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Value of CHA2DS2-VASc Score in Predicting Intracoronary Thrombus Burden in Patients with Non ST-Elevation Myocardial Infarction

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ABSTRACT

Background: The fundamental pathophysiological basis of acute coronary syndrome (ACS) is the creation of an intracoronary thrombosis as a result of atherosclerotic plaque rupture and disruption of coronary blood flow (CBF). The amount of intracoronary thrombus load is related to a poor outcome among individuals with ACS.

Objective: To assess the ability of CHA2DS2-VASc score to predict high pre procedural intracoronary thrombus burden among individuals with non-ST segment elevation myocardial infarction (NSTEMI) who were undergoing revascularization therapy [Percutaneous Coronary Intervention (PCI)].

Patients and Methods: This prospective study enrolled 100 patients above 18 years and admitted/referred to our hospital with acute NSTEMI. The patients underwent PCI for the evaluation of cardiac risk assessment at Cardiology Department in Benha University and Materia Teaching Hospital during the period from January 2023 to January 2024.

Results: No significant differences in ischemic changes, arrhythmia and RWMA were found among groups $p>0.05$. CHA2DS2-VASc and Killip class were independent predictors for high thrombus burden (HTB) with p values < 0.001. Cut-off value of CHA2DS2-VASc score was ≥ 3.5 with sensitivity of 68 %, specificity of 74%, and AUC of 0.758.

Conclusion: When the cutoff value is ≥ 3.5, CHA2DS2-VASc score is a reliable indicator of the intracoronary thrombosis load in individuals with NSTEMI receiving initial PCI.

Key words: CHA2DS2-VASc Score, Intracoronary Thrombus Burden, Myocardial Infarction.

INTRODUCTION

When a patient has suspected ACS, the most common symptom that sets off the diagnostic and treatment process is chest pain. The ECGs of these individuals indicate that they have STEMI, unstable angina, or NSTEMI. The latter is associated with immediate chest pain but no sustained ST- segments elevation. T-wave inversion, flat T wave, pseudo-normalization of T wave, transient ST-elevation, brief or persistent ST-segment depression, and normal ECG are among the possible ECG findings [1].

Eighty percent of patients experience prolonged angina, and twenty percent experience de novo/crescendo angina. Angina, or retrosternal pain, radiating to patient's left arm (or, less commonly, the right arm), neck, or jaw, is a characteristic of typical chest pain. It can be intermittent, lasting few minutes, or chronic. Sweating, nausea, stomach discomfort, dyspnea, and syncope are possible further symptoms. Epigastric discomfort, symptoms resembling indigestion, and isolated dyspnea are examples of unusual presentations. Elderly people, women, individuals with diabetes, chronic renal illness, and dementia are more likely to experience atypical symptoms [1].

The primary pathophysiology of ACS is the production of intracoronary thrombus as a result of ruptured atherosclerotic plaque and disruption of CBF. In patients with ACS, the amount of intracoronary thrombus load is linked to a dismal outcome [2,3].

Despite the development of several pharmacological and surgical therapies, including thrombectomy and glycoprotein IIb/IIIa antagonists, intracoronary thrombus management remains complicated. Patient care for ACS patients may benefit from the identification of predictors of the intracoronary thrombus load [4].

This study evaluated the ability of CHA2DS2-VASc score to predict high pre procedural intracoronary thrombus burden among NSTEMI individuals undergoing revascularization therapy.

PATIENTS AND METHODS

This study was a cross-sectional study included 100 patients above 18 years who were admitted/referred to our hospital because of having acute NSTEMI. The patients underwent PCI for the evaluation of cardiac risk assessment at Cardiology Department in Benha University and Materia Teaching Hospital during the period from January 2023 to January 2024.

Inclusion criteria: Patients > 18 years who underwent PCI for NSTEMI. Very high risk NSTEMI that undergone immediate invasive strategy (<2 h) include: AHF with refractory angina or ST deviation, recurrent dynamic changes of ST or t-wave (especially intermittent ST-elevation), mechanical complications of myocardial infarction, life-threatening arrhythmia or cardiac arrest, hemodynamic instability or cardiogenic shock, recurrent or chest pain non-responding to medications, A high-risk NSTEMI patient underwent an early invasive approach (~24 hours) that included the following: Increase or decrease in cardiac troponin that is consistent with MI and dynamic shifts in the ST or T waves (whether audible or not). This patient had an invasive strategy (about 72 hours) for intermediate risk

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NSTEMI. The invasive strategy included diabetes mellitus (DM), kidney failure (eGFR ~<60 ml/minute/1.73 m^2), congestive HF (LVEF ~<40%), early post-infraction angina, recent percutaneous coronary intervention, history of CABG, and ischemia or recurring symptoms during non-invasive testing.

Exclusion criteria: Patients with haemorrhagic disorders, liver diseases (or transplantation), end stage renal disease (or renal transplantation), patient on anticoagulants and hypercoagulability state.

METHODS

Every patient was subjected to the following: A thorough physical assessment and a detailed medical history that included: general examination: regional cardiac examination. According to their Killip class, patients were ranked as follows: Killip classes I, II, III, and IV [5]. Prior to PCI, blood samples were obtained, the levels of creatinine and creatine kinase MB (CKMB) were assessed. For all patients with NSTE-ACS, high-sensitivity cardiac troponin was utilized as a biomarker of cardiomyocyte damage. Within 10 min from the initial medical contact, a standard 12-lead ECG was conducted, and patients with acute chest pain who were identified with non-ST-segment elevation did not have persistent ST-segment elevation. Regional wall motion and left ventricular systolic function were evaluated, and wall motion anomalies were found using resting transthoracic echocardiography (TTE). A Philips Echo machine was utilized for assessing EDD, ESD, PWD, IVSD, FS, and LVEF. Two echo specialists blinded reviewed the findings in accordance with ASE guidelines [1,6].

Assessment of CHA2DS2-VASc Score:

HF is a condition characterized by symptoms such as shortness of breath, inability to lie flat, and fluid retention. Hypertension is a common cardiovascular condition characterized by persistent elevation in arterial pressure. Diabetes mellitus is diagnosed when a patient presents with hyperglycemia symptoms and plasma glucose levels exceed 200 mg/dL, HB A1C over 6.5 mg/dL, fasting plasma sugar over 125 mg/dl, or 2 hours plasma glucose over 200 mg/dL. Stroke is a clinical illness defined by the fast onset of clinical indications of a disruption in brain function that lasts longer than twenty-four hours and has no other known cause outside vascular origin. Increased risk of myocardial infarction and HF, as well as a greater prevalence of concurrent coronary artery disease, are linked to vascular disease [7,8].

Age is a definitive risk factor for HF, while age below 75 and 65 years is a combination risk factor. Female sex is also considered a combination risk factor for developing ischemic cerebrovascular health problems [9]. **CHADSVASc score**: Based on the definition of the definitive risk factor (history of stroke/TIAs/TEs and age over 75 years) and combination risk factors (HF/moderate-severe cardiac dysfunction, hypertensive heart disease, DM, vascular diseases, female sex, and age between 65 and 74 years), CHA2DS2-VASc is utilized to evaluate the risk for thrombo-embolism [9].

PCI procedure:

A study of 100 patients underwent coronary angiography utilizing the Seldinger approach, with all lesions evaluated using criteria such as degree of stenosis, coronary flow evaluation, and thrombus load. The angiographer, who was blinded to the patients' clinical state, evaluated the grade of stenosis by the percent reduction in lumen diameter relative to the proximal healthy section of the artery. The left and right coronary systems were assessed using right and left anterior oblique views. The thrombus burden was graded as Grade 0 (no evidence of thrombus), Grade 1 (suspected thrombus), Grade 2 (definite thrombus and greatest dimensions >1/2 diameter of the coronary artery), Grade 3 (definite thrombus and greatest dimensions >1/2 to <2 diameter of the coronary artery), Grade 4 (definite thrombus and greatest dimension>2 diameter of the coronary artery), and Grade 5 (complete thrombotic occlusion). The study population was split into two groups: 50 cases with low thrombus burden (LTB) (i.e. grades 0–3) and 50 cases with HTB (i.e. grades 4–5).

Ethical guidelines:

This study obtained its approval from Benha Faculty of Medicine's Ethics Committee. Written consents were taken from all patients before participation. Each patient has an individual file that was coded. All queries and research results were kept anonymous while being utilized solely for academic purposes. The Helsinki Declaration was followed at every stage of the research.

Statistical analysis

The gathered data were evaluated with SPSS version 22.0 for Windows®. For the qualitative data, percentage and numerical descriptors were employed and they were compared using the X^2-test. Continuous variables were expressed as means ± standard deviations (SDs) or median and range. The Student t-test was utilized to evaluate two independent sets of parametric data and Mann Whitney-U test was utilized for comparison between two different sets of non-parametric data. Significance was set at $p \leq$ to 0.05.

RESULTS

There was statistically significant difference between the two groups regarding the age, but no significant difference was found as regards gender, DM, hypertension, smoking, and dyslipidemia (Table 1).

Table (1): Demographics and risk factors of the two groups

Variable	LTB (n=50)	HTB (n=50)	Test of significance	P value
Age (years) Mean ± SD	61.54±8.67	66.54±8.89	t=-2.846	0.005*
Sex Male Female	 34 (68.0%) 16 (32.0%)	 38 (76.0%) 12 (24.0%)	χ^2=0.794	0.373
Smokers	19 (38.0%)	28 (56.0%)	χ^2=3.252	0.071
HTN	33 (66.0%)	37 (74.0%)	χ^2=0.762	0.2383
Dyslipidemia	27 (54.0%)	35 (70.0%)	χ^2=2.716	0.099
DM	27 (54.0%)	31 (62.0%)	χ^2=0.657	0.418

*: Significant

There was a highly statistically significant difference between the two groups regarding congestive HF, vascular disease and CHA2DS2-VASc score and a statistically significant difference as regards patient age more than 75 years and history of stroke, but no significant difference was found regarding hypertension, diabetes, sex and age (Table 2).

Table (2): CHA2DS2-VASc score in the two groups

CHA2DS2-VASc Score	LTB (n=50)	HTB (n=50)	Test of significance	P value
CHF	10 (20.0%)	29 (58.0%)	χ^2=15.174	<0.001*
HTN	31 (62.0%)	37 (74.0%)	χ^2=1.654	0.198
Age 65-75	11 (21.0%)	18 (36.0%)	χ^2=2.38	0.123
Age >75	8 (16.0%)	18 (36.0%)	χ^2=5.198	0.023*
DM	28(56.0%)	33 (66.0%)	χ^2=1.056	0.305
Stroke	9 (18.0%)	18 (36.4%)	χ^2=4.110	0.043*
Vascular disease	7 (14.0%)	32 (64.0%)	χ^2=26.272	<0.001*
Sex	16 (32.0%)	12 (24.0%)	χ^2=0.794	0.373
Score: Median (Min-Max)	2.5 (2-4)	4 (3-6)	Z=4.513	<0.001*

*: Significant

Regarding Killip class, the main difference between the two groups was statistically significant (Table 3).

Table (3): Killip class in the two groups

Killip class	LTB (n=33)	HTB (n=33)	P value
I **II** **III** **IV**	42 (84.0%) 6 (12.0%) 2 (4.0%) 0 (0%)	21 (42.0%) 7 (14.0%) 18 (36.0%) 4 (8.0%)	<0.001*

*: Significant.

Regarding ischemic changes and arrhythmia, the primary difference between both groups was statistically non-significant (Table 4).

Table (4): ECG among low thrombus and high thrombus burden groups

ECG	LTB (n=50)	HTB (n=50)	Test of significance	P value
Ischemic changes	20 (40.0%)	23 (46.0%)	0.367	0.545
Arrhythmia	18(36.0%)	25(50.0%)	1.999	0.157

Regarding RWMA the main difference among both groups was non-significant, while LVEF was statistically significant (Table 5).

Table (5): Comparison of ECHO among the two groups

Echo	LTB (n=50)	HTB (n=50)	Test of significance	P value
RWMA	68 (82%)	68 (82%)	**X^2 =0**	1
LVEF	56.94±9.18	49.15±10.18	T= 4.018	<0.001*

*: Significant

CHA2DS2-VASc and Killip class were independent predictors for HTB (Table 6).

Table (6): Multivariate logistic regression analysis for independent predictors of HTB

		B	S.E.	P value	P value	95% C.I.	
						Lower	Upper
High risk	**KILLIP CLASS (III, IV)**	3.008	0.815	< 0.001*	20.24	4.100	99.933
	CHA2DS2-VASc	0.628	0.163	< 0.001*	1.873	1.362	2.576

CI: confidence interval, *: Significant

Cut-off value of CHA2DS2-VAS score was ≥ 3.5, with sensitivity of 68 %, specificity of 74% and area under the curve of 0.758 (Table 7).

Table (7): Diagnostic accuracy of CHA2DS2-VASc as a predictor for HTB

AUC	95% CI	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
0.758	0.66-0.85	3.5	68.0%	74.0%	72.3	69.8	71.0%

CASE PRESENTATION

Case (1)

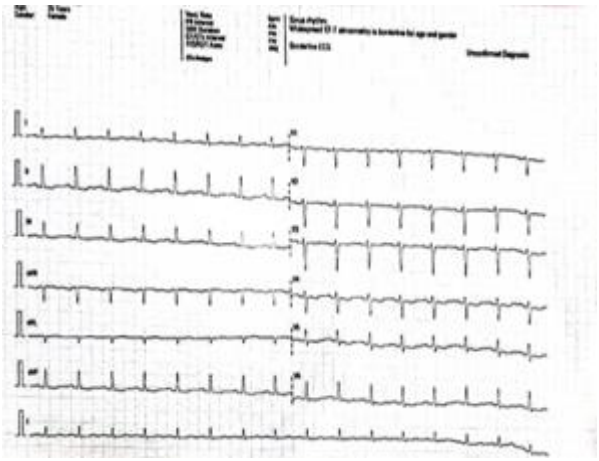
Patient No. (81) High thrombus burden group:

68 years old female patient, HTN, DM, ICM and CVS 5 years ago with residual right-side weakness. She presented with retrosternal refractory agonizing chest pain described as heaviness radiating to left shoulder, started 30 min. before presentation. Examination: Blood pressure: 90/40 mmHg, pulse: 98 beats/minute, auscultation: S1, S2, S3 no detected murmurs and congested neck veins, BMI: 31 kg/m^2, Killip class: II, CHA2DS2-VASc score: 8, Risk: very high risk NSTEMI and **ECG:** shows ST-segment depression in leads V4_V5_V6, and T-wave inversion in leads II – III – avF and V4_V5_V6.

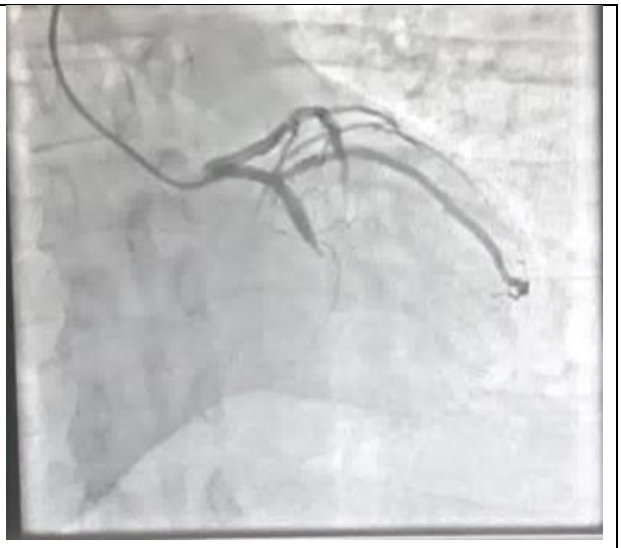
Echocardiography: EF 37 %, LVEDD 5.9 cm, LVESD 3.7 cm, resting wall motion abnormality in form of anterior, antroseptal and inferior walls hypokinesia and no mechanical complication.

Lab Findings: Hemoglobin 15 g/dl, Ck-mb 133 U/L, troponin 540 ng/ml and creatinine 1.2 mg/dL.

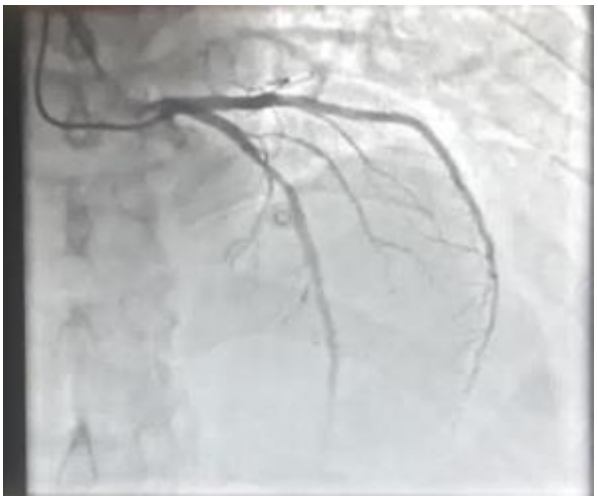
Coronary angiography showed: **LAD**: mid significant lesion, **RCA**: mid significant lesion, **LCX**: proximal total occlusion and **Complications**: none.



ECG: shows ST-segment depression in leads V4_V5_V6, and T-wave inversion in leads II – III – avF and V4_V5_V6



RAO view with caudal projection showed mid total occlusion of LCX



PA view with cranial projections, showed mid LAD significant lesion

LAO view, showed proximal RCA significant lesion

Case (II)

Patient NO. (40) Low thrombus burden group:

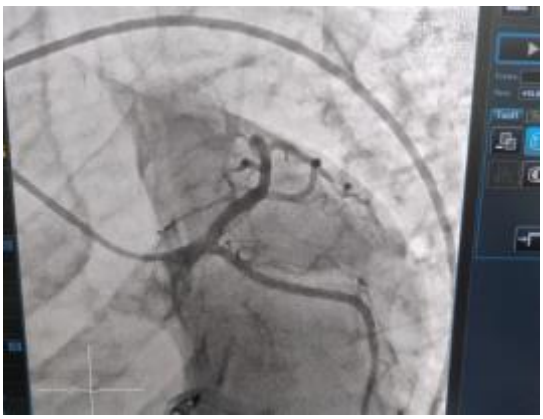
61 years old male patient, diabetic and dyslipidemic. He presented with precordial chest pain described as tightness, started 9 hours before presentation. Examination: Blood pressure: 110/60 mmHg. Pulse: 65 beats/min. Auscultation: normal S1 and S2, no detected murmurs and not congested. BMI: 27 kg/m^2, No signs of HF, Killip class: I CHA2DS2-VASc score: 1, Risk: intermediate risk NSTEMI, **ECG:** sinus rhythm with non-specific T wave abnormality. **Echocardiography:** EF 50%, LVEDD 4.6 cm, LVESD 3.1 cm, resting wall motion abnormality in form of inferior and inferolateral wall hypokinesia and no mechanical complications.

Lab Findings: Hemoglobin 11 g/dl, Ck-mb 69 U/L, Troponin 360 ng/ml and Creatinine 1.4 mg/dL.

Coronary angiography showed: LAD: Normal Vessel, **LCX:** Normal Vessel, **RCA**: Normal Vessel. **Complications:** none.

ECG: sinus rhythm with non-specific T wave abnormality.

LAO view showed Normal RCA



LAO view with caudal projection showed normal LCX and LAD

DISCUSSION

Group I's mean age was 61.54±8.67 years, whereas group II's mean age was 66.54±8.89 years, indicating a significant difference (P = 0.005) in terms of age.

This was consistent with the findings of **Mirbolouk *et al.* [10],** who assessed the CHA2DS2-VASc score as a straightforward tool for forecasting the total occlusion by a thrombus in ACS cases undergoing primary PCI and discovered a significant age difference (P <0.001) among the groups under investigation.

In terms of gender, there were 68.0% of males in group I and 76.0% of males in group II with no significant difference among both groups (P =0.373).

This finding aligns with the research conducted by **Satilmiş and Durmuş [11]** who examined the accuracy of CHA2DS2-VASc score in identifying cases with NSTEMI and separated the study population into two groups based on thrombus burden. Their findings revealed a non- significant difference in gender among both groups (P = 0.72).

In our study, a statistically non-significant difference existed between both groups with respect to the following: smoking (19 cases in LTB group and 28 cases in HTB group with p= 0.071), dyslipidemia (27 cases in LTB group and 35 cases in HTB group with p = 0.099), DM (27 cases in LTB group and 31 cases in HTB group with p = 0.418), and hypertension (33 cases in LTB group and 37 cases in HTB group).

This was in opposition to **Barman *et al.* [12],** who split the study population into two groups and discovered a significant difference in the study groups as regards hypertensive heart disease (P= 0.004) and diabetes (P= 0.009). The researchers studied the ability of CHADS-VASc score to predict thrombus burden and no-reflow in NSTEMI cases.

It's possible that the limited sample size in our investigation contributed to the disparity between the results of the prior study and our findings regarding DM and hypertension.

Our results revealed a significant difference between both groups regarding congestive HF (group I had 10 patients with CHF (20.0%), while group II had 29 patients with CHF (58.0%) and vascular disease (group I had 7 patients with vascular disease (14.0%), and group II had 32 patients with vascular disease (64.0%), with a p value of ≤0.001).

This was consistent with the findings of **Satılmış and Durmuş [11],** who examined the accuracy of the CHA2DS2-VASc score in identifying HTB in 251 NSTEMI cases that underwent PCI during their hospital stay. They also reported a significant difference with regard to CHF (p <0001) between LTB and HTB groups.

In addition, our analysis revealed a significant difference (p = 0.043) in the number of individuals with a history of stroke (18.0% of cases in LTB group versus 36.0% of cases in HTB group).

This agrees with **Barman *et al.* [12]** who evaluated 428 consecutive NSTEMI patients to evaluate the correlation between the CHA2DS2-VASc score and thrombus load. They discovered a statistically significant difference with respect to prior stroke or TIA (p value <0001).

The CHA2DS2-VASc score demonstrated a significant difference (P ≤0.001) among both groups, with the median in group I being 2.5 (2–4) and group II being 4 (3-6).

Consistent with the findings of **Seyis *et al.* [13],** the CHA2DS2-VASc score demonstrated a significant difference among their study groups (P< 0.001), with the mean values of 1 ± 2 and 4 ± 3 in group I and group II, respectively. The difference in Killip class was statistically significant between the 2 groups, with a P value of 0.001.

This was consistent with the findings of **Ipek and co-workers [14],** who reported that Killip class was significant (P <0.001) in their investigation of the ability of CHA2DS2-VASc score to predict thrombus load and no-reflow in NSTEMI cases. In terms of LVEF, group I had a mean of 56.94±9.18, whereas group II had a mean of 49.15±10.18. This difference was significant (P = 0.002).

This was in opposition to **Duman *et al.* [15],** who used the CRP to albumin ratio as a predictive value to determine the incidence of thrombus burden in ACS cases. They also separated the study population into LTB and HTB groups and discovered that LVEF did not show significant difference between both groups.

The difference between the results of the prior study and ours on LVEF may be caused by our sample size, which only included one type of ACS—NSTEMI—while the other studies included both STEMI and NSTEMI.

To determine the impact of CHA2DS2-VASc, Killip class (III, IV), and other risk variables on the probability that individuals will have a HTB, a multivariate logistic regression model was run.

The outcome showed that CHA2DS2-VASc is a significant independent predictor of HTB incidence (p < 0.001).

The ROC curve analysis indicated that a CHA2DS2-VASc score higher than or equal to 3.5 predicted thrombus burden with a sensitivity of 68.0% and a specificity of 74.0% (AUC = 0.758).

This agrees with the findings of **Ipek *et al.* [14],** who discovered that HTB group had substantially higher CHA2DS2-VASc ratings than controls. Following a multivariate regression analysis, the CHA2DS2-VASc score continued to be an independent predictor of HTB with complete blockage (OD: 1.58, 95% CI: 1.33-1, 88%, P < 0.001).

With a sensitivity of 66% and a specificity of 59%, ROC analysis showed that the cut-off of CHA2DS2-VASc score was predictive of high thrombus with complete blockage, which went against our findings. Furthermore, a strong association was found between in-hospital mortality and CHA2DS2-VASc scores [14].

Furthermore, consistent with the findings of **Mirbolouk *et al.* [10],** the CHA2DS2-VASc score could independently predict HTB with total occlusion (OD: 3.06, 95%, CI: 2.23-4.21, P <0.001), provided that the CHA2DS2-VASc score has a cut off of ≥ 2. The score has a sensitivity of 88%, specificity of 67%, AUC: 0.83 with 95% CI (0.79-0.88).

LIMITATIONS

We require a larger research to corroborate our findings since the sample size is insufficient to continue the analysis of the relevant groupings. Lastly, the definition of coronary artery disease was established using angiographic images obtained from a 2D X-ray; the size of the thrombus and, consequently, the thrombus load were not evaluated using IVUS or FFR, which might have affected the interpretation of coronary angiography.

CONCLUSION

When the cutoff value is ≥ 3.5, the CHA2DS2-VASc score is a reliable indicator of the intracoronary thrombus load in individuals with NSTEMI receiving initial PCI.

RECOMMENDATIONS

This study only contained one center; thus, it must be replicated with recruitment from a wider population and several locations. Before doing primary PCI, CHA2DS2-VASc score is applied to NSTEMI patients in the emergency room to estimate the intracoronary thrombus load.

Conflict of interest: none declared
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