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Thirty day mortality of high risk patients with acute st segment elevation myocardial infarction. Does syntax score apply?

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ABSTRACT

Introduction: Acute STEMI is a life threatening condition with in-hospital mortality varies between 6-14%. Primary PCI had reduced the incidence of death and recurrent MI. Risk stratification is mandatory prior to intervention to identify high risk patients and optimize their therapeutic intervention. The aim was to define the high risk patients with acute STEMI undergoing primary PCI using TIMI risk score & SYNTAX score and to investigate the incidence of thirty day mortality among these patients.

Methodology: This prospective study was done on 175 patients with acute STEMI subjected to primary PCI excluding those with previous CABG, renal impairment or acute in-stent thrombosis. Patients were stratified using TIMI risk score and SYNTAX score into low and high risk groups. The primary end point was 30-day mortality & MACE starting from day of admission.

Results: The study included 139 male (79.4%) and 36 female (20.6%) with mean age of 55.1± 10.5 years. Risk factors for CAD: smoking in (67.4%), hypertension in (46.9%), diabetes mellitus in (38.9%) and dyslipidemia was in (12.6%). Multi-vessels affection was noticed in 52 patients (29.7%). SYNTAX score value of >21.5 and TIMI risk score was >5 identified as effective cut-off points for risk stratification of high risk patients (p<0.0001). In the entire cohort, 30-day mortality was 8%. A statistically significant higher 30 day mortality of patients with high TIMI risk score >5 [27.5% vs 2.2%,P=0.0001]. It was also noticed a statistically significant higher 30 day mortality of patients with high syntax score > 21.5 [P<0.001]. Mean survival for a TIMI risk score of >5 was lower than that of a TIMI risk score of ≤5 (p-value <0.0001). Mean survival for a syntax score of >21.5 was lower than that of a syntax score of ≤21.5 (p-value <0.0001).

Conclusion: TIMI risk score and Syntax score accurately identify high risk STEMI patients. High risk patients with TIMI risk score >5 and/or SYNTAX score >21.5 had a higher incidence of 30 day mortality than low risk patients.

Key words: STEMI: ST, PCI:, MI, TIMI: SYNTAX:, CAD: CABG: Coronary artery bypass graft

INTRODUCTION

Acute ST elevation myocardial infarction (STEMI) is a potentially life threatening medical condition with an in-hospital mortality varies between 6% and 14% in the European countries [(1)]. Immediate intervention in the early hours following an acute STEMI has been shown to reduce the incidence of death, recurrent MI, and hospital readmission, and shorten the length of in-hospital stay [(2)].

The aim of reperfusion therapy is to achieve epicardial artery patency at the site of the occlusive thrombus. TIMI (Thrombosis in Myocardial Infarction) III flow is possible to be achieved in 95% of patients through advances in interventional techniques and adjunctive pharmacological treatment [(3, 4)].

However, it has been observed that the benefit of primary PCI is variable in different groups of patients and the benefit is greatest in those at high risk [(5)]. Thus, risk stratification preceding intervention has great clinical importance to identify the higher risk group of patients and to optimize their therapeutic management [(6)].

Several clinical variables have been reported to be independent predictors of mortality among patients with acute STEMI including heart rate, hypotension, Killip classification, infarction area, symptom of onset-to-therapy time interval, and the presence of acute kidney injury [(7)].

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Risk stratification using the Thrombolysis in Myocardial Infarction (TIMI) risk score for STEMI is a complex assessment based on clinical data at the time of patient's hospital admission [8].

Synergy between percutaneous coronary intervention (PCI) with TAXUS and Cardiac Surgery (SYNTAX) score is a quantitative tool of assessment based on the results of coronary angiography incorporating characteristics of atherosclerotic lesions, the complexity of coronary artery anatomy, lesion location and the number of lesions [9].

In addition, SYNTAX score, including only angiographic features and the complexity of coronary lesions, is a good predictor of major adverse cardiovascular events in multi-vessel diseases treated with percutaneous coronary intervention (PCI) or surgery in elective patients [10].

We hypothesized that applying TIMI risk score and SYNTAX score to patients with acute STEMI who are treated with primary PCI would identify patients at high risk and predict short term mortality.

Another point of interest was to highlight the usage of SYNTAX score in acute STEMI & observe whether it will generate the same cut-off points as for the elective casas.

Aim of the Study:

To identify the high risk patients with acute STEMI undergoing primary PCI using TIMI and SYNTAX score to correlate it with the incidence of thirty day mortality in these patients. Another aim was to apply SYNTAX score to acute STEMI patients going for primary PCI and observe the cut-off points

PATIENTS AND METHODS

The study was conducted prospectively on 175 patients admitted to Cairo University hospitals, Critical Care Department, with the diagnosis of acute STEMI and subjected to primary percutaneous coronary interventions available 24/7.

Inclusion criteria:

Patients presented with acute STEMI within ≤ 12 hours from symptom onset.

Exclusion Criteria:

Patients with a previous coronary artery bypass grafting (CABG) in whom the syntax score could not be calculated, patients with acute in-stent thrombosis following elective PCI and patients with co-existing sepsis, infection, renal impairment or acute stroke during the course of their hospital stay. Patients with life expectancy less than one year due to any cause of co-morbidity was also excluded from the study.

All patients had their TIMI risk score for STEMI calculated at the time of presentation done by simple arithmetic sum of point values assigned to each risk factor based on the multivariate-adjusted risk relationship [7].

All patients were transferred to the cardiac catheterization laboratory for diagnostic coronary angiography. Assessment of the extent and number of affected coronaries, determination of TIMI flow grading before and after the procedure and identification of infarct related artery (IRA) for which primary PCI was done [11].

The SYNTAX score for each patient was calculated from initial angiogram by scoring all coronary artery lesions with at least 50% stenosis of vessels at least 1.5 mm in diameter using the SYNTAX scoring online Calculator version 2.11, which is described on the SYNTAX score website (http://www.syntaxscore.com) [12]. Infarct-related artery (IRA) with TIMI flow of 0 or 1 were accepted as total occlusion with thrombus. All lesions were scored before any intervention (prewiring). Total occlusion in IRA was scored as less than 3 months' duration [9].

The primary end point was 30-day mortality and MACE starting from day of admission.

Statistical analysis:

Data were analyzed using IBM© SPSS© Statistics version 21 (IBM© Corp., Armonk, NY, USA) and MedCalc© version 13 (MedCalc© Software, Ostend, Belgium).

The D'Agostino-Pearson test was used to examine the normality of numerical data distribution.

Continuous numerical variables were presented as mean (SD), and intergroup differences were compared using the unpaired t test. The Welch test was used in place of the t test whenever equality of variance could not be assumed.

Skewed continuous data and discrete numerical data were presented as median (interquartile range) and comparisons were done using the Mann-Whitney test.

Categorical data were presented as number and percentage and differences were compared using the Pearson chi-squared test or Fisher's exact test when appropriate. Ordinal data were compared using the chi-squared test for trend.

Receiver-operating characteristic (ROC) curve analysis was used to examine the value of the TIMI risk score and the SYNTAX score for prediction of 30-day mortality. The DeLong method was used to compare the area under individual ROC curves (AUC).

Survival analysis was done using the Kaplan-Meier method. The log-rank test was used to compare individual Kaplan-Meier curves. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

The study included 175 patients presented to the Critical Care Department at Cairo University with acute ST segment elevation myocardial infarction and were treated with primary percutaneous coronary intervention.

The study included 139 male (79.4%) and 36 female (20.6%) with mean age of 55.1± 10.5 years. Smoking was found in 118 patients (67.4%), hypertension in 82

(46.9%), diabetes mellitus in 68 (38.9%), dyslipidaemia in 22 (12.6%) and family history of CAD in 33 (18.9%). History of CAD in 72 (41.1%), previous PCI in 15 (8.6%) and previous MI in 17 (9.7%).

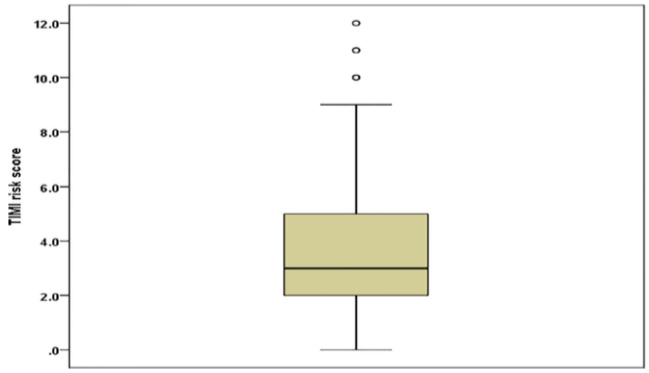
Table-1. Killip classification of studied cohort

Killip class	No. & %
Killip I	140 (80%)
Killip II	4 (2.3%)
Killip III	9 (5.1%)
Killip IV	22 (12.6%)

Killip classification among studied patients is shown in table-1.

TIMI Risk score ranged between 0 and 12 with median and interquartile range was 3 (2-5) as in figure-1.

Figure-1. TIMI risk score of studied population



ECG showed anterior MI in 100 patients (57.2%), inferior MI in 65 patients (37.1%), infero-lateral MI in 10 patients (5.7%), ventricular tachycardia (VT) and/or ventricular fibrillation (VF) in 5 patients (2.8%), complete heart block (CHB) in 11 patients (6.2%) and atrial fibrillation in 5 patients (2.8%).

Coronary angiography showed that single vessel affection was present in 62 patients (35.4%), two vessels in 61 patients (34.9%) while multi vessel disease was found in 52 patients (29.7%).

Left anterior descending artery (LAD) was the infarct related artery in 100 patients representing (57.2%), right coronary artery (RCA) was the culprit in 59 patients (33.7%) while 16 patients (9.1%) had the left circumflex artery (LCX) as the infarct related artery.

Median and interquartile range of SYNTAX score was 19 (13-24) as shown in figure-2.

After stenting 155 patients had a TIMI flow grade III and they represent (88.1%), while TIMI II flow was achieved in 16 patients (9.1%) and TIMI I in 4 patients (2.3%).

In a receiver-operating characteristics (ROC) curve analysis, SYNTAX score value of >21.5 and TIMI risk score >5 were identified as effective cut-off points for high risk STEMI patients as shown in table (2) and figure (3).

Figure-2. SYNTAX score of studied patients

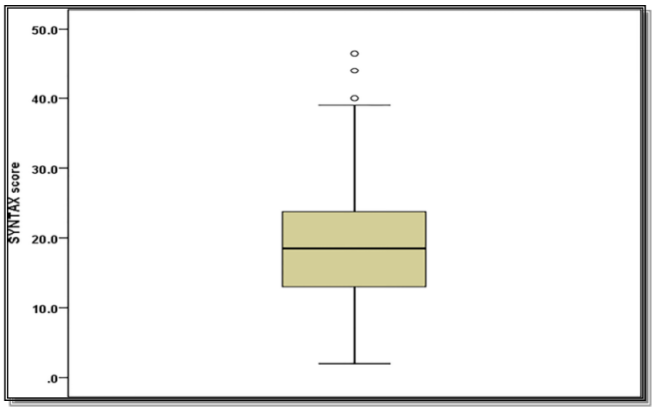
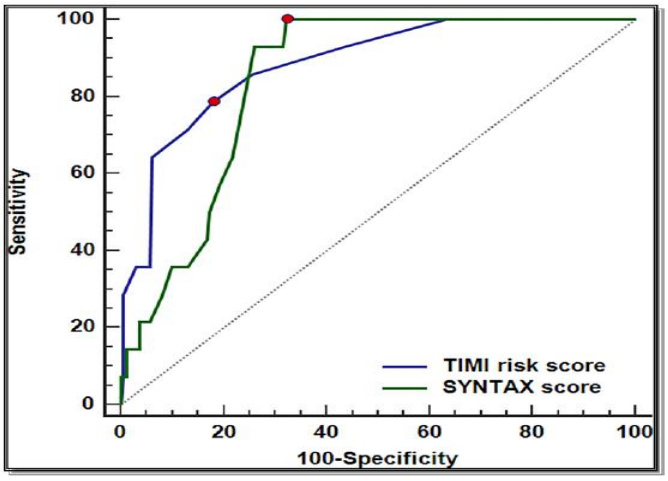


Table-2. ROC curve analysis of SYNTAX & TIMI risk

Index	TIMI risk score	SYNTAX score
Area under the	0.884	0.843
ROC curve (AUC)	(0.799 to 0.969)	(0.776 to 0.911)
p-value (AUC0=0.5)	<0.0001	<0.0001
Youden index J	0.606	0.677
Best cutoff criterion	>5	>21.5
Sensitivity	78.57 (49.2 - 95.3)	100 (76.8 - 100.0)
Specificity	81.99 (75.2 - 87.6)	67.7 (59.9 - 74.8)
PPV	27.5 (14.6 - 43.9)	21.2 (12.1 - 33.0)
NPV	97.8 (93.6 - 99.5)	100 (96.7 - 100.0)

Figure-3. ROC curve analysis of SYNTAX & TIMI risk scores



Accordingly, patients were classified into two groups, low TIMI risk score ≤5 and high TIMI risk score >5. While group I included 135 (87.1%) patients with low TIMI risk score, 40 (22.9%) patients had high TIMI risk score with a statistically significant higher 30 day mortality of patients with high TIMI risk score >5 [27.5% vs 2.2%, P=0.0001] .

Also, based on SYNTAX score, patients were classified into two groups, low SYNTAX score ≤ 21.5 and high SYNTAX score > 21.5. While 109 (62.3%) patients

had low SYNTAX score, 66 (37.7%) patients had high SYNTAX score with a statistically significant higher 30 day mortality of patients with high SYNTAX score > 21.5 [P<0.001] .

Table-3. MACE among studied population

MACE	No. (%)
Heart failure	20 (11.4%)
Acute coronary syndrome	22 (12.5%)
Target vessel revascularization	8 (4.6%)
In stent thrombosis	2 (1.1%)
30-day mortality	14 (8.0%)

In the entire cohort, 30-day mortality was 8%, reported in patients with TIMI risk score >5 and SYNTAX score > 21.5.

Survival analysis for patients using TIMI risk score **s**howed that mean survival time for a TIMI risk score of ≤5 was higher (29.4, 95%CI: 28.7 to 30.1) than that for a TIMI risk score of >5 was (23.4, 95%CI: 20.0 to 26.8), with significant log rank test (p-value <0.0001) as in figure-4.

Also, survival analysis for patients with SYNTAX score showed that mean survival time for SYNTAX score of ≤21.5 was higher (30, 95%CI: 30 – 30) than that for a TIMI risk score of >21.5 (24.7, 95%CI: 22.3 – 27.2), with significant log rank test (p-value <0.0001) as in figure (5).

In hospital MACE was recorded for all patients and recorded in table-3.

DISCUSSION

The significant decrease of in-hospital mortality related to ST-segment elevation acute myocardial infarction (STEMI) has been related to the adoption of primary percutaneous coronary intervention (PCI). STEMI patients with cardiogenic shock tend to have a higher mortality even after PCI and the implantation of mechanical circulatory support devices [13].

STEMI population are highly heterogeneous regarding their risk of adverse events. Thus, risk stratification becomes essential to evaluate their prognosis [14].

Risk stratification and identification of individuals at high risk of death remains a significant issue in patients with STEMI. High risk patients become candidates for

Figure-4. Kaplan-Meier survival analysis for patients using TIMI risk score.

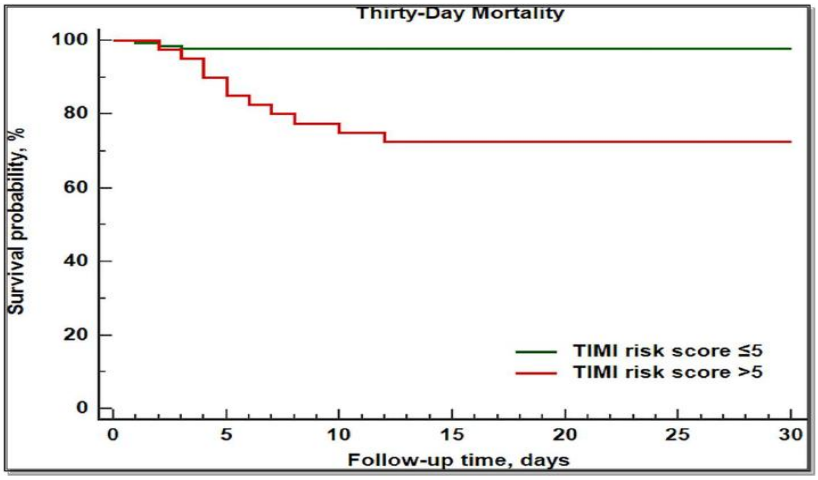
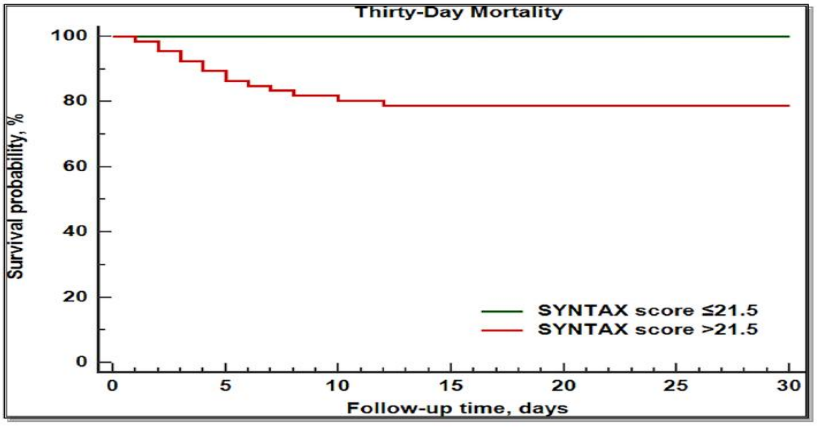


Figure-5. Kaplan-Meier survival analysis for patients using SYNTAX score



aggressive therapy including decisions regarding transfer to tertiary centers. On the contrary, the capacity to reliably identify patients at low risk for fatal recurrent events may offer the opportunity for early hospital discharge [15].

This study investigates determinants of high risk STEMI patients and 30 day mortality of these patients. In our group of STEMI patients treated with primary PCI, the TIMI risk score has a high predictive value for mortality at 30 days with a c-statistics of 0.884 (95% CI: 0.799 to 0.969, p<0.0001). It featured excellent discrimination power regarding 30-day follow-up.

This was evident using data from patients treated with thrombolytic therapy in a randomized In TIME II trial done by *Morrow et al.2001,* which showed a strong association with mortality at 30 days, predictive value for the first 30 days was 0.779. At the high end, a score >5 identified 12% of patients with a mortality risk >2-fold higher than the mean for the population [16].

It was also supported by *Lev et al. 2008,* without identifying a high-risk group, reported that stratification with the TIMI risk score in patients undergoing primary PCI predicts mortality and major adverse cardiac events (death, myocardial infarction, target vessel revascularization) [17].

The present study revealed that 22.9% were classified as high risk (TIMI risk score >5) before the procedure. Those high risk patients (TIMI risk score >5) had a higher incidence of mortality than the low-risk group (27.5% vs. 2.2%, p=0.0001).

González-Pacheco H. et al., 2011 study analysed 572 patients with STEMI, and showed that 32% of patients classified as high risk (TIMI ≥5) had a higher incidence of mortality than the low-risk group 14.8% vs. 2.1%, (p=0.0001). High TIMI risk score is associated with increased frequency of in-hospital death and has a high predictive value for mortality that is comparable with the CADILLAC risk score [18].

Also, *Anna Kozieradzka et al.,2007* divided the patient population into 3 groups: low risk (0-5 points), moderate (6-7) and high (≥8) risk. Thirty-day mortality in the individual groups was 2.07% (n=8), 13.58% (n=11) and 44.4% (n=12), respectively. The c-statistic value for TIMI Risk Score referring to 30-day prognosis was 0.834 (95%CI 0.757-0.91; p<0.0001) [19].

The present study is one of a few in the literature evaluating whether SYNTAX score could predict outcomes in patients admitted with STEMI, and show that SYNTAX score is an independent predictor of all cause 30-day cardiac death after an acute STEMI event.

While originally developed to assess lesion complexity in patients having elective PCI, the SYNTAX score was recently validated in patients with ACS including STEMI undergoing primary PCI. Our findings add to recent data on the usefulness of the SYNTAX score for risk stratification in patients with coronary artery disease.

From the ROC curve, we found that STEMI patients with SYNTAX score > 21.5 was associated with a higher risk of cardiac mortality during the initial 30 days, a figure which usually identify a relatively safe patient in the original study of the SYNTAX score. Based on the results of our study, a patient is considered to be at high cardiac risk if they have a SYNTAX score >21.5.

It was found in the study by *Frank Scherff et al, 2011* that elderly (mean age 79.6±4.1 years) patients with ACS having primary PCI with high SYNTAX score >23 had a higher prevalence of three-vessel disease, cardiogenic shock, and cardiac arrest. Interestingly, they found that the SYNTAX score predicted adverse clinical events in 30 days, but it did not predict clinical outcomes in one year. They concluded that with the complexity of coronary lesions, only peri-procedural risk could be predicted in contrast to the long-term outcomes after discharge [20].

Kul et al, 2012 examined the data of 646 patients with STEMI who had undergone primary PCI. This study showed that patients with a high SYNTAX score (>21.75) had worse clinical outcomes and higher in-hospital mortality than patients with a low SYNTAX score [21].

Yang et al, 2012 found similar results in their study. They examined 151 patients admitted with STEMI and found that a SYNTAX score >22 implies a higher risk of cardiac mortality during the initial 30 days following an acute STEMI [22].

Over the last few years, studies on the association of SYNTAX score with cardiovascular mortality and morbidity have been carried out in acute coronary syndromes. Palmerini T. et al, 2011 for the first time, in a large acute coronary syndrome population (acute catheterization and urgent intervention triage strategy, or ACUITY trial) confirmed SYNTAX score to be a strong independent predictor of morbidity and mortality [23].

Magro et al, 2011 examined the data of 736 patients with STEMI who had undergone primary PCI. They found that the SYNTAX score derived from angiography after primary PCI predicted major adverse coronary events and long-term mortality in patients with STEMI [24].

Garg et al, 2011 also evaluated seven contemporary coronary stent trials (6496 patients) and found that SX score was an independent predictor of all clinical outcomes including mortality, MACE and stent thrombosis at 1-year follow-up. [25]

In another study by Genereux P. et al. 2012, SYNTAX score was one of the scores to have both good discrimination and calibration for cardiac mortality [26].

CONCLUSIONS

TIMI risk score and Syntax score reliably identify patients at high risk of MACE in the occasion of the ACS. High risk patients with TIMI risk score >5 and/or Syntax score >21.5 had a higher incidence of 30 day mortality than low risk patients.

Conflicts of Interest

Authors declare that there is no conflict of interests regarding the publication of this paper.

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