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Prediction of No-Reflow Phenomenon Using Newly Defined CHA2DS2-VASc-HSF Score in Diabetic Patients Undergoing Coronary Angiography

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ABSTRACT

Background: Cardiovascular atherosclerosis, and more especially coronary artery disease (CAD), is the main cause of premature death globally. Coronary artery disease treatment must include risk assessment and prevention measures, such as managing risk factors. The risk of thrombosis can be efficiently measured in situations of non-valvular atrial fibrillation (AF) using the CHADS2 and CHA2DS2-VASc scores.

Objectives: This study aimed to determine whether the CHA2DS2-VASc-HSF score could be used to predict the absence of reflow events in elective coronary angiography patients with diabetes.

Patients and methods: The current research was conducted on 361 cases who underwent elective percutaneous coronary artery intervention at Menoufia University and Matrouh Specialized Cardiac Center. They were classified into two groups: Cohort I [those with a low CHA2DS2-VASc-HSF score (≤ 4)] and cohort II [those with a high CHA2DS2-VASc-HSF score (5-13)]. Participants in cohort I had syntactic scores ranging from 2–13 for low, 14–20 for intermediate, and 21–40 for high. The MBG and traditional TIMI flow grading for each case were taken into consideration.

Results: The findings showed that during elective PCI, all cases exhibited TIMI III flow, and no reflow was found in any of them, nevertheless when TIMI flow grade. People with high or intermediate Syntax scores had a higher average CHA2DS2-VASc-HSF score than those with low Syntax scores, showing a strong and significant correlation between the two types of scores. When combined with MBG, it revealed that approximately 2.5% of the cases had no reflow with an increase in cohort II CHA2DS2-VASc-HSF scores, although this relationship was still statistically non-significant. The CHA2DS2-VASc-HSF score was significantly correlated to HbA1c, creatinine, and random blood glucose levels.

Conclusions: Syntax score results demonstrated a relationship between the CHA2DS2-VASc-HSF score and CAD severity and complexity, but no significant correlation was found between the score and the incidence of no reflow in elective PCI cases.

Keywords: CHA2DS2-VASc-HSF score, Coronary artery illness, Elective coronary angiography, No-reflow.

INTRODUCTION

Globally, DM has become an epidemic, and its incidence is increasing [1, 2].

DM or a history of myocardial infarction (MI) increases CV deaths in all age cohorts and for both gender in an equivalent manner, and the two are highly synergistic [3]. Also, diabetes, particularly type 2 diabetes, is linked to a set of risk factors for cardiovascular disease. Hypertension (75–85%), elevated LDL (70–80%), and obesity (60–70%) are common in adults with DM [4]. Coronary artery disease (CAD) is the leading cause of mortality in both type 1 and type 2 diabetes, and the risk of death from heart disorders is two to four times higher in diabetic individuals. More than 70% of diabetics over 65 will pass away from heart illness or stroke [5]. The mortality rate for DM patients after MI is greater, and their long-term prognosis is worse when they have CAD [6, 7].

A no-reflow phenomenon (NRP) occurs when there is inadequate blood flow to the heart from a specific section of the coronary artery and no indications of mechanical arterial blockage are visible. One of the factors that predicts NRP is DM, which illustrates how ischemia preconditioning and preexisting microvascular damage and dysfunction affect the development of no reflow later on.

As clinical predictors, the CHADS2 and CHA2DS2-VASc scores aid in the assessment of risk for cardiovascular thromboembolism and the prescribing of antithrombotic medications [9, 10]. These scores may be an indicator of mortality for patients with acute coronary syndrome, stable CAD, and those who have had coronary artery bypass grafting (CABG) [11]. The CHA2DS2-VASc score is useful for predicting the risk of thromboembolic events and assisting in the selection of anticoagulant or antiplatelet drugs when applied to persons with non-valvular atrial fibrillation [12]. The NRP risk factors microvascular dysfunction, vascular spasm, and atherosclerosis are associated with the components of these two scores [13].

According to multiple studies, the CHA2DS2-VASc scores are linked to various medical conditions, including CAD severity, prognosis, NRP, acute MI, in-stent restenosis, acute stent thrombosis, mechanical mitral valve thrombosis, right ventricular dysfunction, and contrast-induced nephropathy following percutaneous coronary intervention for acute coronary syndrome [14].

Recently, three additional factors were added to the CHA2DS2-VASc score, expanding its components to become the CHA2DS2-VASc-HSF score.

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Hyperlipidemia (H), smoking (S), and coronary heart disease (F) is present in the family tree. In addition, the gender of the male was used instead of the female, as it had been in the earlier scores [15].

PATIENTS AND METHODS

From October 2021 to December 2023, this prospective study included 361 cases with type II DM who had elective coronary angiography performed at Matrouh Specialized Cardiac Center and Menoufia University Catheterization Laboratory.

Cases were divided into two groups according to their CHA2DS2-VASC-HSF scores: those in Cohort I had low scores (⩽4), while those in Cohort II had high scores (5-13).

Inclusion criteria: Cases having elective coronary angiography because they were previously admitted with coronary artery illness or because of possible coronary artery illness investigations.

Exclusion criteria: Acute coronary syndrome, prior PCI or CABG, decreased renal function, advanced liver cell failure, hematological or inflammatory disorders, or neoplasms.

A thorough history was taken for each one. This included the individual's medical history, risk factors such as diabetes, high BP, obesity, hyperlipidemia, smoking, and other co-morbidities.

Comprehensive general examination that included local heart examination, vital signs, resting 12-lead ECG, resting transthoracic echocardiography, and laboratory tests such as HbA1c, serum creatinine and random blood sugar.

Coronary intervention: They performed invasive coronary angiography. The trans-femoral technique was used to insert the left and right diagnostic catheters via the sheath into the femoral artery. Evaluation of lesions from two orthogonal perspectives.

Syntax score calculation:

The Syntax score is the sum of the points given for every coronary tree lesion with a diameter narrowing of more than 50% in arteries greater than 1.5 mm. According to the American Heart Association, the coronary tree is composed of sixteen segments [16].

While evaluating TIMI flow and myocardial blush grade, NRP was found through elective PCI as described in figure (1).

Grade 0 (MBG-0)	Failure of dye to enter the microvasculature. Either minimal or no ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit artery indicating lack of tissue-level perfusion.
Grade 1 (MBG-1)	Dye slowly enters but fails to exit the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that fails to clear from the microvasculature, and dye staining is present on the next injection (approximately 30 seconds between injections).
Grade 2 (MBG-2)	Delayed entry and exit of dye from the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that is strongly persistent at the end of the washout phase (i.e., dye is strongly persistent after three cardiac cycles of the washout phase and either does not or only minimally diminishes in intensity during washout).
Grade 3 (MBG-3)	Normal entry and exit of dye from the microvasculature. There is the ground glass appearance ("blush") or opacification of the myocardium in the distribution of the culprit lesion that clears normally and is either gone or only mildly/moderately persistent at the end of the washout phase (i.e., dye is gone or is mildly/moderately persistent after three cardiac cycles of the washout phase and noticeably diminishes in intensity during the washout phase), similar to that in an uninvolved artery. Blush that is of only mild intensity throughout the washout phase but fades minimally is also classified as grade 3.

Figure (1): Myocardial Blush grades [21, 22].

Ethical Approval: The relevant IRB and Institutional Ethical Committee for Human Research gave their approval to the project. The study was conducted in accordance with the Declaration of Helsinki. Written informed permission about the research protocols was given by each participant.

Statistical analysis

Using SPSS version 20, the data were analyzed. The Kruskal-Wallis and Chi-square tests were utilized for the testing. For statistical purposes, a p-value ≤ 0.05 was considered significant.

RESULTS

Based on their CHA2DS2-VASc-HSF scores, 361 cases were divided into two groups: low and high. Risk factors included in CHA_2DS_2-VASc-HSF score among the studied cases didn't show significant differences (Table 1).

Table (1): The risk factors included in CHA_2DS_2-VASC-HSF score among studied cases

	CHA_2DS_2-VASC-HSFscore				**p**
	Cohort I (≤4) (n= 85)		**Cohort II (5–11) (n= 276)**		
Age (years)	**No.**	**%**	**No.**	**%**	
<65	40	47.1	143	51.8	0.387
65–74	27	31.8	67	24.3	
≥75	18	21.2	66	23.9	
Gender Male	85	100.0	276	100.0	--
Congestive heart failure	21	24.7	71	25.7	0.851
Hypertension	40	47.1	130	47.1	0.995
Diabetes	85	100.0	276	100.0	--
Previous stroke or TIA	51	17.6	42	15.2	0.591
Vascular	13	15.3	35	12.7	0.535
Hyperlipidemia	69	81.2	230	83.3	0.645
Smoking	84	98.8	271	98.2	1.000
Family history	12	14.1	35	12.7	0.731

Data are presented as frequency (%).

Laboratory investigations to the studied participants among the two cohorts showed highly significant relation with creatinine, random blood glucose and HbA1c (P < 0.05) (Table 2).

Table (2): comparison of the studied cohorts of CHA_2DS_2-VASC-HSF score regarding laboratory results

	CHA_2DS_2-VASC-HSFscore		**p**
	Cohort I (≤4) (n= 85)	**Cohort II (5–11) (n= 276)**	
Creatinine			**<0.001***
Mean± SD.	0.75±0.19	0.83±0.1	
Random glucose	182.8±6.01	223.5±7.0	**<0.001***
Mean± SD.			
HbA1c (%)			**<0.001***
Mean± SD.	8.7±1.8	9.6±1.9	

Data presented as mean ± SD or median (IQR), with P values indicating significance between cohorts (P<0.05) for various laboratory markers (creatinine random blood glucose, HbA1c).

Myocardial blush grade didn't show statistically significant relation between 2 cohorts of the studied participants (Table 3).

Table (3): Relation between CHA_2DS_2-VASC-HSF score and MBG

MBG	**CHA_2DS_2-VASC-HSF score**				**FEP**
	Cohort I (≤4) (n= 85)		**Cohort II (5–13) (n= 276)**		
	No.	**%**	**No.**	**%**	
Normal	84	98.4	268	97.1	
No reflow	1	1.2	8	2.9	

Data are presented as frequency (%).

When compared to intermediate and low risk syntax scores, a high syntax score demonstrated a highly significant relationship with the CHA2DS2-VASC-HSF score (p<0.001) (Table 4 & figure 2).

Table (4): Relation between syntax score and CHA_2DS_2-VASc-HSF score

	Syntax score			**P**
	Low (n=243)	**Intermediate (n= 76)**	**High (n= 42)**	
CHA_2DS_2-VASc-HSF score	5.71±1.69	6.49±1.76	7.0±1.94	**<0.001***
Median (min.–max.)	5.0 (3.0– 11.0)	6.0 (4.0–10.0)	7.0 (4.0–11.0)	

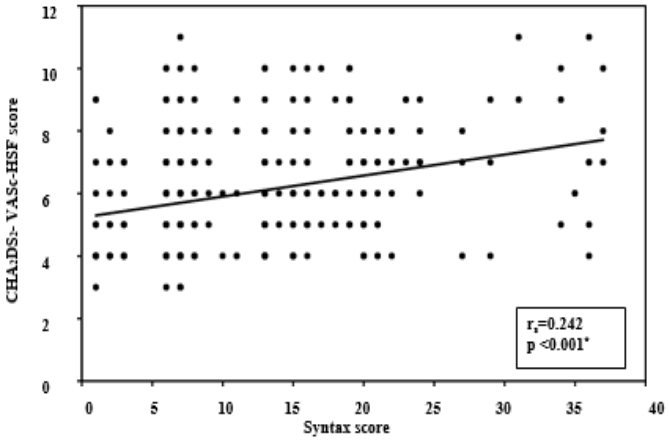

Figure (2): Correlation between Syntax score and CHA_2DS_2-VASc-HSF score.

Data presented as mean ± SD or median (IQR), with P values indicating significance between cohorts (P<0.05)

CHA_2DS_2-VASc-HSF score could predict high syntax score (P=0.001 and AUC=0.665) at cut-off > 5 with 76.19 % sensitivity, 50.16% specificity, 16.8% PPV and 94.1 % NPV (Table 5 & figure 3).

Table (5): Validity for CHA_2DS_2-VASc-HSF score to predict high Syntax score > 20

	AUC	P	95%C. I	Cut off	sensitivity	specificity	PPV	NPV
CHA_2DS_2-VASc-HSF score	0.665	0.001*	0.576–0.754	>5	76.19	50.16	16.8	94.1

*Significant P value <0.05, AUC: Area under curve, PPV: Positive predictive value, NPV: Negative predictive value.

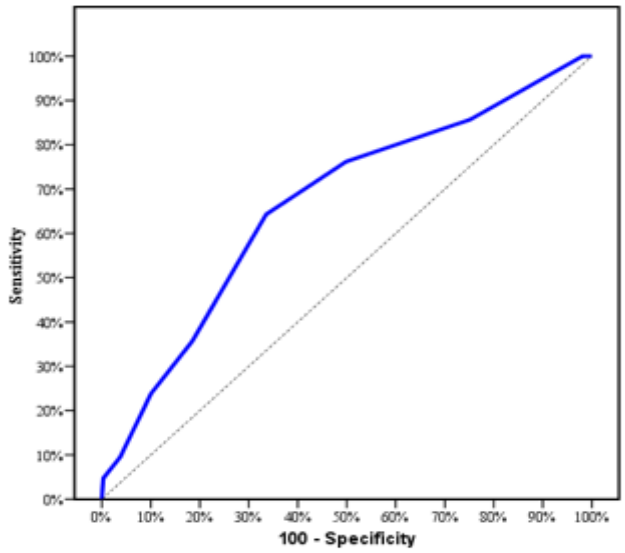

Figure (3): ROC curve for CHA_2DS_2-VASc-HSF score to predict high Syntax score > 20

A high CHA2DS2-VASc-HSF score was independently predicted by creatinine, random blood glucose, and HbA1c in the univariate regression analysis (P<0.001). A high CHA2DS2-VASc-HSF score was independently predicted by random blood glucose and HbA1c in multivariate regression analysis (Table 6).

Table (6): Univariate and multivariate Logistic regression analysis for the parameters affecting high CHA2DS2-VASC-HSF score (n= 276 vs 85)

	Univariate		#Multivariate	
	P	**OR (LL–UL95% C.I)**	**P**	**OR (LL–UL95% C.I)**
Age(years)(>75)	0.602	1.170(0.649–2.109)		
Smoking	0.691	0.645(0.074–5.600)		
Family History	0.731	0.883(0.436–1.790)		
Hyperlipidemia	0.645	1.159(0.618–2.175)		
Vascular	0.536	0.804(0.404–1.602)		
Previous stroke or TIA	0.592	0.838(0.438–1.600)		
Hypertension	0.995	1.002(0.615–1.630)		
Congestive heart failure	0.851	1.056(0.602–1.851)		
Creatinine	**<0.001***	13.854(3.339–57.491)	0.479	1.844(0.339–10.037)
Random glucose	**<0.001***	1.010(1.006–1.015)	**0.025***	1.006(1.001–1.011)
HBA1c	**<0.001***	2.035(1.563–2.650)	**0.004***	1.603(1.167–2.201)
EF	0.055	1.029(0.999–1.059)		
Fractional shortening	0.075	1.052(0.995–1.113)		
LVIDd	0.792	0.993(0.944–1.045)		
LVIDs	0.445	0.984(0.943–1.026)		
IVSd	0.562	0.948(0.790–1.137)		
LVPWd	0.225	0.878(0.712–1.083)		
Left atrium	0.769	1.007(0.959–1.058)		
Aorta	0.358	0.964(0.890–1.043)		
MBG	0.389	2.507(0.309–20.339)		

*Significant P value <0.05, CI: Confident interval.

DISCUSSION

In patients suffering from acute MI, the CHA2DS2-VASc score has been linked to worse outcomes, longer survival times, and NRP of CAD [13]. New scoring methods, such as the CHA2DS2-VASc-HSF, have recently been created. The predictive value increased when male gender, which may be more closely associated with NRP, replaced the female gender, as utilized in the prior ratings. This could be due to the fact that male cases are more likely than female cases to smoke and be obese [15].

The primary objective of our study was to use the newly-developed CHA2DS2-VASc-HSF score to predict NRP in diabetic patients undergoing elective PCI by reviewing their medical records. The additional objective was to determine if the syntactic score, a measure of CAD severity, is related to the CHA2DS2-VASc-HSF score.

Our research demonstrated that elective percutaneous coronary artery intervention using conventional TIMI flow did not result in reflow. Grading, as of total analyzed cases (N= 361 cases) there was no one with no reflow phenomena that may be owing to lack of thrombus load factor, which was present in other studies that performed on STEMI and non-STEMI cases. No-reflow was diagnosed using the TIMI flow grade following the surgery. TIMI flow grade, however does not account for myocardial reperfusion, it merely measures blood flow velocity. The TIMI flow grade in conjunction with MBG, a useful and practically applicable method for evaluating myocardial reperfusion following PCI, was used in this research to define no-reflow. The findings showed that following PCI, all cases exhibited TIMI III flow, and no reflow was found in any of them; nevertheless, when TIMI flow grade. In contrast to other studies conducted on STEMI and non-STEMI cases undergoing emergent PCI, the combination of MBG revealed that approximately 2.5% of the cases had no reflow with an increase in cohort II CHA2DS2-VASc-HSF score. Still, the P value of 0.692 meant that this was not significantly different from the control group.

Therefore, in diabetes cases receiving elective percutaneous coronary intervention, the recently defined CHA2DS2-VASc-HSF score did not provide a prognostic value for the no-reflow phenomena. However, CHA2DS2-VASc-HSF and syntactic score had a strong relationship, as indicated by the statistically significant P value of <0.001.

Findings are in agreement with **Modi *et al.*** [15] who analyzed 2976 patients in a row who underwent coronary angiography. Any degree of coronary artery stenosis greater than 50% was considered significant coronary CAD. There were 804 patients in Cohort 1 with coronary angiography results that were normal. The remaining 2172 CAD cases with stenosis were split into two groups according to the severity of their stenosis: less than 50% and higher than 50%. Cohort 2 consisted of 834 individuals with moderate CAD, while Cohort 3 consisted of 1338 cases with severe CAD. Scores on the CHADS2, CHA2DS2-VASc, and CHA2DS2-VASc-HSF assessments were substantially different across all three categories. An increase in the number of diseased arteries was positively correlated

with higher marks across all grading methodologies. According to the results, the CHA2DS2-VASc-HSF score is the best in predicting the severity of CAD.

Consistent with the findings of **Uysal *et al*.** [17] evaluated the new CHA2DS2-VASc-HSF score for the severity of STEMI coronary artery illness. The investigation included 454 consecutive individuals who underwent PCI. The participants' ages ranged from 57.3 ± 12.9 years, and 79% were males. The objective was to determine the score's predictive usefulness. Multivariate research revealed that CHA2DS2-VASc-HSF scores were higher in patients with older age, greater LVEF, and SYNTAX. Cases were classified as low (> 14), moderate (14-20), or high (> 21) according to the SYNTAX results. Consistent with the results of **Al-Shorbagy *et al.*** [18], the newly-developed CHA2DS2-VASC-HSF score was found to have a significant positive correlation with the previously-established score for coronary artery sickness severity in non-ST segment elevation myocardial infarction, according to researchers who examined its prognostic ability. According to **Ciftci *et al.*** [19], predicting severe CAD was only possible with the CHA2DS2-VASc score (OR=3.03 [95% CI 1.19-7.63]; p<0.05). The following variables were also found to be correlated with severe coronary lesions: Left ventricular hypertrophy (p<0.05), history of coronary artery disease (p<0.05), chronic severe renal illness (p<0.05), hypertension (p<0.05), and the CHA2DS2-VASc-FSH score (p<0.05).

Our research's univariate and multivariate regression analyses revealed a highly predictive and significant relationship between HBA1c and creatinine, which is consistent with the findings of **Alıcı *et al.*** [20] 's univariate analysis.

CONCLUSION

The present study found correlations between the syntax score and the CHA2DS2-VASc-HSF score, the syntax score being a measure of the complexity and severity of CAD. However, there was no association between the score and the occurrence of NRP in individuals who underwent elective coronary artery intervention.

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