Original Article

Correlation of Thrombolysis in Myocardial Infarction (TIMI) risk score with extent of coronary artery disease in patients with acute coronary syndrome

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Abstract

Objective: To determine the correlation of Thrombolysis in Myocardial Infarction (TIMI) risk score with extent of coronary artery disease (CAD) in patients with acute coronary syndrome (ACS).

Methods: We conducted a descriptive study among 200 consecutive patients admitted with ACS at Tabba Heart Institute, Karachi from June to December 2008. The TIMI risk score was stratified on seven standard variables. The extent of CAD was evaluated on angiography and significant CAD was defined as ≥ 70% stenosis in any one of the three major epicardial vessels.

Results: The mean age of the sample was 58.53 ± 10.64 years. Out of 200 patients, there were 142 (71%) patients with TIMI score ≤ 4 (low and intermediate TIMI risk score) and 58 (29%) patients with TIMI score >4 (high TIMI risk score). Patients with TIMI score > 4 were more likely to have significant three vessel CAD (62 %) versus those with TIMI risk score < 4 (46.2 %), (p< 0.04).

Conclusion: Patients with high TIMI risk score were more likely to have severe multivessel CAD compared with those with low or intermediate TIMI risk score. Hence, patients with TIMI score >4 should be referred for early invasive coronary evaluation to derive clinical benefit (JPMA 60:197; 2010).

Introduction

Cardiovascular diseases have emerged as a major health burden in developing countries and are a subject of great concern for its significant contribution to mortality.[1] The acute coronary syndrome is a major cause of cardiovascular morbidity and mortality for which timely diagnosis and appropriate therapy is of paramount importance to improve clinical outcomes.[2] Patients presenting with acute coronary syndrome — unstable angina (UA) and Non-ST-segment elevation myocardial infarction (NSTEMI) and STEMI, are at risk for death, myocardial infarction or recurrent ischaemic events.[3] Identifying such high risk patients, allows aggressive antithrombotic treatment and early coronary angiography to be targeted to those who will benefit.[4,5]

In terms of multivariate analyses, the TIMI risk score has proven to be an effective risk assessment tool for predicting the risk of death and ischaemic events among patients with ACS. The scheme of risk stratification in TIMI risk score is based on seven independent clinical indicators that are evaluated on patient's presentation.[3] It has the advantage of being easy to calculate and has broad applicability in the early assessment of patients.

Mega etal studied the association between the TIMI risk score and high-risk angiographic findings in NSTEMI. They showed that patients with TIMI risk score of 5 to 7 were more likely to have a severe culprit stenosis (81%), p < 0 .001 and multivessel disease (80%), p <0.001 compared to those with scores of 0 to 2.[6] Garcia etal also showed that the severity of coronary artery disease increases as the TIMI risk score increases, p <0.001.[7]

Although studies have looked into the association of TIMI risk score with different clinical parameters — risk of recurrent ischaemic events, mortality and use of glycoprotein IIb/IIIa inhibitors, only limited studies have evaluated the association of TIMI risk score with coronary angiographic findings (in terms of the severity and the extent of CAD) in ACS. Furthermore, there is no local data available. This association is important as patients with low or intermediate TIMI risk score and no high risk features of acute coronary syndrome could be considered to be risk stratified by non-invasive testing only which may prove to be cost-effective. For this purpose we sought to determine the association between TIMI risk score and the extent of CAD in ACS.

Patients and Methods

A cross sectional study was conducted on 200 consecutive patients who presented to the emergency department of Tabba Heart Institute, Karachi from June to December 2008. Written informed consent was obtained in all cases for recruitment in the study and the procedures involved. The study protocol was approved by the institutional review board. Patients who had chest pain suggestive of angina or anginal equivalent symptoms and diagnosis of ACS were included in the study. We excluded those patients who had ST-elevation myocardial infarction (STEMI), new left bundle

branch block on electrocardiogram (ECG), prior revascularization either surgical/ percutaneous and definitive non-ischaemic etiology for their chest pain at the time of presentation.

Patients with ACS included UA, NSTEMI and STEMI. The diagnosis of ACS was based on history, electrocardiographic (ECG) findings and cardiac biomarkers. All enrolled patients received standard medical therapy for ACS and were admitted in either the coronary care unit or in the cardiac step-down unit according to the American College of Cardiology (ACC) /American Heart Association (AHA) guidelines.[8] Blood samples for cardiac troponin I were immediately drawn upon presentation to the emergency room and a second sample was drawn 8 hours later after admission. Cardiac troponin I was determined using AxSYM Troponin - I ADV (Abbott Laboratories, Abbott Park, Illinois) which is a three-step assay based on the microparticle enzyme immunoassay (MEIA) technology with an analytical sensitivity of 0.02 ng/ml and a diagnostic cutoff for myocardial infarction of 0.40 ng/ml. The 99th percentile was 0.04 ng/ml as described by the manufacturer. The assay was designed to have a precision $\leq$ 10% total coefficient of variation with 95% confidence for concentration from 0.27 ng/mL upto 4.00 ng/mL. All assays were done by technologists unaware of the clinical and angiographic data.

Patients with ACS were further risk stratified with TIMI risk scores. The seven predictor variables for this score are: (1) age $\geq$ 65 years, (2) 3 or more cardiovascular risk factors (family history of premature coronary artery disease, diabetes mellitus, hypertension, dyslipidaemia or current smoking), (3) previous CAD ($\geq$ 50% stenosis at angiography) (4) severe anginal symptoms (2 episodes in last 24 hours), (5) use of aspirin in the last 7 days, (6) ST segment deviation $\geq$ 0.5 mm and (7) elevated serum troponin I level.

Patients with ACS were further evaluated with coronary angiograms to assess the extent of CAD. The angiography was performed by the primary physician who had experience of performing coronary angiography. The extent of CAD evaluated on angiography was classified as follows: significant CAD was defined as $\geq$ 70% stenosis in any of the three major epicardial coronary arteries or a left main coronary artery stenosis $\geq$ 50%. Angiograms revealing coronary artery stenosis < 70% in major epicardial coronary arteries were termed non-obstructive CAD. Extent of CAD was defined as significant single, two or three vessel CAD.

A proforma was designed inquiring about age, gender, presence of major cardiac risk factors (diabetes, hypertension, family history of premature CAD, dyslipidaemia and cigarette smoking), chest pain episode during last 24 hours, use of aspirin during last 7 days and prior known CAD.

The collected data was entered and analyzed by the Statistical Package for Social Sciences version 15.0 Software (SPSS Inc., Chicago, Illinois). Descriptive statistics were computed and presented as means and standard deviations for continuous variables like age. Frequencies and percentages were computed for gender, risk factors (hypertension, diabetes, smoking, dyslipidaemia and family history of premature CAD). Chi-square test was applied to determine the proportions difference between groups $\leq$ 4 and >4 TIMI risk score. A p value <0.05 was considered as significant.

Results

A total of 200 patients were included in this study. The age range was 33-86 years, mean 58.53 ± 10.64 years. There were 139 (60%) males and 61 (30%) females. Of the total 98 (49%) patients were diabetics, 140 (70%) were hypertensives, 60 (30%) were smokers, 44 (22%) had positive history for premature coronary artery disease and 127 (64%) were dyslipidaemic. Table-1 shows the baseline demographic and clinical characteristics of the patients with TIMI score $\leq$ 4 and TIMI score > 4.

Table-2 shows the TIMI risk score variables in the

Table-1: Baseline characteristics of patients according to the TIMI risk score status.

Variable	TIMI Risk score ≤ 4 (n= 142)	TIMI Risk score > 4 (n= 58)
Age (years)	56.23 ± 9.69	64.43 ± 10.9
Gender		
Male	100 (70.4)	39 (67.2)
Female	42 (29.6)	19 (32.8)
Diabetes Mellitus	64 (45.1)	34 (58.6)
Hypertension	89 (62.7)	51 (87.9)
Family history of premature CAD	29 (20.4)	15 (25.9)
Dyslipidaemia	85 (59.9)	42 (72.4)
Smoker	41 (28.9)	10 (17.2)

Data expressed as the mean value ± SD or number (%) of patients.
TIMI = Thrombolysis in Myocardial Infarction, CAD= Coronary artery disease.

Table-2: TIMI Risk score variables in the study population.

TIMI Risk score variables	TIMI Risk score ≤ 4 (n= 142)	TIMI Risk score > 4 (n= 58)
3 or more common risk factors for CAD	54 (38)	39 (67.2)
Chest pain	130 (91.5)	54 (93.1)
Use of aspirin	63 (44.4)	53 (91.4)
Prior known CAD	15 (10.6)	23 (39.7)
ECG ST changes	62 (43.7)	51(87.9)
Positive Troponin I	94 (66.2)	55 (94.8)
Age $\geq$ 65 years	26 (18.3)	35 (60.3)

Data expressed as the number (%) of patients.
TIMI = Thrombolysis in Myocardial Infarction,
CAD= Coronary Artery Disease, ECG= Electrocardiography.

Table-3: Extent of coronary artery disease in the study population based on the TIMI risk scores.

Extent of CAD	TIMI Risk score ≤ 4 (n= 142)	TIMI Risk score > 4 (n= 58)	p value
Single vessel CAD	39 (27.5)	7 (12)	0.02
Two vessel CAD	40 (28.3)	15 (26)	0.74
Three vessel CAD	63 (44.2)	36 (62)	0.04

Data expressed as the number (%) of patients.
Extent of CAD= significant CAD ≥ 70% stenosis of major epicardial vessels, TIMI = Thrombolysis in Myocardial Infarction.

study population divided on the basis of a score ≤ 4 and > 4. Among the TIMI risk score variables: chest pain was most prevalent and involved 184 (92 %) patients, troponin I was positive in 149 (75%), 116 (58%) patients used aspirin within seven days, ST segment depression ≥ 0.5 mm were observed in 113 (57%) patients. Three or more risk factors for CAD were present in 93 (47%), age ≥ 65 years was found in 52 (26%) and prior known CAD figured in 38 (19%) patients.

In Table-3, one hundred and forty two (71%) patients with TIMI score ≤ 4, single vessel CAD occurred in 39 (27.5%) patients, while two vessel and three vessel CAD figured in 40 (28.3 %) and 63 (44.2 %) patients respectively. In 58 (29%) patients with TIMI risk score > 4, single vessel CAD occurred in 7 (12%), while two vessel and three vessel CAD figured 15 (26%) and 36 (62%) respectively. The results showed that TIMI risk score is significantly associated with single vessel CAD ($p < 0.02$) and three vessel CAD ($p < 0.04$).

Regarding the predominant vessel involvement in both the TIMI risk score groups, left anterior descending artery (LAD) was the predominant vessel involved. It figured in 95 (66.9%) patients in the ≤ 4 TIMI risk score group and in 46 (79.3%) patients in the > 4 TIMI risk score group. Significant left main coronary artery stenosis (≥ 50% stenosis) was found in 3 (2.1%) in the ≤ 4 TIMI risk score group and 2 (3.4%) in the > 4 TIMI risk score group.

Discussion

The study revealed that patients with higher TIMI risk score were associated with a greater extent of significant CAD. Risk stratification in the setting of UA/NSTEMI has been addressed in several large studies for predicting the risk of death and ischaemic events.[3,9,10] The severity of CAD has been correlated with different risk stratification schemes like the PURSUIT,[11] AHCPR[12] and the GRACE risk scores.[13]

The TIMI risk score was developed and adapted for patients with UA and NSTEMI. The TIMI risk score is an effective tool for predicting the risk of death and ischaemic events. The TIMI risk score is used for objective risk stratification of patients into one of three groups: low score (0 to 2; 5-8% risk); intermediate (3 to 4; 13-20% risk); and high (5 to 7; 26-41% risk).The risk corresponds to future cardiac events including death, myocardial infarction or urgent revascularization within 14 days.[14] It also identifies those who are likely to benefit most from an early invasive strategy.[3]

The usefulness of this score has been validated by the results of the PRISM-PLUS.[15] and TACTICS-TIMI 18 trials.[16] The TIMI risk score based on the TIMI IIB[14] and ESSENCE trials,[17] incorporates the combination of age, clinical characteristics, ECG changes and cardiac biomarkers for risk stratification. Additional biomarkers have also been investigated to increase the predictive accuracy of this score. Montoliu et al investigated the role of N-terminal pro brain natriuretic peptide (NT-proBNP), C-reactive protein (CRP), troponin T and D-dimer in improving the predictive accuracy of the TIMI risk score in patients with NSTE-ACS. Troponin T, CRP and NT-proBNP were all predictors of adverse events. In all patient groups with a low, moderate or high risk profile based on the TIMI risk score, the presence of two or three elevated biomarkers increased the event rate twofold in comparison with no or one elevated biomarkers. They also found positive correlations between these biomarkers.[18]

In our study we divided our patients into two groups based on the TIMI risk scores of ≤ 4 and looked at the association with the extent of CAD. The results of our study compare well with the findings of Mega et al,[6] who studied the correlation between the TIMI risk score and high-risk angiographic findings in NSTE-ACS. Patients with risk scores of 5 to 7, were more likely to have a severe culprit stenosis (81% vs 58%, $p < 0.001$) and multivessel disease (80% vs 43%, $p <0.001$), compared to those with scores of 0 to 2. The probability of significant left main disease ($p <0.001$), also increased progressively with rising TIMI risk scores ($p <0.001$). The authors did not find any significant correlation between TIMI risk score and left Main Disease because of low prevalence of left Main Disease. A significant correlation was observed between single vessel disease and low TIMI risk score and triple vessel disease and high TIMI risk score.[6] Zheng and colleagues in their study found that TIMI risk score correlated well with the severity of CAD ($p< 0.001$).[19] Garcia and coworkers also showed that the extent and severity of CAD increases as the TIMI risk score increases ($p < 0.001$).[7]

Risk scoring systems should ideally be validated, practical and easy to use at the patient bedside in day-to-day clinical practice.[20] There is presently no risk model conforming to all the above. The simplified version of the GRACE risk score, for instance relies on a computed algorithm for calculation. The TIMI risk score, on the other

hand is a validated scoring system and is a useful bedside tool in the evaluation of risk for patients presenting with acute coronary syndromes.

Our study represents the experiences of a single institution. The severity and location of the coronary lesions was based on the operator visual estimation without quantitative or physiological evaluation.

Conclusion

Our study demonstrates that among patients presenting with ACS- UA / NSTEMI who are referred for coronary angiography, clinical risk stratification according to the TIMI risk score correlates with the angiographic extent of CAD. Patients with high TIMI risk scores were more likely to have severe multivessel CAD compared with those who have low scores. A routine invasive strategy in high TIMI risk score patients should be considered as the preferred strategy.

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