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CHA2DS2-VASc Score as a Predictor of Thrombus Burden in Patients with Non ST-Elevation Myocardial Infarction

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ABSTRACT

Background: CHA2DS2VASc score is a predictive tool that enables estimation the risk of developing ischemic stroke and thrombo-embolism in cardiac patient. Intracoronary thrombus formation due to atherosclerotic plaque rupture and the interruption of coronary blood flow constitute the main pathophysiology underlying acute coronary syndrome Objective: Assessment of the ability of CHA2DS2-VASc score for predicting high intracoronary thrombus and to evaluate the prognostic value of it in assessment of stroke, re-infarction and mortality in patients with Non- ST-Elevation Myocardial Infarction (NSTEMI). Methods: Sixty-six patients were enrolled in our study, divided into 2 groups; Group I (n = 33 patients) represents low thrombus grade, Group II (n = 33 patients) represents high thrombus grade. All patients were subjected to coronary angiography to assess degree of stenosis and coronary flow by thrombolysis in myocardial infarction (TIMI) grade score. Sensitivity, specificity and diagnostic accuracy of CHA2DS2-VASc in prediction of high thrombus burden were assessed. Results: The mean age for Group I and II was 62.21±9.51 and 66.67±9.14 years respectively. LV average global systolic strain (AGS) was significantly lower in group I and II when compared to group III. Age, Killip class and LA diameters are highly significant predictors for incidence of high CHA2DS2-VASc. The diagnostic accuracy of CHA2DS2-VASc in prediction of high thrombus burden was 83.3% with cut-off value 4. Conclusion: CHA2DS2-VASc score is a good predictor of intracoronary thrombus burden in non ST segment elevation myocardial infarction patients undergoing primary PCI at a cutoff value equal or more than 4 and also can be a predictor of the outcomes after primary PCI.

Key words: CHA2DS2-VASc score, NSTEMI, Thrombus burden.

Introduction:

Acute coronary syndrome (ACS) is the most common cause of cardiac morbidity and death **(1).** Intracoronary thrombus formation due to atherosclerotic plaque rupture and the interruption of coronary blood flow constitute the main pathophysiology underlying acute coronary syndrome.

The quantity of the intracoronary thrombus burden is associated with a poor prognosis in patients with Acute coronary syndrome **(2)**.

The CHA2DS2VASC risk score was developed to predict the risk of stroke in patients with atrial fibrillation (AF) **(3).** This score includes variables such as heart failure, hypertension, age, diabetes mellitus, gender, vascular disease, and stroke **(4)**

Intracoronary thrombus management is still complex, although many pharmacological and invasive treatments have been developed, such as glycoprotein IIb/IIIa antagonists and thrombectomy. Identifying predictors of the intracoronary thrombus burden may contribute to the management of patients with acute coronary syndrome **(3)**

In our study we investigated the association of both CHA2DS2VASc score and thrombus burden in patients with acute Non-STEMI undergoing revascularization therapy (Percutaneous Coronary Intervention).

Patients and Method:

This study was a prospective cohort study which included a total of 66 patients with acute NSTEMI for PCI and risk assessment admitted to Zagazig university hospitals and National Heart Institute. Patients were enrolled in the study after obtaining their written informed consent, and approval of the local ethics committee of the hospital.

Patients included in the study who had very high risk, high risk and intermediate risk NSTEMI, they were divided according to their coronary angiography into 2 groups; Group I (n = 33 patients): patients with low thrombus grade, Group II (n = 33 patients): patients with high thrombus grade.

Patients who were excluded included: Patients with, low risk for NSTEMI and no recurrent symptoms, history of hemorrhagic disorder, history of liver disease or transplant, history of liver disease or transplant, and patients on anticoagulant medication were excluded from our study.

After exclusion of non-responders, drop out participants and those with exclusion criteria, 66 patients completed the study (this number was considered suitable enough sample for statistical analysis with significant results and correlations).

All patients were subjected to detailed history, including CAD risk factors, physical examination including Killip class, Electrocardiography (ECG) within 10 minutes of first medical contact to detect ST segment and T wave abnormalities.

Blood samples were collected before cardiac catheterization. Patients fasted for >12 hours before cardiac catheterization. Blood was collected either from the antecubital vein or indwelling catheter into Two 3.2% trisodium citrate tube after discarding the initial 3 ml of blood. Serum was separated by centrifugation at 2000g for 15 minutes and stored at -70°C. High sensitive troponin and CKMB were measured.

Echocardiographic images were obtained in the parasternal long-axis and short-axis and apical two-chamber and four-chamber views using standard transducer positions. Vivid 9, General Electric Healthcare (GE Vingmed, Norway) equipped with a harmonic M5S variable-frequency (1.7-4 MHz) phased-array transducer was used.

LV dimensions and wall thickness, EF, and left atrial diameter and volume were measured in accordance with the recommendations of the American Society of Echocardiography. **(5)**

Estimating the risk for thrombo-embolism using CHA2DS2-VASc is based on defining the definitive risk factor (previous stroke/TIA/TE and age above 75 years) with 2 points and

combination risk factors (heart failure/moderate-severe cardiac dysfunction, hypertension, diabetes, vascular disease, female gender, and age range from 65 to 74 years) with 1 point.

Right and left coronary angiography was performed using multiple projections and analysis was done by professional interventionists who were blind to the cases. Angiographic CAD is defined as ≥ 50% luminal diameter stenosis of at least one major epicardial coronary artery.

Coronary flow assessment was assessed by thrombus grade after restoring antegrade flow through guidewire or small balloon dilatation. Angiographic thrombus burden was classified as previously defined by the thrombolysis in myocardial infarction (TIMI) study group. **(6)**

Grade 0: no evidence of thrombus, grade 1: suspected thrombus (low contrast density, haziness, irregular lesion contour, or a smooth convex meniscus at the site of occlusion)**,** grade 2: definite thrombus and the thrombus greatest dimensions _1/2 vessel diameter**,** grade 3: definite thrombus and the thrombus greatest dimension >1/2 to <2 vessel diameters,**,** grade 4: definite thrombus and the thrombus greatest dimension>2 vessel diameter**,** grade 5: total thrombotic occlusion.

All patient had undergone follow up for six months by telephone after acute NSTEMI to evaluate stroke, re-infarction and mortality.

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 20. Statistical analysis was performed using Statistical Package for The Social Sciences Version 22 (IBM Corp., Armonk, NY, USA). Quantitative data are expressed as means and standard deviations.

P-Value ≤ 0.05 was considered to indicate significance. Correlation analysis assesses the strength of association between two variables. Multiple logistic regression analysis was used to detect the associations between lipid profile and both maternal and neonatal complications.

Results:

The patients were classified into 2 groups according to thrombus grade into group I, 33 patients with low thrombus grade and group II, 33 patients with high thrombus grade.

There was a non-significant difference between the studied groups regarding to demographic data (age, gender) and risk factors of CAD (Table 1).

There was non-significant difference between group I and II regarding serum creatinine, CMB and troponin with p value 0.575, 0.530 and 0.064 respectively as shown in (Table 2).

Regarding CHA2DS2-VASc Score parameters, there was a significant difference between group I and II regarding congestive heart failure, age more than 75, stroke and vascular disease with p values ≤0.001, 0.048, 0.049 and ≤0.001respectively. On the other hand, there was a non-significant difference regarding hypertension, age 65-75, DM and sex category with p value 0.296, 0.097, 0.177 and 0.306 respectively (Table 3).

Regarding Echo data, there was a significant difference between the two groups regarding LA dimension and LVEF with p values 0.001 and 0.002 respectively (Table 4).

Regarding IRA, in group I there was 20 patients with LAD lesion, 6 with RCA lesion and 7 with LCX lesion while in group II there was 17 patients with LAD lesion, 10 with RCA lesion and 6 with LCX lesion. The difference between the groups was statistically non-significant with P value 0.517. Also, there was non-significant difference between the two groups regarding number of vessels involved with p value 0.612 (Table 5).

In group I, there were 5 patients with G0, 10 with G1, 12 with G2 and 6 with G3 while in group II there was 11 patients with G4 and 22 with G5. The difference between the groups was statistically significant with P value ≤0.001 (Table 5, Figure 1).

Regarding Outcome after 6 months between low thrombus and high thrombus burden groups there was statistically significant difference regarding **stroke** and **death** with p value 0.049 and 0.021 respectively (Table 6, Figure 2).

There was a positive significant correlation between CHA2DS2-VASc Score and age, Killip class and LA dimension with p values 0.002, ≤0.001 and 0.001 respectively. Meanwhile there was a significant negative correlation with LVEF with p value 0.012 (Table 7)

A multivariate logistic regression model was performed to ascertain the effects of age, Killip class and LVEF on the likelihood that participants would have high CHA2DS2-VASc. The result showed that age, Killip class and LA diameters are highly significant predictors for incidence of high CHA2DS2-VASc with p values <0.001, 0.035 and 0.008 respectively (Table 8).

The best cut-off value considering CHA2DS2-VASc in prediction of high thrombus burden is 4 with 87.9% sensitivity, 78.8% specificity and accuracy 83.3% (Table 9, Figure 3).

Table (1): Demographic data and risk factors among the studied groups

Variables	Low thrombus burden (n=33)	High thrombus burden (n=33)	Test of significance	P value
Age (years) Mean ± SD	**62.21±9.51**	**66.67±9.14**	**t=1.94**	**0.057**
Sex Male Female	**23 (69.7%) 10 (30.3%)**	**19 (57.6%) 14 (42.4%)**	**χ^2=1.05**	**0.306**
Smokers	**13 (39.4%)**	**16 (48.5%)**	**χ^2=0.554**	**0.457**
HTN	**20 (60.6%)**	**24 (72.7%)**	**χ^2=1.09**	**0.296**
Dyslipidemia	**16 (48.5%)**	**20 (60.6%)**	**χ^2=0.978**	**0.323**
DM	**19 (57.6%)**	**25 (75.8%)**	**χ^2=2.45**	**0.117**

T:student t- test, χ^2 : Chi square test

Table (2): Laboratory investigations among two groups.

Laboratory investigations	Low thrombus burden (n=33)	High thrombus burden (n=33)	Test of significance	P value
Creatinine Mean ± SD	1.03±0.19	1.00±0.15	t=0.563	0.575
CKMB Median (Min-Max)	54 (5-122)	54 (9-160)	Z=0.629	0.530
TPN Mean ± SD	2.39±0.99	2.85±0.98	t=1.89	0.064

T: student t- test, Z: Mann Whitney test

Table (3): CHA2DS2-VASc Score among two groups.

CHA2DS2-VASc Score	Low thrombus burden (n=33)	High thrombus burden (n=33)	Test of significance	P value
CHF	5 (15.2%)	19 (57.6%)	χ^2=12.83	≤0.001*
HTN	20 (60.6%)	24 (72.7%)	χ^2=1.09	0.296
Age 65-75	7 (21.2%)	12 (36.4%)	χ^2=2.75	0.097
Age >75	5 (15.2%)	12 (36.4%)	χ^2=1.85	0.048*
DM	19 (57.6%)	25 (75.8%)	χ^2=2.45	0.177
Stroke	5 (15.2%)	12 (36.4%)	χ^2=3.88	0.049*
Vascular dse	4 (12.1%)	21 (63.6%)	χ^2=18.61	≤0.001*
Sex	10 (30.3%)	14 (42.4%)	χ^2=1.045	0.306
Score (Min-Max)	**3 (1-4)**	**5 (3-8)**	Z=6.02	≤0.001*

*$\chi^{2:}$ Chi square test, Z: Mann Whitney test, *significant p≤0.05*

Table (4): Comparison of ECHO between the two groups

Echo	Low thrombus burden (n=33)	High thrombus burden (n=33)	t-test	P value
LA.d	3.52±0.42	3.84±0.35	3.34	0.001*
LVEDD	5.08±0.67	5.13±0.72	0.298	0.767
LVESD	3.54±0.69	3.87±0.76	1.79	0.078
LVEF	56.94±9.18	49.15±10.18	3.26	0.002*

Table (5): Coronary angiography among the studied groups

Coronary angiography	Low thrombus burden (n=33)	High thrombus burden (n=33)	Test of significance	P value
IRA **LAD** **RCA** **LCX**	 20 (60.6%) 6 (18.2%) 7 (21.2%)	 17 (51.5%) 10 (30.3%) 6 (18.2%)	χ^2=1.32	0.517
No of vessels involved: **Single vessel** **Double vessels** **Multivessel**	 16 10 7	 11 12 10	χ^2=1.48	0.612
Thrombus grade **G0** **G1** **G2** **G3** **G4** **G5**	 5 (15.2%) 10 (30.3%) 12 (36.4%) 6 (18.2%) 0 (0%) 0 (0%)	 0 (0%) 0 (0%) 0 (0%) 0 (0%) 22 (66.7%) 11 (33.3%)	MC	≤0.001*

*$\chi^{2:}$ Chi square test, MC: Monte carlo test, *significant p≤0.05*

Table (6): Table (6): Outcome after 6 months between the two groups

Outcome	Low thrombus burden (n=33)	High thrombus burden (n=33)	Test of significance	P value
Stroke	3 (9.1%)	9 (27.3%)	χ^2=4.13	0.049*
Re infarction	4 (12.1%)	8 (24.2%)	χ^2=1.63	0.202
Death	2 (6.1%)	9 (27.3%)	χ^2=5.34	0.021*

Table (7): Correlation between CHA2DS2-VASc Score and other variables

Variables	CHA2DS2-VASc Score	
Age (years)	0.378	0.002*
Creat	-0.009	0.940
CKMB	0.157	0.209
TPN	0.160	0.199
Killip class	0.441	≤0.001*
LA.d	0.412	0.001*
LVEDD	0.034	0.783
LVESD	0.186	0.136
LVEF	-0.309	0.012*

Spearman correlation was used

Table (8): Multivariate linear regression analysis for independent predictors of CHA2DS2-VASc Score

Independent predictors	β	Std. Error	p
Age (years)	0.063	0.017	<0.001*
Killip class	0.579	0.30	0.035*
LA.d	1.12	0.411	0.008*
LVEF	0.002	0.025	0.953

Table (9): Diagnostic accuracy of CHA2DS2-VASc in prediction of high thrombus burden

AUC	95% CI	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
0.923	0.86-0.98	4	87.9%	78.8%	80.6	86.7	83.3%

SN: Sensitivity, SP: Specificity, PPV: Positive, Predictive Value, NPV: Negative Predictive Value, AUR: Area Under Receiver Operating Characteristic curve, 95%CI: 95% Confidence Interval

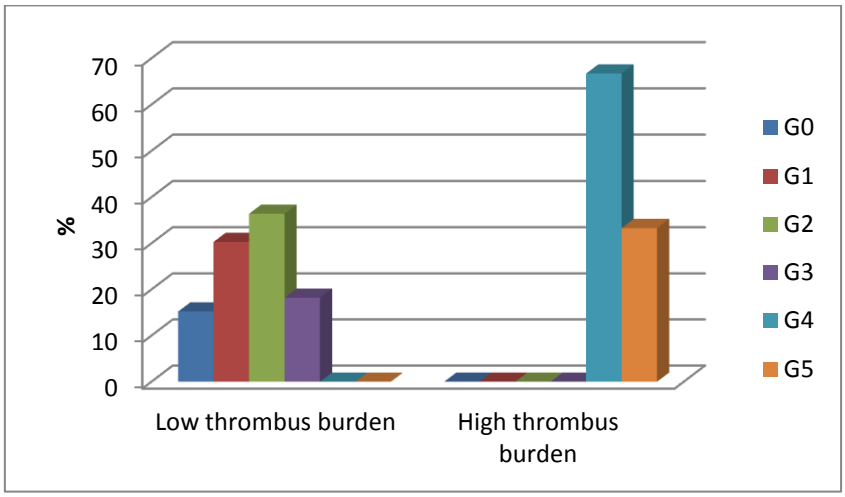

Figure 1: Thrombus grade between two groups

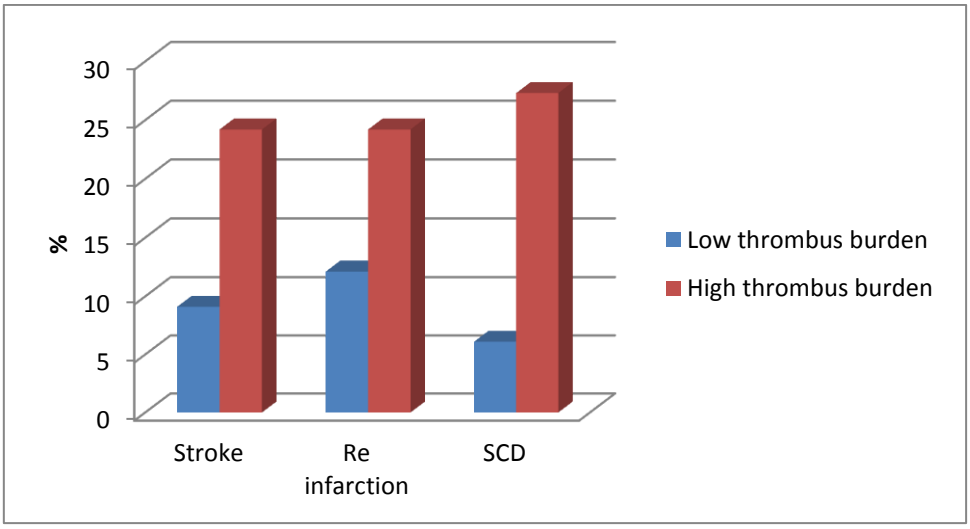

Figure 2: Outcome after 6 months between the two group

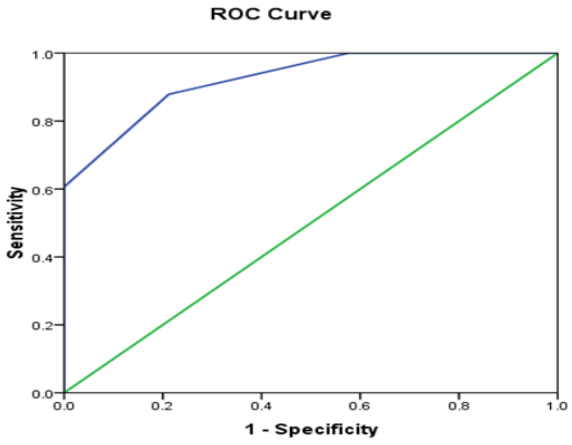

Figure 3: ROC curve for CHA2DS2-VASc Score in prediction of high thrombus burden

Discussion:

Acute coronary syndrome (ACS) is the most common cause of cardiac morbidity and death. Accurate management decisions in light of comprehensive evaluations may improve the outcomes of patients at a higher risk **(7)**

Intracoronary thrombus formation due to atherosclerotic plaque rupture and the interruption of coronary blood flow constitute the main pathophysiology underlying acute coronary syndrome. The quantity of the intracoronary thrombus burden is associated with a poor prognosis in patients with Acute coronary syndrome **(2).**

We enrolled 66 patients in our study with acute NSTEMI, coronary angiography was done to those patients to detect thrombus grade.

Our results found no statistically significant difference between the two groups as regarding demographic data and risk factors. This was in disagreement with **Mirbolouk et al (8)** who found a statistically significant difference between the studied groups regarding the age (P value <0.001), while in agreement with **Bakirci et al (9)** who found a statistically non-significant difference between the studied groups regarding the age (P value 0.129)

Satılmış and Durmuş (10) agreed with our results regarding gender and found a non-statistically significant difference between the groups with (P-value=0.72)

In contrary to our results, Barman et al **(11)** found a statistically significant difference between the studied groups regarding the hypertension (P value 0.004) and DM (P value 0.009). This discrepancy between the previous study and our results regarding hypertension and DM could be due to small sample size in our study.

In our study, there was a statistical non-significant difference regarding serum creatinine p value= 0.575, this was against **Mirbolouk et al (8)** who found a statistically significant difference between the studied groups with p value= 0.002. This discrepancy between the previous study and our results is due to exclusion of CD patients from our study.

Regarding CKMB, there was statistically non-significant difference with P value =0.530. This was against **Hakan Duman et al (12)** who found statistically significant difference regarding CKMB (p value =0.04). This discrepancy between the previous study and our results could be due to early withdrawal of CKMB sample from patients in our study.

Our results regarding CHA2DS2-VASc score was in agreement with **Satılmış and Durmuş (10)** in which 251 patients with NSTEMI who underwent PCI during their hospitalization studied for accuracy of CHA2DS2-VASc score in determining the high thrombus burden and divided the study population into two groups according to thrombus burden and found statistically significant difference regarding congestive heart failure (p value <0001). And also, in agreement **with Barman et al (11)** with statistically significant difference regarding Previous stroke/TIA (p value <0001)

While against our result regarding Vascular disease **Satılmış and Durmuş (10)** found statistically non-significant difference regarding Vascular disease (p value =0.62). This discrepancy between the previous study and our results could be because most patient do not discover peripheral vascular disease as well.

Regarding Echo data, there was a significant difference between both groups regarding LA dimension and LVEF. This was against **Duman et al (13)** who found that the LVEF was statistically non-significant with P value =0.09. This discrepancy between the previous study and our results regarding LVEF could be due to sample size in our study contain only one category of ACS which was NSTEMI but other study contains STEMI and NSTEMI.

Regarding IRA, there was a statistically non-significant with P value 0.517. This was in agreement with **Duman et al (13)** who study the incidence of Thrombus Burden in Patients With Acute Coronary Syndrome and found in group I (Low thrombus burden group) there was 35% of patients with LAD lesion, 20% with RCA lesion and 44% with LCX lesion while in group II (high thrombus burden group) there was 27% patients with LAD lesion, 27% with RCA lesion and 45% with LCX lesion and the difference between the groups was statistically non-significant with P value 0.233. Also **Hakan Duman et al (12)** found the same results.

Regarding Thrombus grade, in group I there was 5 patients with G0, 10 with G1, 12 with G2 and 6 with G3 while in group II there was 11 patients with G4 and 22 with G5 with statistically significant with P value ≤0.001. This was in agreement with **Hakan Duman et al (12)** who found the difference between the groups regarding thrombus grade was statistically significant with P value <0.001.

ROC curve analysis was done to pick up the best cut off value of CHA2DS2-VASc Score and incidence of high thrombus burden which revealed CHA2DS2-VASc Score more than or equal to 4 with sensitivity 87.9 % and specificity 78.8% Area under the curve 0.923.

This was in agreement with Ipek et al **(14)** who found CHA2DS2-VASc scores were significantly higher in the no-reflow group (high thrombus burden) compared to the control group. After a multivariate regression analysis, CHA2DS2-VASc score remained as an independent predictor (odds ratio: 1.58, 95% confidence interval: 1.33-1, 88, P < .001) of high thrombus with total occlusion.

Also, in agreement with **Mirbolouk et al (8)** who found that CHA2DS2-VASc score can predict high thrombus with total occlusion (no-reflow) independently (odds ratio: 3.06, 95%, confidence interval: 2.23-4.21, P <0 .001) with a cut off value of ≥ 2 for the CHA2DS2-VASc score in predicting the no-reflow with a sensitivity of 88% and specificity of 67%, area under curve: 0.83 with 95% CI (0.79-0.88).

Also, in agreement with **Seyis et al (15)** who found that CHA2DS2-VASc score was higher in patients with high thrombus burden compared to patients with low thrombus burden (4.41 ± 1.7 vs. 1.47 ± 1.1, p<0.001). Logistic regression analysis revealed that one-point increment in CHA2DS2VASc score was associated with three times higher risk of having high thrombus burden (odds ratio 3.28, 95% CI: 2.57-5.70). The area under the ROC curve for a cut-off value of CHA2DS2- VASc score>2 to predict high thrombus burden was 0.925, with a sensitivity of 91% and a specificity of 82%.

Limitations

The study lacked a large validation population. Further prospective studies are thus needed to confirm our results. Also, the definition of coronary arteries disease was based on angiographic views y 2D X-ray, we did not use IVUS or FFR which may interfere with the decision of the interpretation of coronary angiography

Conclusion

CHA2DS2-VASc score is a good predictor of intracoronary thrombus burden in non ST segment elevation myocardial infarction patients undergoing primary PCI at a cutoff value equal or more than 4 and also can be a predictor of the outcomes after primary PCI.

Conflict of Interest: No conflict of interest.

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