Association of TIMI Risk Score with Angiographic Severity of Coronary Artery Disease in Patients with Non-ST Elevation Acute Coronary Syndrome

A B K Bashiruddin[1*] Mohammad Ibrahim Chowdhury[2] Biplob Bhattachajee[3] Sukanta Dhar[4] Iqbal Mahmud[5] Md Sahadat Hossain[1] Abdur Rahim[6]

Abstract

Background: Clinical guidelines recommend that optimal management of Non ST Elevation Acute Coronary Syndrome (NSTE-ACS) should include patient risk stratification. Predicting the anatomical extension of Coronary Artery Disease (CAD) is also potentially useful for clinical decision. The objective of our study was to determine whether the TIMI risk score correlates with the angiographic extent and severity of CAD in patients with NSTE- ACS.

Materials and methods: This cross-sectional study was carried out in the Department of Cardiology, Chittagong Medical College Hospital (CMCH) on a total of 200 patients diagnosed with NSTE - ACS. TIMI risk score was calculated for each patient and they were stratified into 3 groups according to the TIMI risk score: low risk (0-2) intermediate risk (3-4) high risk (5-7). The severity of the CAD was assessed by Gensini score.

Results: Mean (± SD) age was 53.7 (±10.8) years and 142 (71%) were male. Regarding cardiovascular risk factors, 68.5% had diabetes mellitus, 41.5% had dyslipidaemia, 77.5% had hypertension, 68% were current smoker and 35% had a family history of CAD. The Gensini score was higher in patients at high risk TIMI group. Moreover, there was a signi cant positive correlation between the TIMI and Gensini score (r=0.446). TIMI score can predict significant CAD moderately well (Area under the curve 0.661). Significantly higher proportion of patients with TIMI score more than 4 (65.9%) had significant three vessels CAD compared to patients with TIMI risk score 3-4 (17.9%) and TIMI risk score less than 3 (2%).

Conclusion: TIMI score had good predictive value in assessment the severity of CAD in patients with NSTE-ACS.

Key words: Gensini score; NSTE-ACS; TIMI score.

1. OSD (DGHS) Deputed to Department of Cardiology Chittagong Medical College Hospital, Chattogram.
2. Associate Professor of Cardiology Chittagong Medical College, Chattogram.
3. Assistant Professor of Cardiology Chittagong Medical College, Chattogram.
4. Consultant of Cardiology Chittagong Medical College Hospital, Chattogram.
5. Lecturer of Dental Unit Chittagong Medical College, Chattogram.
6. Assistant Professor of Medicine Chittagong Medical College, Chattogram.

***Correspondence:** **Dr. A B K Bashiruddin**
E-mail: abk.bashiruddin@gmail.com
Cell : 1712 94 50 56

Submitted on : 21.03.2021
Accepted on : 18.06.2021

Introduction

Coronary Artery Disease (CAD) is the leading cause of death globally.[1] Recent studies observed that prevalence of cardiovascular diseases, especially CAD is high in Bangladeshalong with an upward trend and its associated risk factors are on the rise too in Bangladeshi adults.[2,3] The term Acute Coronary Syndrome (ACS) distinguishes acute myocardial ischemia from stable CAD. It includes ST-Segment Elevation Myocardial Infarction (STEMI) Non-ST-Segment Elevation Myocardial Infarction (NSTEMI) and unstable angina.[4] Registry data consistently show that NSTE-ACS is more frequent than ST-ACS.[5]The incidence of NSTE-ACS, both absolute and relative to STEMI, 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.[6]

Current NSTE-ACS guidelines recognize the importance of early risk stratification in the management of NSTE-ACS and recommend an integrated approach to risk assessment.[7] Several model of risk scores are developed in predicting short and mid-term outcomes in patients with ACS and to distinguish the patients at the highest risk or an adverse outcome, who may benefit from aggressive therapies. The TIMI risk score is one of the most popular risk score in clinical practice.[8,9] The TIMI score has been derived from Thrombolysis In Myocardial Infarction (TIMI) IIB trial and has also been published as online TIMI risk score calculator (http://www. timi.org). This score has seven variables (Age, Prior CAD, Risk factors, History of Angina episodes in 24 h, History of Aspirin intake, ST segment deviation on ECG and elevated cardiac biomarker) with the scoring from 0 to 7.[10,11]

The TIMI score was derived from clinical trial databases. Although TIMI risk score is an important and validated tool for assessing prognosis, the literature lacks studies that demonstrate the correlation between the scores and the magnitude of coronary lesions found by coronary angiography.[12] So, the objective of this study was to evaluate the association between hospital TIMI score with angiographic severity of CAD in patients with NSTE-ACS. Knowledge of correlation between TIMI score and angiographic severity of coronary diseases would help clinicians to do triage of NSTE-ACS patients.

Materials and methods

This cross sectional study was conducted in the Department of Cardiology, Chittagong Medical College Hospital, Chattogram, Bangladesh from September 2017 to May 2018. A total of 200 patients with NSTE-ACS were studied who agreed to underwent coronary angiography during the period of index hospitalization. The patients with history of prior myocardial infarction, severe comorbid conditions like uncontrolled DM, ESRD and who underwent prior PCI or CABG were excluded from the study. The study protocol was approved by ethical review committee of the Chittagong Medical College.

The study was aimed to determine the correlation between TIMI score and Gensini score. So, a total of 200 cases were required to determine whether this correlation coefficient differs from zero, assuming correlation coefficient of 0.3 between TIMI score and Gensini score, at 95% confidence level with a power of 80%.[13]

Demographic data, risk factors and data related to drug history were recorded in case record form. A 12-lead resting ECG was done on admission. The TIMI scores werecalculated by using the online calculator (https://www.mdcalc.com/timi-risk-score-ua-nstemi) during hospital admission. Coronary Angiogram (CAG) was done during index hospitalization. All CAG were evaluated by one experienced cardiologist who was blind to the TIMI risk score of individual patient and the severity of CAD were assessed by vessel score and Gensini score. After Gensini score was determined, 36 points was chosen as an appropriate cut-off value and patients were divided into two groups, those with a Gensini score ≤36 were considered as absent or mild coronary artery disease and those with a Gensini score >36 were considered as moderate to severe coronary artery disease.[14]

Aiming at assessing the association between TIMI risk scores and CAD extension, some analyses were used. Chi-square test was applied to determine the proportions difference among three TIMI risk groups. Considering that both TIMI score and the Gensini score showed non-normal distribution (Kolmogorov-Smirnov test), the statistical analyses were mainly non-parametric. First, the linear association of risk score with the Gensini score was assessed by use of Spearman correlation. Second, the Independent sample Kruskal-Wallis test was used to compare the Gensini score values among the three TIMI risk groups. Third, the Receiver-Operating Characteristics (ROC) curve was used to test the predictive accuracy of TIMI risk score regarding the presence of obstructive CAD. Significant prediction occurred when the area under the ROC curve (AUROC) was statistically different from 0.5. p value of less than 0.05 was considered as significant. Data were analyzed by using SPSS (Windows version 23.0).

Results

The mean age of the study population was 53.7±10.8 years. Male patients were predominant (71%). HTN was the most prevalent (77.5%) risk factor in this study. Among the other risk factors, the frequency of diabetes mellitus was 68.5%, 68% were smoker, 35% patients had positive family history of premature CAD and 41.5% patients were dyslipidemic. Among the TIMI risk score variables: chest pain was most prevalent and involved 131 (66%) patients, followed by 107 (54%) patients used aspirin within seven days, ST segment depression >0.5 mm was observed in 98 (49%) patients, troponin I was raised in 63 (32%) and 15 (8%) patients had prior CAD. Out of 200 patients, 100 (50%) were in low risk group with a TIMI score 0-2, 56 (28%) were in intermediate risk group with a TIMI score 3-4 and 44 (22%) were in high risk group with a TIMI score 5-7 (Table I).

Out of 200 patients, 70 (35%) had two vessel CAD, 48 (24%) had normal coronary artery, 41 (20.5%) with single vessel CAD and 41 (20.5%) had three vessel CAD. Median Gensini score was 24 (IQR: 12-40.7). Table I shows that, median Gensini score was the highest in the patients with TIMI high risk and the lowest in TIMI low risk group. These differences of median Gensini score was highly significant statistically ($p < 0.001$).

Table I : Association between TIMI score and Gensini score (n=200)

TIMI risk score	Gensini score		p value
	Mean ± SD	Median (IQR)	
Low risk group (0-2) n=100	20±12.9	18.5 (12-27.8)	
Intermediate risk group (3-4) n=56	31.9±15.2	32 (22.5-44)	<0.001*
High risk group (5-7) n=44	51.9±34.1	52 (23-23.5)	

SD: Standard Deviation, IQR: Interquartile Range,
* Kruskal-Wallis test.

According to the Gensini score patients were categorized as having either non-severe CAD (Gensini score ≤36) or severea CAD (Gensini score >36). Table 2 shows that, angiographic severity was increased as the TIMI risk group increased, with most of the patients in non-severe CAD had low TIMI risk group in contrast to most of the patients in the severe CAD group had high TIMI risk group.

Table II : Association between TIMI risk group and CAD type

TIMI risk group	CAG findings		P value
	Non severe (Gensini score ≤36)	Severe (Gensini score >36)	
Low risk group (0-2) n=100	83 (60.6%)	17 (27.0%)	
Intermediate risk group (3-4) n=56	34 (24.8%)	22 (34.9%)	<0.001*
High risk group (5-7) n=42	20 (14.6%)	24 (38.1%)	
Total	137 (68.5%)	63 (31.5%)	

Data are presented as frequency (Percentage). *Chi-square test and significant.

Gensini score was positively (Correlation co-efficient r=0.446) and significantly (p<0.001) associated with the TIMI score in the present study (Figure 1).

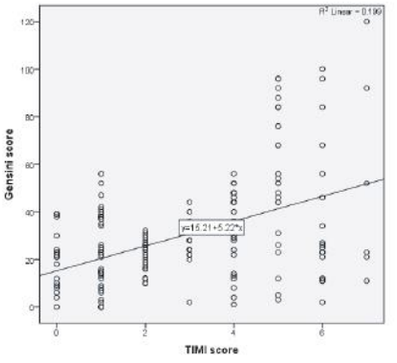

Fig 1 : Correlation between TIMI risk score and Gensini score

As shown in Table III, as the TIMI score increases the extent of CAD is also increased. Among the 100 patients with low risk TIMI score, majority 69 (69%) had normal angiography finding and rest 31 (31%) had single vessel disease. Patients with intermediate TIMI risk group majority (89.7%) had two vessel disease and patents with high risk TIMI score majority (81.8%) had three vessel disease.

Table III : Extent of CAD in the study population based on TIMI risk score (n=200)

Extent of CAD	TIMI risk group			p value
	Low risk (n=100)	Intermediate risk (n=56)	High risk (n=44)	
Normal	48 (48%)	0 (0%)	0 (0%)	
Single vessel CAD	30 (30%)	6 (10.7%)	5 (11.4%)	<0.001*
Two vessel CAD	20 (20%)	40 (71.4%)	10 (22.9%)	
Three vessel CAD	2 (2%)	10 (17.9%)	29 (65.9%)	

Data are presented as frequency (Percentage). *Chi-square test.

The discriminator accuracy of TIMI risk score to predict significant CAD was analyzed by ROC curve. The TIMI score discriminated accurately patients with or without obstructive CAD (Area under the ROC curve of 0.563; 95% CI: 0.573-0.748, p <0.001) (Figure 2).

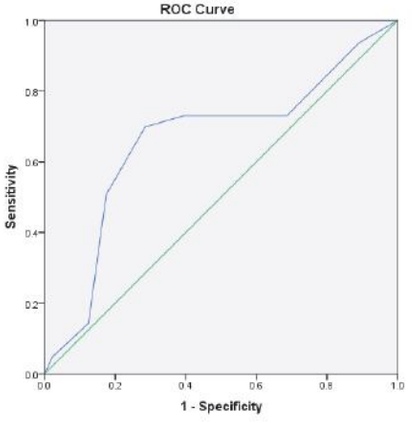

Fig 2 : ROC curve of the TIMI score for detecting significant CAD

Discussion

The findings of the present study confirmed strong association of TIMI score more than 4 with multivessel and severe CAD and the low TIMI score with normal or non-obstructive CAD. Half of our studied patients were in low risk group and the proportion of intermediate risk group and high

risk group were nearer to each other. Among the TIMI score variables, most prevalent one was angina pain in last 24 hours, followed by history of taking aspirin in last 7 days, ST depression and raised Troponin-I. this findings were in accordance to the findings of Roy et al who found 58% patients had more than 2 episodes of angina in last 24 hours, 57% had ST depression of more than 0.5 mm, 22.9% patients had history of taking aspirin in last 7 days, 18% patients having T wave inversion, 23% patients having no specific ST-T changes in contiguous leads on ECG and 56.1% had raised Troponin-I.[15]

Patients with high TIMI risk score were more likely to have multi-vessel CAD compared with those with low or intermediate TIMI risk score. The results compare well with the findings of Mahmood et al and Mega et al.[16,17] A significant correlation was found between single vessel disease and low TIMI risk score and triple vessel disease and high TIMI risk score which were also similar to the findings of Zheng et al and Lakhani et al.[18,19] Correlation co-efficient between the TIMI score and Gensini score was 0.446. These findings were also in agreement with the study findings of Roy et al and Barbosa et al.[15,20]

ROC curve was used to test the predictive accuracy of TIMI risk score regarding the presence of significant CAD. The TIMI score showed a modest discriminatory capacity between patients with and without significant CAD, having an AUROC curve of 0.661. Similarly, Lakhani et al, Barbosa et al, Correia et al and Yan et al, also reported a good predictive utility of TIMI score for severe CAD.[19-22]

Our findings have some important clinical implications. In our hospital there is over burden of patients. We cannot perform index hospital coronary intervention to all patients. If we can predict severe CAD clinically by TIMI score then we can do early PCI to those patients whichmay reduce mortality and morbidity. Patients with low TIMI score can be given medical management followed by coronary intervention later on. From our country's perspective, in a resource poor setting where only coronary care is available without diagnostic angiography facility, patients with low TIMI score can be given medical management and high TIMI score can be referred to centers equipped with diagnostic and therapeutic intervention facilities.

Limitations

This study results should be interpreted considering few limitations. Number of patients with high risk score was low in the study. All the patients were selected from a single center. So, results can be generalized.

Conclusions

The present study shows a significant correlation between TIMI clinical risk score and the angiographic Gensini score as well as with the number of diseased vessel. It helps in predicting severe CAD among NSTE-ACS patients.

Recommendations

TIMI risk score can be used in our clinical setting for CAD risk assessment in patients presented with NSTE-ACS. A routine invasive strategy in high TIMI risk score patients should be considered as the preferred strategy. However, it is worth noting that future studies with a higher number of patients with multicenter approach will provide more precision to our estimates.

Acknowledgement

The authors thank to all th patients, nurses and staff of Cardiology Department of CMCH.

Contribution of authors

ABKB: Conception, design, data collection, manuscript drafting & final approval

MIC: Acquisition of data, manuscript drafting & final approval.

BV: Data collection, critical revision & final approval.

SD: Data analysis, manuscript drafting & final approval.

IM: Data collection, critical revision & final approval

MSH: Data collection, interpretation of data, drafting & final approval

AR: Interpretation of data, manuscript drafting & final approval.

Disclosure

All the authors declared no competing interest.

References

1. Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. World Health Organization. 2018.
Available from: https://www.who.int/healthinfo/global_burden_disease/estimates/en/

2. Khanam F, Hossain MB, Mistry SK, Afsana K, Rahman M. Prevalence and Risk Factors of Cardiovascular Diseases among Bangladeshi Adults: Findings from a Cross-sectional Study. Journal of Epidemiology and Global Health. 2019; 9(3):176–184

3. Chowdhury M, Haque MA, Farhana Z, Anik AM, Chowdhury AH, Haque SM et al. Prevalence of cardiovascular disease among Bangladeshi adult population: A systematic review and meta-analysis of the studies. Vascular health and risk management.2018;14:165–181.

4. Wardhan H, Bhattacharyya K. Prognostication of A case of NSTEMI, in P. K. Deb (ed.) Cardiology update. Kolkata: Indian Heart House. 2012;52-58.

5. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, AndreottiF, et al ESC Scientific Document Group. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). European Heart Journal. 2016; 37(3):267–315.

6. Giugliano RP, Cannon CP, Braunwald E. Non–ST Elevation acute coronary syndrome. In: Bonow RO, Mann DL, Zipes DP, Libby P, editors. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, Tenth Edition ed. Philadelphia: Saunders, an imprint of Elsevier Inc. 2016;1155-1157.

7. Khalill R, Han L, Jing C, Quan H. The use of risk scores for stratification of non-ST elevation acute coronary syndrome patients. Experimental & Clinical Cardiology. 2009;14:e25-e30.

8. Backus BE, Six AJ, Kelder JH, Gibler WB, Moll FL, Doevendans PA. Risk scores for patients with chest pain: evaluation in the emergency department. CurrCardiol Rev. 2011;7(1):2-8.

9. Bueno H, Ferna´ndez-Avile´s, F. Use of risk scores in acute coronary syndromes. Heart. 2012;98 (8):162-168.

10. Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA. 2000; 284(7):835-842.

11. TIMI Risk Score for UA/NSTEMI (Onlne).
Available from: https://www.mdcalc.com/timi-risk-score-ua-nstemi.

12. Manini AF, Dannemann N, Brown DF, Butler J, Bamberg F, Nagurney JT, et al. Rule-Out Myocardial Infarction using Coronary Artery Tomography (ROMICAT) Study Investigators. Limitations of risk score models in patients with acute chest pain. Am J Emerg Med. 2009;27(1):43-48.

13. Hulley SB, Cummings SR, Browner WS, Grady D, Newman TB, Designing clinical research : an epidemiologic approach. 4th ed. 2013, Philadelphia, PA: Lippincott Williams & Wilkins; Appendix 6C. 2013;79.

14. Ling S, Shu-Zheng LU. Association between non-alcoholic fatty liver disease and coronary artery disease severity. Chin Med J (Engl). 2011;124(6):867–872.

15. Roy SS, Abu Azam STM, Khalequzzaman M, Ullah M, Arifur Rahman M. GRACE and TIMI risk scores in predicting the angiographic severity of non-ST elevation acute coronary syndrome. Indian Heart J. 2018;70Suppl 3(Suppl 3):S250-S253. .

16. Mahmood M, Achakzai AS, Akhtar P, Zaman KS. Comparison of the TIMI and the GRACE risk scores with the extent of coronary artery disease in patients with non-ST-elevation acute coronary syndrome. J Pak Med Assoc. 2013;63(6):691-695.

17. Mega JL, Morrow DA, Sabatine MS, Zhao XQ, Snapinn SM, DiBattiste PM et al. Correlation between the TIMI risk score and high-risk angiographic findings in non-ST-elevation acute coronary syndromes: Observations from the Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) trial. Am Heart J. 2005;149(5):846-850.

18. Zheng XY, Meng XK, Li WG, Yang J, Wei G, Fang R. Clinical study on value of severity of patient with coronary artery disease evaluated with the thrombosis in myocardial infarction risk score. Zhongguo Wei Zhong Bing JiJiu Yi Xue. 2004;16(4):239-241.

19. Lakhani MS, Qadir F, Hanif B, Farooq S, Khan M. Correlation of thrombolysis in myocardial infarction (TIMI) risk score with extent of coronary artery disease in patients with acute coronary syndrome. J Pak Med Assoc. 2010;60(3):197-200.

20. Barbosa CE, Viana M, Brito M, Sabino M, Garcia G, Maraux M, Souza AC, Noya-Rabelo M, Esteves JP, Correia LC. Accuracy of the GRACE and TIMI scores in predicting the angiographic severity of acute coronary syndrome. Arq Bras Cardiol. 2012;99(3):8118-8124.

21. Correia LC, Freitas R, Bittencourt AP, Souza AC, Almeida MC, Leal J, Esteves JP. Prognostic value of GRACE scores versus TIMI score in acute coronary syndromes. Arq Bras Cardiol. 2010;94(5):613-619. .

22. Yan AT, Yan RT, Tan M, Casanova A, Labinaz M, Sridhar K, Fitchett DH, Langer A, Goodman SG. Risk scores for risk stratification in acute coronary syndromes: Useful but simpler is not necessarily better. Eur Heart J. 2007;28(9):1072-1078.