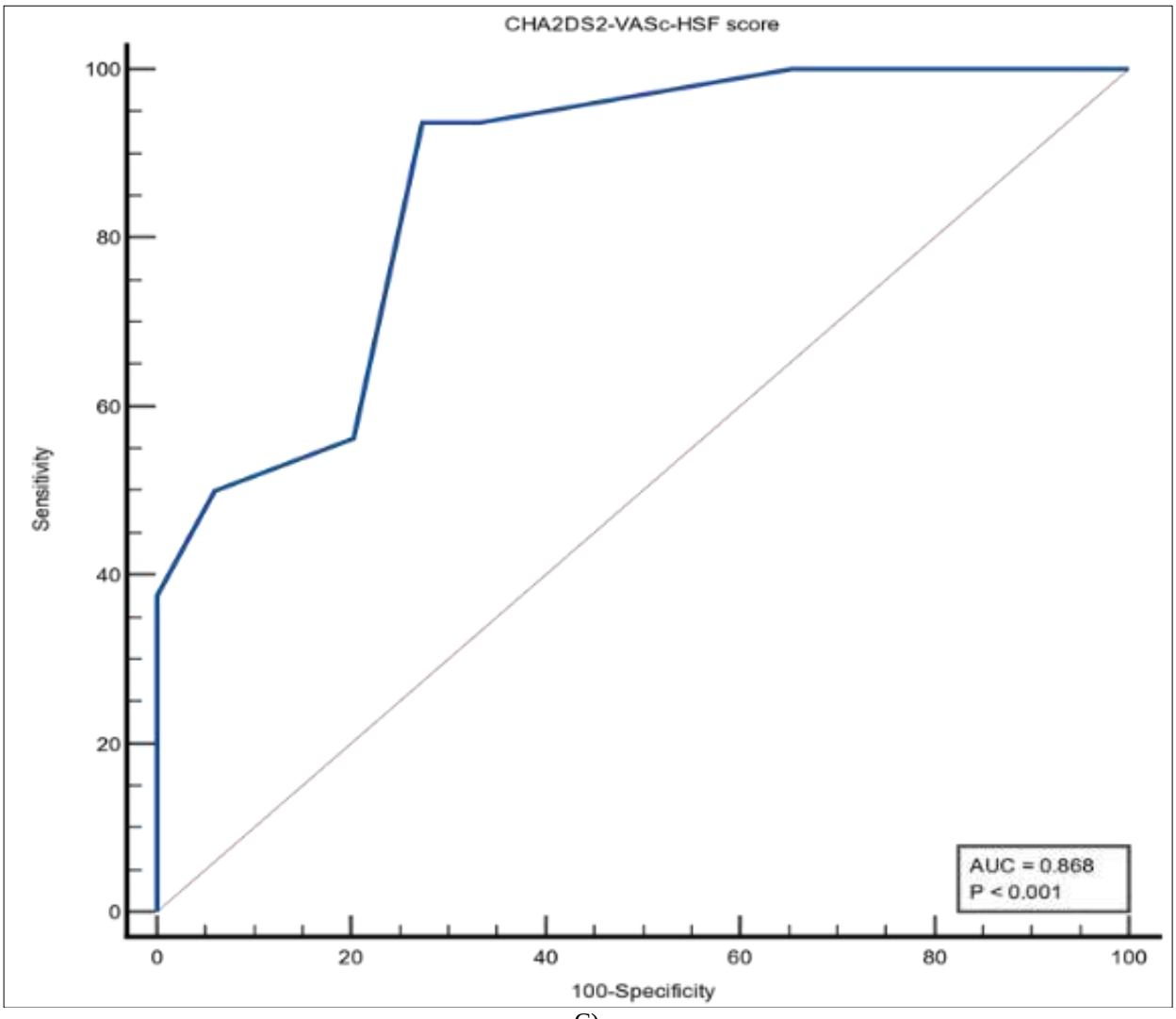

C)

Fig 1: ROC curve analysis of (A) CHADS2, (B) CHA2DS2-VASc (C) CHA2DS2-VASc-HSF scores in the prediction of the incidence of no reflow

Figure 2 illustrates the outcomes of pairwise comparisons of the AUCs, revealing that the CHA2DS2-VASc-HSF score emerged as the most effective predictor for the incidence of no-reflow.

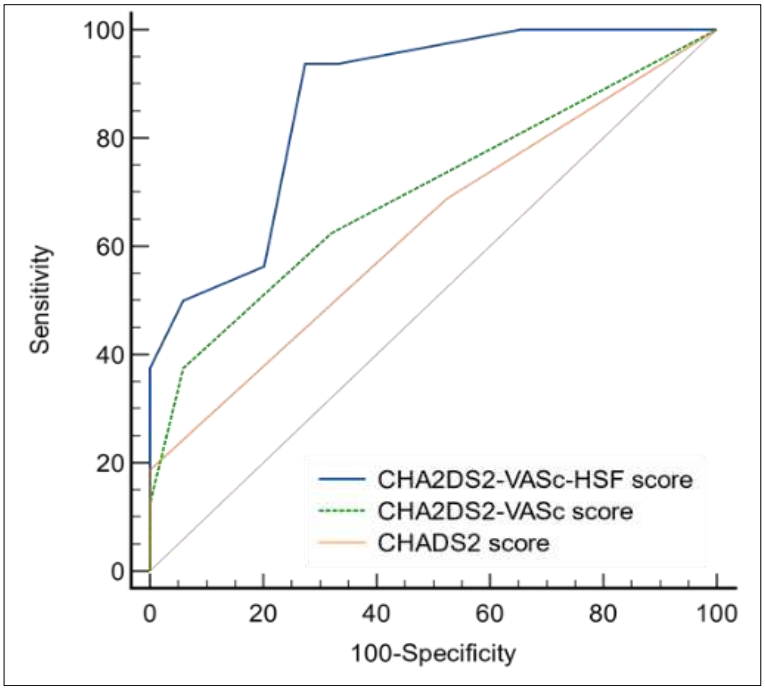

Fig 2: ROC curves comparisons of the AUC in prediction of the incidence of no reflow.

Univariate logistic regression analysis revealed that factors such as age, eGFR, CK-MB, EF, Killip classification, and the CHADS2, CHA2DS2-VASc-HSF, and CHA2DS2-VASc scores were significant predictors for the occurrence of no-reflow. Upon conducting multivariate logistic regression analysis, it was found that CK-MB levels, Killip classification, the presence of multi-vessel coronary artery disease, stent length, tirofiban infusion, along with the CHADS2, CHA2DS2-VASc, and CHA2DS2-VASc-HSF scores remained statistically significant predictors for the likelihood of no-reflow phenomenon Table 6.

Table 6: Logistic regression analysis for prediction of the incidence of no reflow

	Univariate			Multivariate		
	OR	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Age	1.285	1.156- 1.429	<0.001*	1.060	0.994-1.129	0.072
eGFR	1.141	1.047- 1.242	0.002*	1.139	0.992-1.309	0.065
CK-MB	1.807	1.161- 2.812	0.009*	1.916	1.030-3.564	0.040*
EF	0.779	0.663- 0.915	0.002*	0.792	0.618-1.015	0.065
Killip class	6.333	1.868- 21.468	0.003*	4.242	1.075-16.733	0.039*
Multivessel disease	1.200	0.395- 3.638	0.747	0.196	0.040-0.962	0.044*
Stent length	0.866	0.349- 2.143	0.756	0.360	0.131-0.987	0.047*
Tirofiban infusion	2.191	0.728- 6.591	0.162	0.018	0.001-0.412	0.012*
$CHADS_2$ score	5.640	1.847- 17.219	0.002*	11.067	2.423-50.530	0.001*
CHA2DS2-VASc score	3.509	1.836- 6.707	<0.001*	4.927	2.190-11.086	<0.001*
CHA_2DS_2-VASc-HSF score	1.877	1.338-2.634	<0.001*	2.405	1.544-3.744	<0.001*

eGFR: estimated glomerular filtration rate, CK-MB: creatine kinase-myocardial band, EF: ejection fraction, OR: odds ratio, CI: confidence interval, *: statistically significant as P value <0.05.

Discussion

The CHA2DS2-VASc-HSF score, a novel risk stratification tool, has been proposed to predict angiographic outcomes in patients with STEMI undergoing PPCI [13-14]. This study aimed to evaluate the predictive value of the CHA2DS2-VASc-HSF score in relation to the angiographic TIMI blood flow grade.

Regarding medical history, hypertension, history of heart failure, diabetes mellitus, history of stroke/TIA, vascular disease, and hyperlipidemia were significantly more prevalent in the no-reflow group compared to the normal/slow flow group (p<0.05). Smoking showed no significant difference between the groups.

In a similar vein, Zhang *et al*. (2020) utilized multivariate regression analysis to demonstrate that male sex, family history, hypertension, vascular disease, age ranges of 65-74 years and ≥75 years, a history of TIA or stroke, and hyperlipidemia were independently correlated with the occurrence of NRP. Additionally, their investigation identified peripheral vascular disease, heart failure, advanced age, and atherosclerosis as additional known risk factors that contribute to NRP [4].

The CHA2DS2-VASc model's independent predictive value for evaluating the risks of no-reflow and overall in-hospital mortality is demonstrated by the current study, with odds ratios of 1.59 (1.30–2.25) and 1.60 (1.17–2.19), respectively. Additionally, the odds ratios of abortive reperfusion were significantly predicted by BMI, elevated thrombus burden, and cardiogenic shock, with values of 1.07 (1.01–1.35), 1.59 (1.28–1.76), and 8.65 (3.76–24.46), respectively. A CHA2DS2-VASc cutoff score of two has a sensitivity of 69.7% and a specificity of 64.4% for

predicting increased mortality risk, with an area under the curve of 0.72 (95% CI: 0.62–0.81). In addition, the study groups did not exhibit any substantial variations in their lipid profiles, which included total cholesterol, triglycerides, HDL, and LDL levels [20]

In our study, cardiac biomarkers (Troponin I and CK-MB) were significantly elevated in the NR group compared to the normal/slow flow group (P=0.001, 0.005, <0.001 respectively).

Similarly, Zhang *et al*. divided patients into NRP and control groups based on post-PPCI thrombolysis in myocardial infarction flow rates. They analyzed 454 patients, including 80 in the NRP group and 374 controls, finding an NRP incidence of 17.6%. They identified CK-MB levels, Killip class, stent length, and the presence of multivessel disease as independent predictors of NRP. The CHA2DS2-VASc-HSF score demonstrated superior predictive capability, with a score of ≥4 yielding a sensitivity of 72.5% and a specificity of 66.5% for predicting NRP (AUC: 0.755, 95% CI [0.702–0.808]). In line with our findings, the no-reflow group exhibited significantly elevated CK-MB and Troponin levels when compared to the normal/slow-flow group [4].

In terms of laboratory findings, this study revealed that the mean peak levels of CPK and CKMB were significantly elevated in patients experiencing NR. These results align with the findings of Liang *et al*., who also reported higher peak CPK levels in patients with NR [15].

The EF was markedly reduced in the no-reflow group compared to the normal/slow flow group (P=0.001). There was also a significant difference in Killip class distribution between the two groups, with Class 1 being substantially less common in the NR group than in the normal/slow flow group (25% vs. 67.86%), while classes greater than 1 were significantly more prevalent in the no-reflow group (75% vs. 32.14%) (p<0.001). Additionally, the pain-to-balloon time was notably longer in the no-reflow group compared to the normal/slow flow group (P=0.004).

Echoing our findings, Zhang *et al*., in their investigation of the predictive power of the new CHA2DS2-VASc-HSF score for the no-reflow phenomenon post-PPCI in STEMI patients, corroborated the significant association we observed between EF and Killip class across the two group [4].

The development of NR following primary PCI in patients suffering from STEMI was significantly correlated with a marked decrease in myocardial salvage, an enlargement of infarct size, diminished LVEF at the six-month follow-up, and an increased risk of mortality within one year, as elucidated by Ndrepepa *et al*. (2010). Incredibly, four out of five patients who initially experienced no-reflow post-PCI, normal blood flow was restored within a six-month period following reperfusion. In contrast, patients who continued to suffer from impaired tissue perfusion, despite initial PCI, exhibited significantly worse left ventricular function compared to those whose blood flow was fully restored within six months [16].

Patients who demonstrated no-reflow exhibited significantly higher CHADS2, CHA2DS2-VASc, and CHA2DS2-VASc-HSF scores than those who had normal or sluggish flow (P = 0.001, <0.001, and 0.001, respectively). This observation is consistent with the study conducted by Ipek *et al*. (2016), in which patients were categorized into no-reflow (n = 111) and control (n = 1670) cohorts based on their post-PCI reflow status. The no-reflow group exhibited a significant increase in CHA2DS2-VASc scores, which were systematically calculated for all subjects. The CHA2DS2-VASc score was further confirmed as an independent predictor of no-reflow by multivariate regression analysis, with an odds ratio of 1.58 (95% CI: 1.33-1.88, p<.001). A threshold of 2 for the CHA2DS2-VASc score was identified by the ROC analysis as indicative of no-reflow, with a specificity of 59% and a sensitivity of 66%. Additionally, in-hospital mortality was significantly correlated with elevated CHA2DS2-VASc scores. In summary, the CHA2DS2-VASc score is inextricably associated with an elevated risk of in-hospital mortality and no-reflow following primary PCI [17].

Regarding angiographic data, no statistically significant differences were observed between the studied groups, initial TIMI flow grade, stent length, tirofiban infusion, or thrombus aspiration.

The CHADS2 score demonstrated significant predictive ability for no reflow with an AUC of 0.651 (P = 0.038). Using a cutoff value >2, it showed 81.25% sensitivity, 35.71% specificity, 19.4% PPV, and 90.9% NPV. These metrics indicate that while the CHADS2 score can effectively identify true positive cases (No reflow) with high sensitivity, it also has a notable rate of false positives.

Similarly, the CHA2DS2-VASc score significantly predicted the incidence of no reflow with an AUC of 0.697 (P = 0.010). At a cutoff value >2, it demonstrated 62.5% sensitivity, 67.86% specificity, 27% PPV, and 90.5% NPV. These findings suggest moderate discriminatory power, particularly in ruling out no reflow (high NPV), while balancing sensitivity and specificity.

In line with these results, Avci *et al*. (2018) found that the CHA2DS2-VASc score was significantly higher in the no-reflow group compared to the control group. They also observed that combining the CHA2DS2-VASc score with the pre-PCI thrombus load score improved predictive accuracy for no reflow compared to using either score alone. This combination showed enhancements in AUC, net reclassification improvement, and integrated discrimination improvement, highlighting its value in forecasting the no-reflow phenomenon in STEMI patients undergoing PPCI [18].

The CHA2DS2-VASc-HSF score predicted no reflow effectively (AUC = 0.868, p< 0.001) with a cutoff >2, showing 93.75% sensitivity, 66.67% specificity, 34.9% PPV, and 98.2% NPV. Consistent with Zhang *et al*. (2020), it was the most predictive score, highlighting its utility in identifying high-risk patients. In contrast to the normal cohort, the no-reflow group displayed a markedly higher incidence of factors such as advanced age, hypertension and previous stroke or TIA, and vascular pathology. Conversely, variables including male gender, the presence of DM, smoking, a history of heart failure, hyperlipidemia, and familial predisposition to cardiovascular conditions did not exhibit any statistically significant variation between the two groups [4].

The CHA2DS2-VASc-HSF score emerged as the most effective predictor of no reflow phenomenon. In comparison to CHADS2 and CHA2DS2-VASc scores, CHA2DS2-VASc-HSF demonstrated superior sensitivity and specificity in identifying patients at high risk for no reflow. In univariate logistic regression analysis, several factors including age, eGFR, CK-MB, EF, Killip class, CHADS2

score, CHA2DS2-VASc score, and CHA2DS2-VASc-HSF score were significant predictors of no reflow. Numerous predictors have been identified in prior research, including advanced age, higher Killip class, thrombus burden, protracted pain-to-balloon time, lower-left ventricular EF, and longer stent lengths.

Additionally, no reflow has been linked to factors such as hypertension, dyslipidemia, anterior infarctions, and a history of smoking. Our study substantiates that Killip class, stent length, and CK-MB levels serve as independent predictors of the no-reflow phenomenon. Moreover, the presence of multivessel disease, administration of tirofiban, a history of stroke or TIA, familial predisposition, and vascular disease are also significantly correlated with its incidence. Additionally, the CHA2DS2-VASc score independently predicts the absence of reflow, which is in accordance with previous research [19].

These findings highlight how cardiac biomarkers, clinical severity, procedural factors, and angiographic characteristics interact in microvascular dysfunction. Integrating these predictors into a unified risk assessment model could improve outcomes in PPCI for STEMI by better identifying high-risk individuals and tailoring interventions.

Conclusion

In conclusion, our study demonstrates that the CHA2DS2-VASc-HSF score emerged as a significant predictor of no reflow in STEMI patients post-PPCI, surpassing the predictive capabilities of CHADS2 and CHA2DS2-VASc scores. CK-MB, Killip class, and scores like CHA2DS2-VASc-HSF, CHADS2, and CHA2DS2-VASc were significant independent predictors for no reflow.

Conflict of Interest

Not available

Financial Support

Not available

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