Original Article

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Association of CHA2DS2-VASc-HS Score with Adverse In-hospital Outcomes in Patients with Non-ST Segment Elevation Myocardial Infarction

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Key words: *Ischaemic heart disease, Myocardial infarction, CHA2DS2-VASc-HS score*

Abstract

Background: *Early detection of patients with non-ST segment elevation myocardial infarction (NSTEMI) who would suffer from adverse in-hospital outcomes is important for the therapeutic decision. Recently it was described that CHA2DS2-VASc-HS and CHA2DS2-VASc score is a predictor for severity and adverse in-hospital outcomes in patients with stable coronary artery disease (CAD) and acute coronary syndrome. The aim of our study was to assess the accuracy of the CHA2DS2-VASc-HS score predicting adverse in-hospital outcomes in NSTEMI patients.*

Methods: *120 patients with NSTEMI were enrolled in this study. The CHA2DS2-VASc-HS score was calculated. The study subjects were divided into two groups. Patients' with CHA2DS2-VASc-HS score>4 were put into group I and scored" 4 into group II. They were treated as per hospital treatment protocol and followed-up for adverse in-hospital outcomes (Heart failure, cardiogenic shock, recurrent ischemic pain, significant arrhythmia and death).*

Results: *It was observed that, patients with CHA2DS2-VASc-HS score >4 had more adverse in-hospital outcomes than CHA2DS2-VASc-HS score d" 4 (20% vs. 3.3%, p=0.01). Group I patients developed cardiogenic shock 10%, heart failure 4%, recurrent ischemia 11.7%, significant arrhythmia 1.7% and death 1.7% than group II patients (1.7%, 3.3%, 3.3%, 0% and 0% respectively). By risk measurement, CHA2DS2-VASc-HS score >4 emerged as a risk factor for developing adverse in-hospital outcome (Relative risk=6).*

Conclusion: *NSTEMI patients with high CHA2DS2-VASc-HS score have more adverse in-hospital outcomes. This score, which involves only clinical parameters, can be used as a predictor of outcomes in this group of patients.*

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Introduction:

Cardiovascular diseases account for more than 17 million deaths globally each year. It contributes 30% of all deaths. Among them 80% occur in low and middle-income countries. This figure is expected to grow to 23.6 million by the year 2030. Coronary artery disease alone caused 7 million deaths worldwide in 2010 and it is an increase of 35% since 1990.[1]

Estimates from the global burden of disease study suggest that by the year 2020 the South Asian part of the world will have more individuals with atherothrombotic cardiovascular disease than any other region.[2] The exact prevalence of coronary artery disease in Bangladesh is not known. More recent data indicates that coronary artery disease prevalence is 1.85% to 3.4% in rural population and 19.6% in an urban population.[3]

The clinical presentations of coronary artery disease include silent ischemia, stable angina pectoris, non-ST segment elevation acute coronary syndrome (NSTE-ACS) comprising unstable angina and non-ST segment elevation

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myocardial infarction (NSTEMI), ST elevation myocardial infarction (STEMI), heart failure and sudden death.[4]

The incidence of NSTE-ACS compare to ST elevation myocardial infarction (MI) is increasing, probably as a result of demographic changes in the population, including progressively increasing numbers of older persons and higher rates of diabetes mellitus.[5] NSTEMI currently accounts for about 50% of all myocardial infarctions. With the increasing use of beta blockers and aspirin, the incidence of NSTEMI is increasing.[6] Prognosis in patients with NSTEMI depends on several factors and those include the extent of coronary stenosis, left ventricular dysfunction, short-term risk associated with the culprit lesion and the state at presentation.[7]

Patients with NSTEMI typically have more comorbidities, both cardiac and non-cardiac than patients with STEMI.[8] In patients with NSTE-ACS the in-hospital mortality is 3-5%.It is lower than those with STEMI, which comprises 7%. But at 6 months, the mortality rates are very similar in both conditions comprising 13% and 12% respectively. Long-term follow-up showed that the death rates were higher among patients with NSTE-ACS than with STEMI, with a two-fold difference at 4 years.[4]

This in-hospital and 6 months mortality difference between NSTE-ACS and STEMI may be due to different patient profiles, since NSTE-ACS patients tend to be older, with more co-morbidities, especially diabetes and renal failure. The lesson from this epidemiological observation is that the treatment strategies for NSTE-ACS not only need to address the acute phase but also with the same intensity on longer term management.[5]

Risk evaluation is important for the management of patients with NSTE-ACS. The risk of morbidity and mortality in NSTE-ACS patients varies according to the presence of baseline risk factors, clinical syndrome features and the management strategy. Current guidelines for the risk stratification of patients with NSTE-ACS recommend the use of the Thrombolysis in Myocardial Infarction (TIMI) risk score or the Global Registry for Acute Coronary Events (GRACE) score.[9]

Clinicians need simple, reliable, reproducible, and quantitative tools to identify patients' risks and recommend prevention strategies. The TIMI and GRACE scoring systems used for the risk stratification of NSTE-ACS patients are primarily based on multivariable models that include components of the medical history, admission electrocardiogram, and cardiac biomarker variables.[10]

The CHADS2 and CHA2DS2-VASc scores are clinical predictors used to evaluate the risk of cardiac thromboembolism in non valvular Atrial Fibrillation and to guide antithrombotic therapy. CHADS2 and CHA2DS2-VASc scores are widely used in clinical practice and include similar risk factors for the development of coronary artery disease (CAD). These scores have been demonstrated to have predictive value in terms of the risk of death after stroke, after coronary artery bypass grafting (CABG),[11] and with stable CAD and acute coronary syndrome.[12]Age, DM, male gender, hyperlipidemia, smoking, and family history of CAD are traditional risk factors for CAD. There was a strong correlation between degree of peripheral artery disease and severity of coronary atherosclerosis.[13]

Recently CHA2DS2-VASc-HS score is described as a novel predictor of CAD severity in stable CAD patients who underwent diagnostic coronary angiography. The CHA2DS2-VASc-HS nomenclature represents congestive heart failure (C), Hypertension (H), age e"75 years (A2), Diabetes Mellitus (D), and history of stroke or TIA (S2), vascular disease (V), age 65–74 years (A), and male gender (as the sex category), hyperlipidemia (H) and smoking (S). In comparison to CHA2DS2-VASc score, this scoring system includes hyperlipidemia and smoking as other major risk factors for CAD, in addition to using males rather than females.[14]

The CHA2DS2-VASc-HS risk scores were increased in patients with severe CAD and also correlated significantly with the number of diseased vessels.[14] A recent study shows CHA2DS2-VASc-HSF (Family history) score was independently associated with the severity of

atherosclerosis in patients with STEMI.[15] Another study compared the CHA2DS2-VASc-HS score with the TIMI and GRACE risk score, which have no differences.[16]

The purpose of this study is to evaluate the association of CHA2DS2-VASc-HS score in prediction of adverse in-hospital outcomes in patients with NSTEMI. This scoring is an easily remembered formula that includes multiple risk factors, which is practical, simple, and useful.

Methods:

This was a Prospective cohort study performed over a period of 1 year from September, 2016 to September, 2017 at Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka. The study protocol conformed to the principles of the Declaration of Helsinki and was approved by NICVD Ethics Committee. Informed consent was obtained from all participants. Total 120 patients with NSTEMI were selected by purposive sampling technique based on predefined enrollment criteria. NSTEMI was defined as presenting with typical chest discomfort at rest for the past 48 h along with in the absence of persistent STelevation on the electrocardiogram suggestive of myocardial ischemia and positive cardiac enzymes. Cardiac troponin I was taken as a positive biomarker with a threshold of 1.0 ng/mL by the machine "SIEMENS IMMULYTE 1000"in NICVD, Dhaka. Patients with valvular heart diseases, congenital heart diseases, cardiomyopathy, myocarditis, pericarditis, significant co-morbidities and who underwent revascularization (PCI or CABG) during index hospitalization were excluded.

Demographic characteristics including age, gender, Diabetes mellitus, Hypertension, Hyperlipidemia, current cigarette smoking, family history of premature CAD, Chronic heart failure, previous ischemic stroke or transient ischemic attack (TIA), peripheral artery disease (PAD),), presenting symptoms, biochemical and Electrocardiography findings and echo-cardiography data were obtained. Then the CHA2DS2-VASc-HS score was calculated and the study subjects were divided into two groups. Patients' with the CHA2DS2-VASc-HS score>4 put into group I and score ≤4 into group II.

Table-I

CHA2DS2-VASc-HS score:

C	Congestive heart failure	1 point
H	Hypertension	1 point
A2	Age >75 years	2 points
D	Diabetes mellitus	1 point
S2	Previous stroke or TIA	2 points
V	Vascular disease	1 point
A	Age 65–74 years	1 point
Sc	Sex category, male gender	1 point
H	Hyperlipidemia	1 point
S	Smoker	1 point

Total score=11 points

DM was diagnosed as a fasting blood glucose ≥126 mg/dL or the current use of anti-diabetic medications. HT was diagnosed if repeated measurements of systolic and diastolic blood pressure were ≥140 mm Hg and e"90 mm Hg, respectively, or if the patient received chronic anti-hypertensive medication treatment. A level of low-density lipoprotein cholesterol above 160 mg/dL according to the National Cholesterol Education Program Adult Treatment Panel III recommendations or the usage of lipid lowering medications was defined as HL. Cigarette smoking was defined as smoking a minimum of 10 cigarettes per day for at least 1 year in patients who had never stopped smoking before the day of evaluation. Family history was defined as the presence of ischaemic heart disease or sudden cardiac death in a male first degree relative aged <55 years or in a female first-degree relative aged <65 years. Chronic heart failure was defined as Killip Classification. Vascular disease was considered to be the presence of PAD where at least 50% stenosis diagnosed by Dupplex-sonographyof the non-coronary artery circulation. When the stroke or TIA was due to thromboembolism in the carotid or vertebral arteries, they were included in the scoring.

Then in-hospital outcomes were observed and recorded. Outcome variables were comprises of recurrent ischemia, heart failure, cardiogenic shock, significant arrhythmia and death. Overall adverse outcomes was defined as consisting of the occurrence of any one of a set of multiple outcomes is classified as an outcome. Patients

who had experienced any one of the individual events specified by the components in the outcome variables were considered to have experienced the composite outcome or overall adverse outcomes.[17]

Data was processed and analyzed manually by using SPSS (Statistical Package for Social Sciences) Version 16.0.Quantitative data was expressed as mean and standard deviation and comparison was being done by "t" test. Qualitative data was expressed as frequency and percentage and comparison was being done by Chi-square test and Fisher's Exact test as appropriate. Multivariate regression analysis was done to find predictors of in-hospital mortality. A probability (p) value of <0.05 was considered as significant.

Results:

A total of 120 patients were studied, including 78 (65%) male and 42 (35%) female (Fig 1). Patients having CHA2DS2-VASc-HS score>4 were assigned as group I and patients having CHA2DS2-VASc-HS score ≤4 were assigned as group II. Baseline characteristics are mentioned in Tablel.

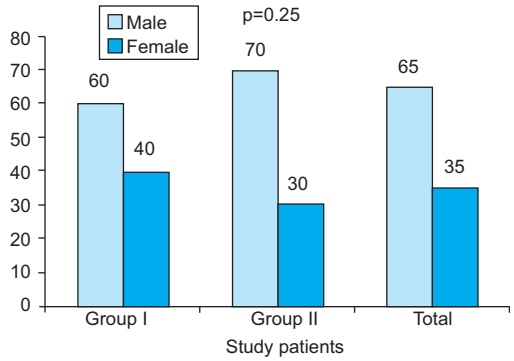


Fig.-1: *Bar diagram showing sex distribution of the study patients (n=120).*

In-hospital adverse events are reported in Table II and III.Cardiogenic shock (p=0.04s), heart failure (p=0.03s) and recurrent ischemia (p=0.04s) were significantly higher with CHA2DS2-VASc-HS score >4. The significant arrhythmia and death occurred in group I and none in group II.20% of 60 patients in group I experienced combined adverse in-hospital outcomes, on the contrary 3.3% of the patients in group II which was significantly higher(p=0.01) with RR= 6. The prediction by the area under the ROC curves for CHA2DS2-VASc-HS score>4 was good with accuracy 89%. (Fig. 2) with sensitivity 85.7% and specificity 54.7% (Table IV).

Table-I

Baseline characteristics of study population (N=120).

Variables	Group I (n= 60) Mean±SD	Group II (n = 60) Mean±SD	p value
S. creatinine (mg/dl)	1.25±0.31	1.13±0.30	0.19^{ns}
RBS (mg/dl)	8.4±4.8	7.3±2.6	0.14 ^{ns}
Cardiac troponin I (ng/dl)	4.0±2.3	3.1±2.2	0.03^{S}
Total Cholesterol(mg/dl)	203.5±35.6	198.6±30.2	0.26^{ns}
Triglyceride (mg/dl)	200.8±40.9	170.2±32.5	0.27^{ns}
LDL cholesterol (mg/dl)	112.1±30.2	98.6±11.2	<0.02^{s}
HDL cholesterol (mg/dl)	39.4±6.4	42.±4.6	0.22^{ns}
ST segment deviation in ECG	28	22	0.22^{ns}
Ejection fraction (percent)	53.2±6.3	56.9±7.1	0.03s

Table-II

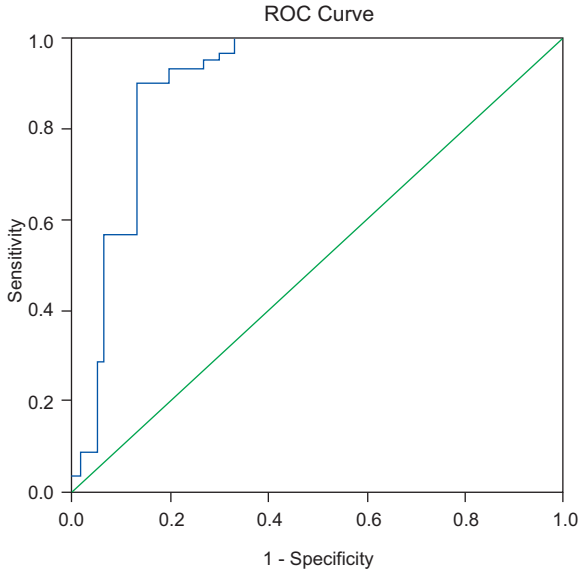
Adverse in-hospital outcomes variables of the study population (N=120).

Outcomes variables	Group I (n= 60)		Group II (n = 60)		Total (N=120)		p value
	Number	%	Number	%	Number	%	
Cardiogenic shock	6	10.0	1	1.7	7	5.8	0.04^{s}
Heart failure	10	16.7	2	3.3	12	10	0.03^{s}
Recurrent ischemia	7	11.7	2	3.3	9	7.5	0.04^{s}
Significant arrhythmia	1	1.7	0	0.0	1	0.8	0.97^{ns}
Death	2	3.3	0	0.0	2	1.7	0.47^{ns}

Table-III

Combined adverse in-hospital outcome among the study population (N=120).

Group	Adverse in-hospital outcome		Adverse in-hospital outcome			p value
	Present	%	Absent	%		RR
Group I (n= 60)	12	20.0	48	80.0	0.01[s]	6
Group II (n = 60)	2	3.3	58	96.7		
Total (N=120)	14	11.7	106	88.3		



Area Under the Curve
Test Result Variable(s):Predicted probability

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.899	.032	.000	.836	.961

Fig.-2: *Receiver operating characteristic (ROC) curves for CHA_2DS_2-VASc-HS score >4 in the prediction of occurring adverse in-hospital outcomes.*

Table IV

Performance test of CHA2DS2-VASc-HS score in the setting of NSTEMI (N=120).

CHA_2DS_2-VASc-HS score	Adverse in-hospital outcomes		Sensitivity	Specificity	Accuracy
	Occurred	Not occurred			
High: score>4	12	48	85.7%	54.7%	89%
Low: scored”4	2	58			
Total	14	106			

Discussion:

The main objective of the study was to find out the association of CHA2DS2-VASc-HS score with adverse in-hospital outcomes in patients with non- ST segment elevation myocardial infarction (NSTEMI) patients. Total 120 patients with NSTEMI of both gender and all ages were included considering the inclusion and exclusion criteria.

Male patients were predominant in study population which was 65%. Female patients were 35%. In almost all studies related to coronary artery disease (CAD) similar male preponderance was found. As females are given less attention and access for them to the health care facilities is limited particularly in low socioeconomic population like our country may contribute for this male predominance.

No statistically significant difference was observed regarding clinical parameters between the study groups. We found 46.6% patients having ST deviation in group I which was higher than group II (41.6%). In 2011 study was conducted one cross sectional study in NICVD, Bangladesh, which found that magnitude of ST-segment depression positively correlate with the severity of coronary artery disease.[18]

Average left ventricular ejection fraction (LVEF) of the study population was 54.6 ± 7.1. LVEF was decreased in Group I (53.2±6.3) than Group II (56.9±7.1) with statistically significant difference. Recent study conducted in NICVD on NSTEMI patients and found that average LVEF was 54.8 ± 2.1.[19]More risk factors and severe disease in group II may be responsible for lower LVEF.

In Lipid profile, the mean LDL cholesterol (112.1±30.2) was found significantly higher in group I. Elevated LDL was identified as a major cause of Atherosclerotic Cardiovascular Disease (ASCVD). Ta°olar, et al. found that mean LDL cholesterol was 112.1±43. Total cholesterol and triglyceride level had higher in group II than group I but did not reach the level of significance ($p>0.05$).[16] HDL cholesterol was lower in group I than group II with no statistical difference. Among biochemical parameters only cardiac troponin level were found higher in group I compared to group II and reached the level of significance. Cohen also found that raised troponin I is an independent predictor for adverse outcome. But no significant difference in serum creatinine and RBS between two groups in.[20]

Among the NSTEMI patients with CHA2DS2-VASc-HS >4 (Group I), 16.7% developed heart failure, 11.7% suffered from recurrent ischemia and 10% developed cardiogenic shock. Only 1.7% developed significant arrhythmias and 3.3% died in group II. 3.3%, 3.3% and 1.7% developed heart failure, recurrent ischemia and significant arrhythmia respectively among patients with CHA2DS2-VASc-HS score ≤4 (Group II). Heart failure, cardiogenic shock and recurrent ischemia was higher in Group I than Group II and reached the level of significance ($p<0.04$). Islamconducted a study in NICVD on NSTEMI patients which correlates with adverse outcome of this study.[19] The same study showed total 6.4% suffered from recurrent ischemia, 5% developed cardiogenic shock and 1.4% patients died compare to 7.5%, 5.8% and 1.7% experienced recurrent ischemia, cardiogenic shock and death in this study. Another study showed that in case of NSTEMI in-hospital recurrent ischemia was 10%, heart failure 18% and death 6%.[21]

Regarding the total patients with adverse in-hospital outcomes, 20% of the patients in group I had adverse in-hospital outcome while in group II 3.3% patients had adverse in-hospital outcome and the difference was statistically significant. Here some patients experienced more than one adverse in-hospital outcomes. In a similar study Ta°olar, et al. found 23.2% patients with cardiac events in patients with CHA2DS2-VASc-HS >4 compared to 3.8% in score ≤4.[16] The findings of this study were consistent with the previous study. Risk was measured by relative risk (RR). Relative risk (RR) for developing adverse in-hospital outcomes was more than 1, so CHA2DS2-VASc-HS >4 is a risk factor. Receiver operating characteristic curve (ROC) analysis identified an optimal cutoff value for CHA2DS2-VASc-HS score >4 to predict the cardiac outcomes, with a sensitivity of 85.7% and specificity of 54.7%. Hence the prediction was significantly good with accuracy of 89%.

Recently, CHA2DS2-VASc-HS score has become a new emerging predictor of CAD severity in stable CAD patients and CHA2DS2-VASc score in hospital outcome in ACS patients. In our country, no study has been done using this CHA2DS2-VASc-HS score model for predicting in-hospital outcomes in patients with NSTEMI. This study was designed to address the CHA2DS2-VASc-HS as a risk factor predicting tool of adverse in-hospital outcomes after NSTEMI.

In clinical practice, simple risk scores are preferred. The ideal score should be easy to calculate and convenient for the rapid screening of high-risk patients for preventing adverse outcomes. The outcomes of high-risk patients can be predicted with comorbidity findings using this CHA2DS2-VASc-HS scoring system without the need for information regarding vital signs at admission, which is simple to use, time-saving, does not require any software to calculate the total risk assessment, and does not entail additional costs in a real-life. So the CHA2DS2-VASc-HS score may play an important role as a predictive model of adverse outcomes in hospitalized NSTEMI patients.

Study Limitations:

Although adequate number of study population was used in this study, it is still limited in number to generalize the results. Patients who underwent CAG and revascularization by PCI/ CABG were not included in this study and thus excluding an important sub-population of NSTEMI patients.So whether this study is also applicable for those patients who were treatedby early invasive treatment is not known. Sampling method was not random rather purposive, so there is risk of selection bias. It was conducted in a single center.

Conclusion:

CHA2DS2-VASc-HS scores can be used to predict the risk of clinical adverse events in patients with NSTEMI. Identifying higher risk patients with CHA2DS2-VASc-HS score >4, we are able to pay special attention to them and formulate an optimized treatment strategy, which might reduce risks of subsequent adverse events. In conclusion, our study demonstrated that patients with high CHA2DS2-VASc-HS score had more adverse in-hospital outcomes.

Conflict of Interest - None.

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