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Navigating the Risk: "Unraveling the Relationship between Thrombolysis in Myocardial Infarction ("TIMI" Risk Score) and Coronary Vessel Involvement in Non-ST-Elevated acute Coronary Syndrome with Respect to "Syntax" Score – A Cross-sectional Study"

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ABSTRACT

Objectives: Patients with unstable angina and non-ST-elevated myocardial infarction (NSTEMI) present with a spectrum of cardiac events and death. Hence, early accurate management should be initiated. This can be achieved by risk stratifying the patients as early as possible on hospital admission. Thrombolysis in myocardial infarction (TIMI) risk score assessment is used widely for this purpose. It helps to standardize the approach of management and compare the extent and number of vessels involved in the coronary angiogram. This research aims to assess coronary artery disease (CAD) in individuals with NSTEMI by examining the extent of vessel involvement and the complexity of coronary artery blockages, using the SYNTAX score about the TIMI risk score.

Materials and Methods: This cross-sectional observational study involved 60 participants who were selected based on specific inclusion and exclusion criteria. The TIMI risk score was computed for each individual, categorized as either <4 or \geq 4, and the results of their coronary angiogram were analyzed to assess the degree of vessel involvement, categorizing it as either single-vessel disease (SVD) or multi-vessel disease (MVD). The Syntax score was computed for all angiograms and divided into two groups based on whether it was \leq 22 or >22.

Results: The average age of the participants in our study was 56 ± 10.64 , with an age range of 34. Gender distribution revealed a higher proportion of males, constituting 68.3% (41 individuals), while females accounted for 31.7% (19 individuals). The angiogram results demonstrated that among the patients with TIMI score <4, 70% (14 individuals) had SVD, 30% (6 individuals) had MVD, and among those with score \geq 4, 15% (6 individuals) had SVD while 75% (34 individuals) had MVD. In the subgroup analysis of TIMI <4, a Syntax score <22 was observed in 15 cases of SVD and a score >22 was observed in cases of MVD. Likewise, in the TIMI >4 group, a Syntax score <22 was observed in 12 cases of SVD and a score >22 was observed in 28 cases of MVD.

Conclusion: This study noted that patients with non-ST-segment elevation acute coronary syndrome who underwent coronary angiogram and had a TIMI score of \geq 4 were observed to have a 13-fold increased likelihood of having multi-vessel Coronary artery disease (CAD) compared to those with a TIMI score of <4. TIMI score of \geq 4 had a 7 times higher chance of getting a SYNTAX score >22.

Keywords: Non-ST-elevated myocardial infarction, Thrombolysis in myocardial infarction score, Angiography, Single-vessel disease, Multi-vessel disease, SYNTAX score

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INTRODUCTION

Coronary artery disease (CAD) is a major health hazard in both industrialized and developing nations, and it is of great concern due to the high mortality rate that it causes.^[1] Acute coronary syndrome (ACS) includes acute myocardial infarction and unstable angina, which together result in approximately 7 million deaths each year.^[2] The majority of ACS patients (70%) present with non-ST-elevated myocardial infarction (NSTEMI), for which treatment options are not clear.^[3] Despite advances in therapeutic interventions, NSTEMI patients still experience high morbidity and mortality rates. Therefore, it is crucial to assess risk factors early on for prognosis and to initiate treatment during the critical early hours. Several scoring systems have been developed to stratify ACS patients based on their risk. The thrombolysis in myocardial infarction (TIMI) risk score is widely used due to its simplicity, as it involves evaluating seven independent clinical indicators in each patient.^[4] The SYNTAX score which incorporates characteristics of lesion complexity, lesion location, and the number of lesions was developed during the SYNTAX trial to classify patients according to the severity of their CAD [Table 1].

MATERIALS AND METHODS

Design and setting

It was a cross-sectional observational survey of 60 patients with non-ST-segment elevation ACS (NSTE-ACS) presented to the cardiology unit of ASRAM Institute. The study was completed in 2 months (March-April 2023).

Sample collection and criteria

All patients with NSTE-ACS under the age group of 30–80 years irrespective of gender were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

- Hemodynamic instability due to mechanical complications (e.g., acute Mitral regurgitation [MR] and Ventricular septal defect [VSD])
- Unstable ventricular arrhythmias
- Congenital heart disease
- Prior percutaneous transluminal coronary angioplasty/ coronary artery bypass grafting
- Myocarditis/pericarditis.

All patients were tested for cardiac enzymes by immunometric assay.

Data collection methods

After obtaining proper consent, a thorough history was taken and an examination was done on the patients. Risk factors including diabetics, hypertension, dyslipidemia, and family H/o of CAD were noted. Electrocardiogram (ECG) and echocardiography were done according to standard protocols. All the data were recorded on a short structured questionnaire. TIMI risk score was calculated for each patient. All patients were categorized into TIMI scores of <4 and ≥4. Patients were further evaluated with coronary angiograms to assess CAD. All the angiograms were performed by a single physician. Vessels with >70%

were considered to have significant disease in our study. The online latest version was used for the calculation of the Syntax score (http://www.SYNTAXscore.com). The coronary artery lesions were divided into two groups: those with a SYNTAX score of 22 or lower, representing lesions of low to moderate complexity, and those with a score above 22, indicating higher complexity of lesions.

Statistical technique

Both descriptive and inferential statistical analysis was done in a Statistical Package of the Social Sciences version trail version 26.0. Data were presented in the form of frequencies and percentages; categorical data were analyzed using the Chisquare test. $P \le 0.05$ was considered statistically significant.

RESULTS

A total of 60 patients having NSTE-ACS presenting to the cardiac department in our Institute were studied. There was a male predominance of 68.3%, male-to-female ratio was 2.1:1, and the mean age of study was 56 years. Among risk factors recurrent episodes of angina (98.7%), elevated cardiac enzymes (75%), and prior documented CAD (63.3%) were common in our study.

The demographic profile is mentioned in Table 2.

The percentage of each TIMI risk factor for all cases in our study is shown in Table 3.

Table 4 illustrates the distribution of TIMI scores, coronary vessel involvement, and SYNTAX scores in male and female subsets of the population.

In this study, it was noted that among males, there was a higher prevalence of TIMI scores \geq 4, multivessel disease (MVD), and SYNTAX scores >22. In females, TIMI scores <4 and single-vessel disease (SVD) were slightly more common, while SYNTAX exceeding 22 was observed to be higher in both men and women, with a somewhat higher proportion in men.

Table 5 shows that 14 patients (70%) had SVD, 6 patients (30%) had MVD with a TIMI score <4, 6 patients (15%) had

Table 1: TIMI UA/NSTEMI risk score.				
1	Age≥65	1 point		
2	\geq 3 risk factors for CAD	1 point		
3	Use of ASA (past 7 days)	1 point		
4	Known CAD (prior stenosis≥50%)	1 point		
5	>1-episode rest angina in<24 h	1 point		
6	ST-segment deviation	1 point		
7	Elevated cardiac markers	1 point		
UA/NSTEMI: Unstable angina non-ST-elevated myocardial infarction, TIMI: Thrombolysis in myocardial infarction, CAD: Coronary artery disease, ASA: Acetyl salicylic acid				

SVD, and 34 patients (75%) had MVD with TIMI risk score of \geq 4. TIMI risk score is significantly associated with several vessels in CAD (*P* < 0.001). TIMI score of \geq 4 had a 13 times higher chance of getting multivessel CAD compared to patients with a TIMI score of <4. (Crudes Odds ratio: 13.22; 95% confidence interval: 3.6343–48.1047; *P* = 0.0001).

Table 6 shows in the subgroup analysis of TIMI <4, a SYNTAX score <22 was observed in 13 cases of SVD and two cases of MVD, and a score >22 was observed in single case of SVD and four cases of MVD. Likewise, in the TIMI ≥4 group, a SYNTAX score <22 was observed in two cases of SVD and ten cases of MVD, and a score >22 was observed in four cases

Table 2: Demographic features of the study patients.		
Age in years (mean±SD)	56±10.64	
Age in range	74-40	
Males	41 (68.3%)	
Females	19 (31.7%)	
Hypertension	37 (61.7%)	
Diabetes mellitus	36 (60%)	
Dyslipidemia	42 (70%)	
Smoker	22 (36.7%)	
Family history of CAD	1 (1.7%)	
SD. Stondard deviation CAD. Conservation	urr diasaa	

SD: Standard deviation, CAD: Coronary artery disease

Table 3: TIMI risk score n (%).	
Age>65 years	13 (21.7%)
>3 risk factors of CAD	27 (45%)
Prior documented CAD>50% stenosis	38 (63.3%)
ST deviation>0.5 mm	23 (38.3%)
>2 episodes of angina within the past 24 h	58 (98.7%)
ASA usage within the prior week	34 (56.7%)
Elevated cardiac enzymes	45 (75%)
TIMI: Thrombolysis in myocardial infarction, CAD: C disease, ASA: Acetyl salicylic acid	Coronary artery

Table 4: Distribution of TIMI scores, coronary vessel involvement, and SYNTAX scores in male and female subsets of the population.

Total <i>n</i> =60	Males (41)	Females (19)
TIMI		
<4	19 (46.3%)	13 (68.4%)
≥4	22 (53.7%)	6 (31.6%)
Coronary vessel involvement		
SVD	12 (29.3%)	10 (52.6%)
MVD	29 (70.7%)	9 (47.4%)
SYNTAX		
<22	11 (26.8%)	8 (42.10%)
>22	30 (73.17%)	11 (57.89%)

SVD: Single-vessel disease, TVD: Triple-vessel disease, MVD: Multi-vessel disease, TIMI: Thrombolysis in myocardial infarction, SYNTAX: Synergy between percutaneous intervention with taxus and coronary artery bypass surgery

Table 5: TIMI risk scores and angiographic disease correlation.				
Number of vessels		Number of vessels	Chi-square value P-v	
	SVD	MVD (DVD+TVD)		
TIMI score				
TIMI score<4	14 (70%)	6 (30%)	18.15	< 0.001
TIMI score≥4	6 (15%)	34 (85%)		
TIMI: Thrombolysis in myocardial infarction SVD: Single-vessel disease DVD: Double-vessel disease TVD: Triple-vessel disease MVD: Multi-vessel disease				

Table 6: The relationship between the TIMI score and the SYNTAX score with respect to Coronary vessel involvement.						
	TIMI score<4		TIMI score≥4		Chi-square value	P-value
	SVD	MVD (DVD+TVD)	SVD	MVD		
SYNTAX score SYNTAX score<22	13	2	2	10	10.9091	< 0.001
SYNTAX score>22	1	4	4	24	100001	(01001

SYNTAX: Synergy between percutaneous intervention with taxus and coronary artery bypass surgery, TIMI: Thrombolysis in myocardial infarction, SVD: Single-vessel disease, DVD: Double-vessel disease, TVD: Triple-vessel disease, MVD: Multi-vessel disease

of SVD and 24 cases of MVD. TIMI risk score is significantly associated with SYNTAX score. TIMI score of \geq 4 had a 7 times higher chance of getting a SYNTAX score of >22.

DISCUSSION

As per the World Health Organization, cardiovascular disease is expected to become the leading cause of death in developing nations.^[5] Despite therapeutic advances, CAD remains the leading cause of death worldwide.^[6] Knowing the low survival rate in high-risk patients, giving the right and early treatment becomes important. As NSTEMI patients are more prone to cardiac complications, early risk stratification plays the main role in the optimal management of the NSTE-ACS group.^[7] Guidelines from the American Heart Association, American College of Cardiology, and European Society of Cardiology recommend that suitable pharmacotherapy and early therapeutic interventions would decrease the adverse outcomes in high-risk patients of NSTE-ACS.^[7,8] A new study has found that in NSTE-ACS patients, cardiac catheterizations are not being performed optimally due to less or no correct knowledge about risk assessment.^[9] To overcome this problem, different risk assessment scores have been developed but only a few have been put forward. Thrombolysis in myocardial infarction (TIMI), Platelet glycoprotein IIb/IIIa in unstable angina: Receptor suppression using integrilin therapy (PURSUIT), and global registry of acute coronary events (GRACE) scores have established their roles in risk stratification and predicting prognosis (5.6).^[10-14] Out of these, the "TIMI risk score" system is widely used due to its simplicity and its bedside easy assessing ability. TIMI risk score is an effective risk assessment tool for in-hospital mortality and 14-day mortality among NSTEMI patients.

Various studies have validated its use.^[15-17] It is effective in both chronic (6-month) and acute (14-day) presentations of patients with chest pain.^[18-20] When originally developed, the TIMI risk score was correlated by Antman *et al.*^[4] with clinical endpoints of non-ST-elevation ACS, such as death and myocardial infarction. The use of the TIMI score for NSTE-ACS was validated by TACTICS-TIMI.^[21]

It is beneficial to predict the angiographic assessment of CAD using one of the proven risk-scoring systems, as it has a predictive value for Major Adverse Cardiovascular Events (MACE). A Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) analysis showed that the frequency of high-risk angiographic findings, such as severe (>70%) culprit stenosis, MVD, visible thrombus, and left main disease, increased gradually as TIMI risk scores ranged from low to high.^[22] This also indirectly indicates that as the TIMI risk score rises, the complexity of CAD also increases. Hence, we have evaluated the SYNTAX score, which assesses the angiographic severity and complexity of CAD about the TIMI score.

On analyzing individual variables within the TIMI score in our study, we observed that the majority of patients (98.7%) experienced multiple episodes (more than 2) of angina within the past 24 h, and 75% of patients exhibited elevated cardiac enzymes on presentation with CAD, irrespective of the presentation type. Elevated cardiac enzymes have consistently demonstrated heightened sensitivity in predicting mortality in various studies. Khandelwal *et al.*^[23] reported similar findings in their study. In addition, Van Miltenburg-van Zijl *et al.*^[24] have highlighted the significance of the variable "Severity of angina" about a poor prognosis. Some studies have shown the superiority of GRACE over

Table 7: The results of various studies done on the comparison of TIMI scores and CAD.			
S. No.	Study	Year	Conclusion
1.	Garcia et al. ^[27]	2004	High TIMI correlated with severe CAD and left main CAD
2.	Ben et al. ^[26]	2011	TIMI (0-2) No significant CAD, TIMI (5-7) critical TVD LM disease
3.	Mega et al. ^[22]	2011	TIMI score (5–7) more severe MVD
4.	Bashiruddin et al. ^[29]	2019	TIMI score significantly correlated with Gensini CAD score in NSTEMI
5.	Roy <i>et al</i> . ^[25]	2018	GRACE and TIMI are good predictive valves in the assessment of the severity of CAD in NSTEMI
6.	Khandelwal et al.[23]	2015	GRACE and PURSUIT scores had more correlation than TIMI
7.	Namazi et al.[32]	2022	Direct correlation of TIMI and CAD
8.	Hussein and Sabah ^[33]	2022	Moderate TIMI risk score was associated with double vessel disease
9.	Abbas et al. ^[28]	2020	TIMI score>4 greater extent of CAD
10.	Our study	2023	Patients with a TIMI score of \geq 4 had a thirteen times more severe Multi vessel disease (MVD) and
			seven times higher chance of having a Syntax score >22
CAD: Coronary artery disease, LM: Left main disease, NSTEMI: Non-ST elevation MI, TVD: Triple-vessel disease, TIMI: Thrombolysis in myocardial infarction, MVD: Multi-vessel disease, GRACE: Global registry of acute coronary events, PURSUIT: Platelet glycoprotein IIb/IIIa in unstable angina: Receptor suppression using integrilin therapy, SYNTAX: Synergy between PCI with taxus and cardiac surgery			

TIMI in predicting the extent of CAD, but many other studies have shown that they both were equally good in the correlation to high-risk CAD in angiography.^[25]

In our study, men exhibited higher TIMI scores and a greater prevalence of MVD compared to females. In addition, our study revealed that patients with a TIMI score of \geq 4 had a 13 times higher likelihood of developing multi-vessel CAD compared to those with a TIMI score of <4. Similar findings of the correlation of high TIMI scores with MVD were reported by some previous research also.^[26] In their study, Garcia et al.^[27] and Mega et al.^[22] found that when using a TIMI score cutoff of >5, there was a higher prevalence of MVD and left main disease compared to cases with lower scores. Similarly, another study conducted by Abbas et al.[28] showed that even a TIMI score cutoff of 4 could distinguish a greater extent of disease. A study done by Bashiruddin et al.,^[29] showed a positive correlation between the Gensini score (Severity of Angiographic disease) and TIMI score. Recently, Parikh et al.,^[30] have shown that TIMI risk scores predict severe coronary atherosclerosis in patients with end-stage renal disease.

In our study, a TIMI score of ≥ 4 had a 7 times higher chance of getting a SYNTAX score of ≥ 22 indicating more complexity of angiographic disease in patients with high TIMI score. There have not been many studies comparing the TIMI and SYNTAX scores, and our study is one of those rare studies that have explored this relationship.^[31]

Various studies done on the comparison of TIMI scores and CAD are shown in Table 7.^[22,23,25-29,32,33]

Limitations

The small study population is a major limitation of our study; larger cohorts with multiple centers are needed to further validate the results. Our study has focused only on angiographic severity but not the overall outcome of the patients which is a better marker of prognosis. Angiographic assessment is done by "eyeball" estimation rather than intravascular ultrasound (IVUS)/ fractional flow reserve (FFR) methods which are more validated tools for quantitative and quantitative assessment of CAD. The SYNTAX scoring system may be susceptible to subjective errors, but these errors can be minimized by involving multiple assessors in the scoring process.

CONCLUSION

The TIMI score can serve as a predictor for both the presence and extent of CAD observed during angiography. For patients experiencing NSTE-ACS and having a TIMI score of 4 or higher, an early invasive approach involving coronary angiography and revascularization should be considered as the preferred management strategy. In a developing country like ours, this study helps us to prioritize the limited resources for early interventions in high-risk TIMI scores for decreasing mortality and better patient care.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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