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CHA_2DS_2-VascHSF Score as a Predictor of No-Reflow in Patients with ST-Segment Elevation Myocardial Infarction Who Underwent Primary Percutaneous Intervention

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Abstract: Background: Primary percutaneous coronary intervention is the preferred reperfusion strategy used in patients with acute STEMI to prevent progression of myocardial necrosis. Besides the advantages of this strategy, there are situations in which myocardial reperfusion is not restored to its optimal level. Angiographic no-reflow phenomenon, a reduced coronary antegrade flow (TIMI flow grade ≤ 2) without mechanical obstruction after recanalization, predicts poor LV functional recovery and survival in the early phase of STEMI[1]. The no-reflow phenomenon is critical and, if not reversed, causes a high rate of morbidity and mortality. CHA2DS2-VASc score is used to estimate the risk of thromboembolism in patients with atrial fibrillation[2]. Objectives: The aim of this study was to evaluate the new CHA_2DS_2-VASc HSF Score as a predictor of no-reflow in patients who underwent primary percutaneous intervention. Methods: The present study was conducted on 100 patients admitted with STEMI and treated with 1ry PCI at cardiovascular medicine department Tanta University Hospitals within 6 months from June 2018 to December 2018. Patients were divided into 2 groups according to no-reflow phenomenon. Group 1 consisted of 34 patients that had noreflow phenomenon & group 2 consisted of 66 patients that had normal flow after primary PCI. Results: The occurrence of no-reflow phenomenon after primary PCI can be predicted using the simple CHA_2DS_2-VASc HSF Scoring system with 73.53 % sensitivity and 66.67 % specificity for a cut off level of ≥ 3 with (P=0.002). Conclusion: CHA_2DS_2-VASc HSF score can be used as a new, simple, and reliable tool to predict noreflow in patients with ST elevation myocardial infarction who underwent primary percutaneous coronary intervention.

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Key Words: Percutaneous coronary intervention – ST segment elevation acute myocardial infarction –No-reflow phenomenon.

1. Introduction

The goal of reperfusion therapy by PCI in acute myocardial infarction is to restore optimal blood flow in the infarct-related artery (IRA) to ensure adequate blood supply to the ischemic but yet viable myocardium and to reduce infarct size and mortality. In no reflow, myocardial reperfusion is not achieved in spite of patent IRA. The no-reflow phenomenon is an acute reduction in coronary blood flow in the absence of major epicardial coronary vessel obstruction, flow-limiting dissection, vessel spasm or thrombosis[3].

The European Society of Cardiology has published atrial fibrillation-management guidelines in 2016 to advocate using the CHA2DS2-VASc score as a predictive scoring model for stroke in patients with atrial fibrillation[4]. In addition, the American Heart Association has already released similar recommendations for treatment of patients with atrial fibrillation in 2014[5].

This scoring system can also predict various categories of cardiovascular hospitalization events other than cerebrovascular accident events; the scores themselves were a composite of inflammatory risk factors[6].

The new formulated score, CHA_2DS_2-VASc-HSF which included more variables like Hyperlipidemia (H), Smoking (S) and Family history of CAD (F) in addition to the previous risk factors was used also recently to predict major adverse cardiac events[7].

Aim of the work

The aim of this study was to evaluate the new CHA_2DS_2-VASc HSF Score as a predictor of no-reflow in patients who underwent primary percutaneous intervention.

2. Patients and Methods:

One hundred patients that fulfilled the inclusion criteria were recruited from Cardiology department in Tanta University presented with ST segment elevation acute myocardial infarction, the patients were divided into two groups:

Group 1: consisted of 34 patients with no reflow phenomenon after primary PCI.

Group 2: consisted of 66 patients with normal flow after primary PCI.

Duration of the study:

This study was done in a period of six months starting from June 2018.

Inclusion criteria:

Patients presenting by STEMI within 24 hours and treated with primary PCI.

Exclusion criteria:

Patients presenting after 24 hours of symptoms.

Patient received thrombolytic therapy.

All recruited patients were subjected to:

An informed consent was obtained from all participants in the research.

Detailed clinical history: Age, sex, history of risk factors for coronary artery disease (CAD) as: Diabetes Mellitus, hypertension, smoking, Dyslipidemia, History of previous ischaemic stroke, transient ischaemic attack (TIA) or thromboembolism, past history of premature coronary artery disease, family history of premature CAD and vascular disease (defined as previous myocardial infarction [MI] and peripheral artery disease including prior revascularisation, amputation or angiographic evidence or aortic plaque).

Full clinical examination:

Vital signs: heart rate, blood pressure and respiratory rate.

General examination: with attention to Height, weight, body mass index (BMI), patient look, decubitus, cyanosis, jaundice, with special attention to signs of heart failure.

Local cardiac examination: abnormal pulsation, Heart sounds & murmurs.

Standard12-lead ECGwasobtainedwithin10minutesoffirstmedicalcontact (FMC) according to ESC guidelines2018(5).

Trans Thoracic Echocardiography (TTE) in the four standard views (Apical four, apical two, long parasternal, short parasternal) which was done either immediately on admission when hemodynamic instabilitywaspresentand/orwithinthefirst24hsincaseofstablepatients.

Routine laboratory investigation including:

-CKMB/Troponin.

-Fasting and 2 hours post prandial blood sugar level.

-Total cholesterol, LDL, HDL, Triglycerides.

-Urea/Creatinine level before and 24hs after primary PCI.

-Liver function tests.

-Complete blood count.

-CRP.

CHA_2DS_2-VASc and CHA_2DS_2-VASc HSF scores were calculated for each patient according to the following table:

	Risk Factor	Points
C	Congestive heart failure	+1
H	Hypertension	+1
A_2	Age ≥ 75	+2
D	Diabetes Mellitus	+1
S_2	Previous Stroke or TIA	+2
V	Vascular disease	+1
A	Age (65- 74)	+1
SC	Sex category (Female)	+1
H	Hyperlipidemia	+1
S	Smoking	+1
F	Family history of premature CAD	+1

Reperfusion through primary percutaneous intervention for Infarct related artery (IRA).

Angiographic films were reviewed and interpreted by an experienced interventional cardiologist as regard to TIMI flow before and after revascularization and myocardial blush grade.

Statistical methods

Normally distributed scale variables were expressed as mean + standard deviation. Non-normally distributed variables were expressed as median and range. Categorical variables were expressed in numbers and percentages. Analyses of categorical variables were performed by chi-square test. Parametric scale variables were analyzed by independent sample t test, and nonparametric scale variables were analyzed by Mann-Whitney U test. Multivariate logistic regression analyses were performed to determine the independent predictors of no-reflow in patients with STEMI.

3. Results

Patient demographics:

Age: The age of the study population ranged from 34 to 85 years. In Group I, the age of the patients ranged from 39.0 – 85.0 years with a mean age of 61.29 ± 12.8 years. In Group II, the age ranged from 34.0 – 85.0 years with a mean age of 55.83 ± 11.52 years. There was statistically significant difference between the studied groups (P value < 0.04).

Gender distribution: 100 patients included in the study, 62 of the study population were males and 38werefemales. Group Iincluded18males (52.9%) and 16 females (47.1%). Group IIincluded44 males (66.7%) and 22 females (39.4%). There was no

statistically significant difference between the two groups (P value =0.18).

		No-reflow (N=34) Mean ± SD (range)	Normal flow (N=66) Mean ± SD (range)	T. test	P. Value
Age (n=100)		61.29 ± 12.8	55.83 ± 11.52	2.0892	0.04
		39 –85	34 –85		
sex	Male	18 (52.9%)	44 (66.7%)	1.794	0.18
	Female	16 (47.1%)	22 (39.4%)		

Prevalence of risk factors within study population:

In our study, some factors were found to be significant predictors of noreflow phenomenon. In the noreflow group, 18 patients were diabetics (52.9 %), 22 were hypertensive (64.7 %), six patients had a history of cerevrovascular stroke (17%) and four had a history of vascular diseases (11.8%).

	No-reflow (N=34)	Normal flow (N=66)	OR (95%C.I)	P value
DM	18 (52.9 %)	19 (29.7%)	2.75 Calculated by Fisher's test 1.08-7.16	0.0314
HTN	20 (58.8%)	26 (39.4%)	2.97 Calculated by Fisher's test (1.17-7.85)	0.0195
Smoking	15 (44.1%)	29 (43.9%)	1 (0.44-2.32)	0.986
Family history of premature CAD	5 (14.7%)	7 (10.6%)	1.45 (0.42-4.9)	0.55
CVS	6 (17.6%)	3 (4.5%)	4.5 (1.05-19.3)	0.03
Vascular diseases	4 (11.8 %)	1 (1.5%)	8.7 (0.93-80.8)	0.044 Calcula ted by Fisher exact
Killip Class	11 (32.4%)	13 (19.7%)	1.9 (0.7-4.99)	0.16
Dyslipidemia	15 (44.1%)	23 (34.8%)	1.47 (0.63-3.4)	0.366

Angiographic and procedural characteristics:

In our study, location of infarction was found to be a predictor of noreflow as noreflow occurred more commonly with anterior myocardial infarction (58%) in comparison to non anterior infarction (41.1%), P.value = 0.009. Also, 66 patients of the study population had multivessel disease. In group I, 27 (79.4%) of patient had multivessel disease while 39 patients (59.1 %) had multivessel disease in group II. There was statistically significant difference between the studied groups (P value0.04).

In addition, we found that the no reflow group had a higher incidence when baseline TIMI flow is ≤ 1 compared with the normal flow group (P value 0.002).

		Noreflo-w (N=34)	Normal flow (N=66)	OR (95%C.I)	P value
Location of infarction	Ext anterior	20 (58.8%)	41 (62.1%)		0.009 Calcul at Ed by Monte Carlo
	Inferior	8 (23.5%)	24 (36.4%)		
	Lateral	6 (17.6%)	1 (1.5%)		
MVD		27 (79.4%)	39 (59.1 %)	2.67(1.01-7)	0.04
IRA	LAD	20 (58.8%)	41 (62.1%)		0.135
	LCX	9 (26.5 %)	8 (12.1%)		
	RCA	5 (14.7%)	17 (25.8%)		
PTCA		31 (91.2 %)	53 (80.3%)	2.53(0.6-9.6)	0.16
GP IIb IIIa		24 (70.6%)	47 (71.2%)	0.97(0.4-2.4)	0.948
Stent	No	1 (2.9%)	4 (6.1%)		0.767 Calculated by Monte Carlo
	BMS	10 (29.4%)	21 (31.8%)		
	DES	23 (67.6%)	41 (62.1%)		

Regarding Ejection Fraction on admission:

In group I, The EF on admission ranged from (25 – 65) % with mean E.F 44.5 ± 10.6 % while it ranged from (23 – 65)% in group II with a mean EF of 48.09 ± 9.2 %, There was no statistically significant difference between the two groups (P value= 0.103).

Comparison between the two studied groups according to Ejection Fraction on admission:

EF (n=100)	No-reflow (N=34) Mean ± SD (range)	Normal flow (N=66) Mean ± SD (range)	T test	P Value
	44.5 ± 10.6	48.09 ± 9.2	-1.65	0.103
	(25 – 65)	(23 – 65)		

Univariate and Multivariate analysis for predictors of no reflow:

Univariate and multivariate regression analysis were performed to investigate the possible predictors of no reflow in the study population.

In univariate regression analysis, age, DM, HTN, history of cerebrovascular stroke or vascular events, anterior wall infarction, multivessel disease, CHA2DS2-VASc and CHA2DS2-VASc-HSF scores, TIMI Flow before Primary PCI were correlated with noreflow.

Variables with a significant P.value in univariate analysis were included into multivariate regression analysis. Risk factors involved in CHA2DS2-VASc score were excluded from this analysis to avoid multicollinearity.

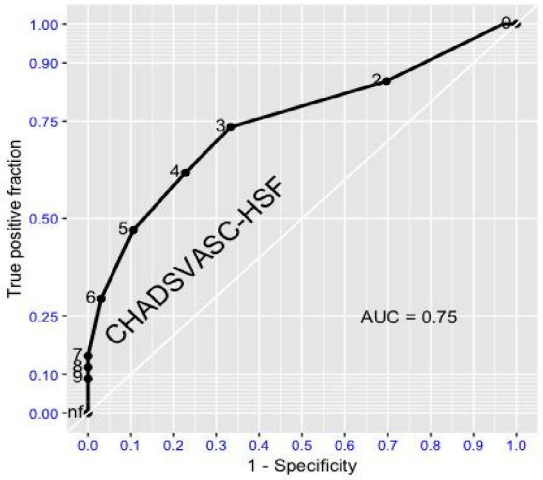
According to the results of the multivariate regression analysis CHA2DS2-VASc-HSF score was an independent predictor (odds ratio [OR]: 1.618 -, 95% confidence interval [CI]: 1.186-1.979, P <.002) of no-reflow.

Multivariate Regression Analysis of Predictors of No-Reflow in Study Population:

	B	S.E.	Wald	Sig.	OR	95% C.I.for OR	
						Lower	Upper
CHA2DS2-VASc-HSF	.417	.135	9.530	.002	1.518	1.165	1.979
Location of infarction	.135	.394	.118	.731	1.145	.529	2.478
MVD	.393	.578	.464	.496	1.482	.478	4.600
TIMI flow before	-18.523	5182.451	.000	.997	.000	.000	.

ROC curve for CHA_2DS_2-VASc-HSF Score to predict no-reflow cases:

The receiver operating characteristic (ROC) analysis showing the performance and predictive accuracy of CHA_2DS_2-VASc - HSF Score in predicting noreflow phenomenon, the area under the curve (AUC) was 0.71 confidence interval (CI) 1.186-1.979 (P value 0.002), with cutoff value CHA_2DS_2-VASc - HSF score equal or more than 3, with 73.53 % sensitivity and 66.67 % specificity.



ROC curve of CHA2DS2-VASc- HSF score in predicting noreflow

4. Discussion

Regarding the demographics in this study:

In the present study, the incidence of noreflow is slightly more common in males (52.9% of noreflow group Vs 44% in normal flow group) but this difference was not statistically significant (P.value=0.18).

The patients in noreflow group were older: Mean age in no reflow group was 61.29 years while it was 55 years in the other group.

In contrast to our study, Ipek et al.[8] revealed that female gender were significantly higher in the no-reflow group (27.9% vs 18.4%, P.value< 0.01)[8].

In a meta-analysis conducted by Fajar et al.[9] that included 46 papers between August and October 2017 and aimed to assess several factors (demographic and clinical characteristics, laboratory parameters, electrocardiogram, echocardiography, and angiographic findings) that might have an impact on noreflow phenomenon after PCI in patients with STEMI. In this study, noreflow phenomenon occurred in elder patients with a mean age of (61 Vs 59 years for no-reflow and normal flow group, respectively). Also, in agreement of our study, it found that noreflow phenomenon occurred more commonly in male patients (71.9%)[9].

Regarding clinical features:

In our study, some factors were found to be significant predictors of noreflow phenomenon. In the

noreflow group, 18 patients were diabetics (52.9 %), 22 (64.7 %) were hypertensive, six patients had a history of cerevrovascular stroke (17%) and four had history of vascular diseases (11.8%).

This came in agreement with a meta-analysis conducted by Fajar et al. which found that diabetes mellitus and hypertension were proven to be associated with the risk of no reflow[9].

Similarly, In a study conducted by Celik et al.[10]on885 patients presented with STEMI and treated with primary PCI in two tertiary centers in Turkey from 2014 to 2015 to asses predictors of no-reflow phenomenon in young patients, patients with no reflow were more likely to have diabetes and hypertension (29.6% vs 11.0%, P.value = 0.013 and 59.3% vs 27.1%, P.value 0.001, respectively)[10].

Also, a study conducted by Tian et al.[11] and included 277 STEMI patients from January 2011 till December 2015 aiming to asses predictive factors for insufficient myocardial reperfusion in ST segment elevation myocardial infarction in patients treated with selective aspiration thrombectomy during primary PCI found that noreflow occurs more common in hypertensive patients in comparison to normal flow group, P.value=0.002[11].

The more prevalence of noreflow in patients with diabetes mellitus[12] and hypertension[13] correlates mainly with endothelial dysfunction.

In concordant with our study, a study conducted by Avci et al.[14] on 497 patients presented with STEMI found that history of vascular diseases and prior ischemic stroke or TIA are more prevalent in noreflow group in relation to normal flow group (5 % vs 9%, P.value = 0.042 and 0.1 % vs 3%, P.value =0.031), respectively[14].

In our study we also found that noreflow phenomenon is more prevalent in smokers, dyslipidemics, those with positive family history of premature coronary artery disease and patients with congestive heart failure but the results were statistically insignificant, P.value> 0.05 for all.

Our results showed that noreflow occurs more common in patients with clinical heart failure at time of admission and that that the mean Ejection Fraction on admission was lower in noreflow group. but the results was statistically insignificant.

However, a study also conducted by Gagliard et al.[15] including 742 patients with acute myocardial infarction treated with primary percutaneous coronary intervention between October 2001 and May 2011 found that heart failure at admission were significantly more common in patients with no-reflow (17.6% vs.10.1%; P.value= 0.01)[15].

Regarding the angiographic results:

In our study, location of infarction was found to be a predictor of noreflow as noreflow occurred more commonly with anterior myocardial infarction (58%) in comparison to non anterior infarction (41.1%), P.value = 0.009.

Also, we found that the infarct-related artery in most cases of noreflow was the LAD (58.8%), while LCX and RCA were the IRAs in (26.5 %) and (14.7%) of cases respectively.

Also, in agreement with our study, the study conducted by Ipek et al.[8] reported that noreflow is more common in patients presented with anterior myocardial infarction (60.4%) in comparison to non-anterior infarction (39.6%)[8].

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Similarly, the study conducted by Hassan et al.[16] in Assiut University hospital between 1st of October 2015 and 30th of November 2016 and enrolled 310 consecutive STEMI patients reported that noreflow is more common in anterior myocardial infarction (52.5%) in comparison to non-anterior infarction (47.5%), P.value =0.009. It also found that the noreflow occurs more commonly when the LAD is the culprit vessel (51.5% of cases of noreflow), P.value=0.002[16].

The association between the infarct size and no reflow may be explainable as local necrosis is associated with tissue destruction, including vascular tissue, edema, and mechanical compression which constitute potential mechanisms of no reflow[17].

Regarding PCI procedural aspects:

our results found no association between different types of intervention (PTCA alone, direct stenting with BMS or DES and usage of balloon for pre or post dilatation) and the risk of no reflow, (P.value>0.05 for all).

In contrast to our study, the no-reflow incidence was significantly higher in patients who had more postdilation (54.3 vs. 30.9%, for no-reflow and reflow, respectively) in the study conducted by Chen et al.[3] on 320 female patients with STEMI and successfully treated with Primary PCI within 12 hours after the onset of symptoms from 2007 to 2010 in tertiary center in China[3].

In addition, we found that the no reflow group had a higher incidence when baseline TIMI flow is ≤ 1 compared with the normal flow group. This finding was also reported by Soeda et al.[18] which concluded that initial TIMI flow is a predictor of noreflow[18].

No-reflow was also found to be more common in patients who had a low (≤ 1) initial TIMI flow (91.5% vs. 47%, P.value<0.001) in a study conducted by Padmajan et al.[19] which analyzed data from 781 consecutive patients who had undergone primary angioplasty from 2008 to 2012 in a tertiary center in India[19].

Several mechanisms may explain the association between initial TIMI and occurrence of noreflow. The protective role of residual blood flow in the infarct-related artery before reperfusion is the corner stone of these mechanisms. First, residual blood flow in the infarct-related artery is associated with smaller infarct size. Second, infarct-related arteries prone to spontaneous recanalization may have less thrombotic burden meaning less distal remobilization, which is considered an important factor for the development of no reflow after PCI. Third, early restoration of blood flow may alleviate tissue ischemia and prevent or attenuate the microvascular damage[20].

Regarding CHA_2DS_2-VASc and CHA_2DS_2-VASc-HSFscores:

CHA_2DS_2-VASc score was found to be associated with higher risk of no-reflow in the study conducted by Ipek et al.[8] on patients undergoing primary PCI after STEMI[8].

Our study showed that CHA_2DS_2-VASc and CHA_2DS_2-VASc-HSFscores can be used as a new, simple, and reliable tool to predict noreflow in patients with ST elevation myocardial infarction who underwent primary percutaneous coronary intervention with superiority to CHA_2DS_2-VASc-HSFas CHA_2DS_2-VASc-HSFScore with a cut off level of ≥ 3 is an independent risk factor for noreflow with 73.53 % sensitivity 66.67 % specificity.

Limitations of The Study

The study had some potential limitations such as; small size of study population, which was due to many factors, one of them was technical error in our catch lab for about 2 months during the period of the study, also some of cases came with late presentation after the accepted window of primary PCI.

Others refused doing PCI at our center due to logistic or cultural issues. Also the assessment of coronary flow was performed by the TIMI flow method which can be subjective, but this was performed by a single experienced cardiologist in order to maintain consistency. Also most previous studies have used TIMI flow as the method for assessing no-reflow it has been shown to be a predictor of mortality in numerous studies and so remains a useful marker that is practical and easy to measure in clinical practice.

Conclusion

The study showed that CHA_2DS_2-VASc HSF score can be used as a new, simple, and reliable tool to predict noreflow in patients with ST elevation myocardial infarction who underwent primary percutaneous coronary intervention.

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