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Comparison of TIMI, Pursuit, Grace Risk Scores in Indians with NSTEMI: A Prospective Cohort Study

Veenu J[1], Srilakshmi Adhyapak[2], GG Shetty[3], Kiron Varghese[4], Chandrakanth B Patil[5]

Authors Affiliation: [1]Consultant Cardiologist, [2]Associate Professor [3-5]Professor, Dept of Cardiology, St Johns Medical College, Bengaluru, Karnataka 560034, India.

Abstract

Background: Patients with non ST elevation myocardial infarction (NSTEMI) are a very heterogenous population, with varying risks of early and longterm adverse events. Early risk stratification at admission seems to be essential for planning therapeutic strategy. There are scores for this. They include the TIMI, PURSUIT and GRACE risk score. In this study we sought to compare these risk scores in a NSTEMI cohort. In the subgroup of patients with syntax score, the TIMI, PURSUIT and Grace risk scores were compared with syntax score in prognosticating patients with NSTEMI. *Materials and methods:* This is a prospective cohort study conducted in a tertiary care hospital catering to patients from Karnataka, Tamil Nadu and Andhra Pradesh states of India. All patients with NSTEMI admitted to the coronary care unit from 01.08.2011 to 30. 04.2013 were included in the study after informed consent. Patients were followed up for adverse cardiac events including NSTEMI, unstable angina, ST elevation myocardial infarction, congestive cardiac failure, interventions and mortality which included in hospital, 30 day and 1 yr mortality. The followup was done till 31st July 2013. *Results:* A total of 213 patients with NSTEMI were included in this study. The mean age of the cohort was 61 ± 12 years. 69.4% (148) were males. Univariate predictors of early mortality included low systolic (p – 0.010), low diastolic blood pressures (p – 0.048) and patient with CCS Class IV at admission (p – 0.019). Univariate predictors of longterm (1 year) mortality includes age (p -0.000), low systolic (p – 0.030) and low diastolic (p -0.001) blood pressure, low ejection fraction (p – 0.002), low hemoglobin (p - 0.004), high serum creatinine (p – 0.009). The GRACE RS was good (AUC – 0.890 CI: 0.77 – 0.99) as compared to TIMI (Fair – AUC – 0.778) and pursuit (good – AUC – 0.865) in predicting In hospital mortality. Long-term mortality prediction was same with all risk scores (AUC – 0.7). Syntax had a better predictability for shorterm and long-term mortality when compared to the other scores. This subgroup is not a random sample and hence may not represent the cohort as a whole. *Conclusion:* In an Indian cohort of NSTEMI, GRACE risk score was better than TIMI and PURSUIT risk scores in discriminative and predictive accuracy for in hospital and shorterm (30 days) mortality. The three risk scores were similar in predicting long-term mortality. Low hemoglobin and diastolic blood pressure are not part of these scores but were independently associated with long term mortality in our cohort.

Keywords: NSTEMI; GRACE risk score; PURSUIT risk score; TIMI risk score; Indian cohort.

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Corresponding Author: Veenu J, Consultant Cardiologist, St Johns Medical College, Bengaluru, Karnataka 560034, India.

E-mail: veenu.remaliya@gmail.com

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Introduction

Patients with non ST elevation myocardial infarction (NSTEMI) are a very heterogenous population, with varying risks of early and longterm adverse events. Early risk stratification at admission seems to be essential for planning

therapeutic strategy. Risk assessment is done by various factors like severity of angina, clinical features, electrocardiography changes and elevated cardiac biomarkers. Integrating all of these factors, several groups have developed comprehensive risk scores that use clinical variables and findings from the electrocardiogram or from serum cardiac markers [1,2]. They include the TIMI, PURSUIT and GRACE risk score. In this study we sought to compare these risk scores in a NSTEMI cohort. The aims and objectives of this study was to compare the TIMI, PURSUIT and Grace risk scores in predicting early and longterm adverse cardiac events and mortality in patients with NSTEMI. Also, to study the significant univariate predictors of adverse outcome or mortality in this cohort. In the subgroup of patients with syntax score, to compare the TIMI, PURSUIT and Grace risk scores with syntax score in prognosticating patients with NSTEMI.

Materials and methods

This is a prospective cohort study conducted in a tertiary care hospital catering to patients from Karnataka, Tamil Nadu and Andhra Pradesh states of India. All patients with history suggestive of angina or electrocardiography changes suggestive of myocardial ischemia (with no sustained ST elevation or new onset LBBB) and rise in cardiac markers of myocardial necrosis (troponin I), admitted to the coronary care unit from 01.08.2011 to 30.04.2013 were included in the study after informed consent. For all these patients the TIMI, PURSUIT and GRACE risk scores were calculated with the data available at admission. The syntax score was calculated using the online syntax calculator version 2.02. All these patients were kept under regular follow-up either on out patient basis or telephonic. Patients were followed up for adverse cardiac events including NSTEMI, unstable angina, ST elevation myocardial infarction, congestive cardiac failure, interventions and mortality which included in hospital, 30 day and 1 yr mortality. The followup was done till 31st July 2013.

Inclusion criteria

1. All patients with history suggestive of angina (OR)
2. Electrocardiography changes suggestive of myocardial ischemia (with no sustained ST elevation or new onset LBBB)
3. And a rise in cardiac markers of myocardial necrosis (troponin I)

Exclusion criteria

1. Perioperative myocardial infarction.
2. Patients not willing for follow-up.

Statistical analysis

Continuous variables with a normal distribution were expressed as mean ± standard deviation. Continuous variables not following the normal distribution are expressed as median with range. Discrete variables were expressed as percentages. The univariate analysis for the baseline characteristics with event or mortality at 30 day and 1 year were performed using Pearson's chi square test or the fisher exact test when appropriate for categorical variables and two tailed student's T test for continuous variables.

For the three risk scores - TIMI, PURSUIT and GRACE, the receiver operator characteristics (ROC) curves were used to relate the calculated scores to the rate of adverse clinical events or mortality and mortality alone at 30 days and 1 year of follow-up. Accordingly the low and high risk cut off values were calculated for each score in accordance with the area under the curve (AUC) obtained from ROC curves. With these values the population was divided into a high and low risk group. This group was used to calculate the sensitivity, specificity, positive and negative predictive value for each risk score.

The predictive accuracy for each of these scores were measured using the sensitivity, specificity, positive and negative predictive value and the difference in the AUC or Pearson's statistic. The relative performance of each test was evaluated with 95% confident interval for difference between the two AUC. The goodness of fit of the risks scores was evaluated by calculating the Pearsons chi square test.

A similar subgroup analysis was performed for the syntax score and the three risk scores, as only a smaller number had coronary angiogram done at our centre.

For the characteristics which had a significant association with event or mortality the logistic regression analysis was performed to rule out the effect of revascularization after the event. For all comparisons, a p – value of <0.05 was considered statistically significant. 95% confidence level was used for confidence interval.

Data obtained was entered in a excel spreadsheet. Statistical analysis was performed using stata.

Table 1: Grace Risk score.

Grace risk score	Age (years) <40	0	Grace risk score	Systolic BP (mm Hg) <80	63
(0 to 300)	40 - 49	18		80 – 99	58
	50 - 59	36		100 – 119	47
	60 - 69	55		120 - 139	37
	70 - 79	73		140 – 159	26
	≥80	91		160 – 199	11
	Heart rate (BPM) <70	0		>200	0
	70 – 89	7		Creatinine (mg/dl) 0 – 0.39	2
	90 – 109	13		0.4 – 0.79	5
	110 – 149	23		0.8 – 1.19	8
	150 – 199	36		1.2 – 1.59	11
	>200	46		1.6 – 1.99	14
	Killip class			2 – 3.99	23
	Class I	0		>4	31
	Class II	21		Cardiac arrest at admission	43
	Class III	43		Elevated cardiac markers	15
	Class IV	64		St – segment deviation	30

Table 2: PURSUIT and TIMI risk score.

PURSUIT risk score	Age (years) 50	11	TIMI risk score	Age (years) ≥65	1
(0 – 20)	60	12	(1 – 7)	≥3 risk factors for cad	1
	70	13		Use of ASA (last 7 Days)	1
	80	14		Known CAD (stenosis ≥ 50%)	1
	Sex			One episode of angina in < 24 hours	1
	Male	1			
	Female	0		ST segment deviation	1
	Worst CCS class in 6 weeks			Elevated cardiac markers	1
	I/II	0			
	III/IV	2			
	Signs of heart failure	2			
	ST depression on ECG	1			

Risk scores: The three risk score were calculated as in table 1 and table 2.

Results

A total of 213 patients with NSTEMI were included in this study. The baseline characteristics, events and mortality are given in table 3. The mean age of the cohort was 61 ± 12 years. 69.4% (148) were males. 48.7% (104) patients presented in CCS class III/ IV at admission. 68.5% (146) patients had diabetes mellitus and 68.1% (145) had hypertension. 86.9% (172) had dyslipidemia with low HDL being the most common type.

In calculating the TIMI risk score, for patients without a prior coronary angiogram, for the variable "known coronary artery disease – stenosis ≥50%" 1 point was given for any patient with prior myocardial infarction or revascularization as validated by TIMI RS authors' earlier 3. The simple score of pursuit risk score for death or myocardial infarction was used. 1 The Grace score was calculated as in Table 1. The syntax score was calculated using the online calculator (version 2.02). 30.5% (65) had known coronary artery disease and 14.5% (31) of patients had prior revascularization. 25.8% (55) were on antiplatelet prior to admission. 48.8% (105) had cardiac failure at admission.

The cardiac In hospital, 30 day and 1 year mortality were 2.8%, 5.5% and 15% respectively. Target vessel revascularization was performed in 21% of patients. NSTEACS and cardiac failure were seen in 16.1% (29) and 21.7% (39) respectively. 33 (15.5%) were lost for follow-up. So calculation of in hospital mortality included 213 patients but all other calculations include 180 patients.

Table 3: Baseline characteristics.

Characteristic	n (percentage)	Characteristic	n(percentage)
Age	61 ± 12©	Hemoglobin	12.5 ± 2.46©
Male	148 (69.4%)	Total WBC count	10656 ± 4471©
Female	65 (30.6%)	Serum creatinine	1.3 ± 0.64©
Presentation with chest pain	140 (65.3%)	0 hour troponin I	0.15 (0.01 – 35)¥
CCS Class I	76 (35.9%)	6 hour troponin I	0.5 (0.5 – 84)¥
CCS Class II	33 (15.4%)	Recurrent angina	9 (4.2%)
CCS Class III	48 (22.5%)	Heart failure during hospital stay	104 (48.8%)
CCS Class IV	56 (26.2%)	Arrhythmias	15 (7%)
Diabetes mellitus	146 (68.5%)	Heart blocks	12 (5.6%)
Systemic hypertension	145 (68.1%)	In hospital mortality	6 (2.82%)
Dyslipidemia	172 (86.94%)	30 day mortality	10 (5.5%)
Mixed hyperlipidemia	74 (34%)		
Low HDL alone	80 (40.4%)		
High LDL alone	19 (9.6%)		
Chronic kidney disease	37 (17.4%)	6 month mortality	21 (11.7%)
Old cerebrovascular accident	15 (7%)	1 Year mortality	27 (15%)
Peripheral arterial disease	11 (16.9%)	Total mortality (Cardiac + non cardiac)	33 (18.3%)
Old Coronary artery disease	65 (30.5%)	Events -NSTE – ACS (unstable angina + NSTEMI)	34 (18.9%)
Prior revascularization - nil	34 (52%)	Events – Cardiac failure	29 (16.1%)
PCI	16 (24.6)	Revascularization	39 (21.7%)
CABG	11 (16.9)	Total hospitalizations	108 (60%)
PCI + CABG	4 (6.2%)	Revascularization	39 (21.7%)
Antiplatelets	55 (25.8%)	Total hospitalizations	108 (60%)
Aspirin alone	22 (10.4%)	LV global hypokinesia on echocardiography	24 (11.6%)
Clopidogrel alone	07 (3.3%)	RWMA	118 (57%)
Aspirin + clopidogrel	26 (12.2%)	Ejection fraction	49.9 ± 14.7
Heart failure at admission	104 (48.8%)		
Heart rate	87.8 ± 21.5©		
Systolic blood pressure	138.1 ± 28.9©		
Diastolic blood pressure	85.9 ± 15.8©		
ECG changes suggestive of ischemia	164 (77%)		
LBBB	18 (8.5%)		
RBBB	15 (7%)		
AV block	3 (1.5%)		
ST depression in more than 5 leads	35 (16.4%)		

© - mean ± standard deviation, ¥ - median with range, CCS – Canadian cardiological society, PCI – percutaneous coronary intervention, CABG –Coronary artery bypass graft surgery, AV block – atrio ventricular nodal block, RWMA – regional wall motion abnormalities, LBBB and RBBB – left and right bundle branch blocks.

Univariate analysis

Univariate predictors of early mortality (Table 4) included low systolic (p – 0.010), low diastolic blood pressures (p – 0.048) and patient with CCS Class IV at admission (p – 0.019). Predictors of early events and mortality include low systolic blood pressure (p – 0.018) and level of 6hour troponin I (p – 0.002). The same parameters showed significant predictors of early mortality after logistic regression.

Table 4: Univariate analysis for predictors of mortality at 30 days

Variable	Mortality at 30 days		P - value
	No	Yes	
Age	61.6 ± 12.5	68.1 ± 9.5	0.079
SBP	138.1 ± 28.89	114.2 ± 17.47	0.010
DBP	85.8 ± 15.4	76 ± 8.4	0.048
CCS Class IV	44 (25.8)	6 (60%)	0.019
CVA	9 (5.29)	2 (20)	0.059

SBP – Systolic blood pressure, DBP – Diastolic blood pressure, CVA – history of cerebrovascular accident.

Univariate predictors of longterm (1 year) mortality (Table 5) includes age (p - 0.000), low systolic (p – 0.030) and low diastolic (p - 0.001) blood pressure, low ejection fraction (p - 0.002), low haemoglobin (p - 0.004), high serum creatinine (p - 0.009), prior history of cerebrovascular accident or presence of peripheral vascular disease and cardiac failure during hospital stay (p - 0.022). The same parameters showed significant predictors of long term mortality after logistic regression.

Table 5: Univariate predictors of mortality at 1 year

Variable	Mortality at 1 year		P - value
	No	Yes	
Age	60.7 ± 11.9	69.3 ± 12.5	0.000
SBP	139.4 ± 28.5	126.7 ± 27.6	0.030
DBP	87.1 ± 15.3	76.7 ± 12.1	0.001
EF	51.1 ±- 14.6	42.1 ± 13	0.002
Hemoglobin	12.8 ± 2.3	11.45 ± 2.4	0.004
Creatinine	1.2 ± .54	1.5 ± 0.73	0.009
CVA	5 (3.42)	5 (17.86)	0.003
Cardiac Failure	8 (5.4)	5 (17.8)	0.022
CKD	20 (13.7)	8 (28.51)	0.050
PAD	4 (2.74)	3 (10.71)	0.049

SBP – Systolic blood pressure, DBP – Diastolic blood pressure, EF – Ejection fraction, CVA – history of cerebrovascular accident, CKD – Chronic kidney disease, PAD – Peripheral arterial disease.

Predictive accuracy for mortality or mortality / events of each risk scores

For in hospital mortality (Table 6) Grace RS was good (AUC – 0.890 CI: 0.77 – 0.99) as compared to TIMI (Fair – AUC – 0.778) and pursuit (good – AUC – 0.865) in predicting in hospital mortality.

Table 6: Area under the curve for in – hospital mortality

Scores	AUC	95% CI
TIMI	0.778	0.61 – 0.94
PURSUIT	0.865	0.76 – 0.97
Grace	0.890	0.77 – 0.99

AUC – area under the curve, 95% CI – 95% confidence interval.

Shorterm mortality at 30 days (Table 7) was again predicted better with GRACE score with good AUC (0.824), sensitivity, specificity and negative predictive value as compared to fair results with TIMI (AUC – 0.687) and PURSUIT (AUC – 0.790).

Long-term mortality (Table 8) prediction was same with all risk scores (AUC – 0.7).

When taking into account the cardiac events either early or long-term, all three risk scores showed a poor performance. (Table 9 and Table 10).

Table 7: Comparison for 30 day mortality

Scores	AUC	95% CI	Sensitivity	Specificity	PPV	NPV
TIMI	0.687	0.52 – 0.85	40	91.7	22.2	96.3
PURSUIT	0.790	0.69 – 0.89	40	82.3	11.7	95.8
Grace	0.824	0.69 – 0.95	80	81.1	20	98.5

AUC – Area under the curve, 95% CI – 95% confidence interval, PPV – Positive predictive value, NPV – Negative predictive value.

Table 8: Comparison of risk scores for 1 year mortality

Scores	AUC	95% CI	Sensitivity	Specificity	PPV	NPV
TIMI	0.704	0.60 – 0.80	50	76.7	29.2	88.9
PURSUIT	0.777	0.70 – 0.85	57.1	75.3	30.8	90.2
Grace	0.778	0.69 – 0.86	67.86	70.3	30.7	91.9

AUC – Area under the curve, 95% CI – 95% confidence interval, PPV – Positive predictive value, NPV – Negative predictive value.

Table 9: Comparison of risk scores for either cardiac event or mortality at 30 days

Scores	AUC	95% CI	Sensitivity	Specificity	PPV	NPV
TIMI	0.507	0.41 – 0.60	25.5	71.4	24	73.1
PURSUIT	0.471	0.38 – 0.57	34	58.7	22.5	71.5
GRACE	0.530	0.43 – 0.63	46.8	48.8	25.3	72.2

AUC – Area under the curve, 95% CI – 95% confidence interval, PPV – Positive predictive value, NPV – Negative predictive value.

Table 10: Comparison of risk scores for either cardiac event or mortality at 1 year

Scores	AUC	95% CI	Sensitivity	Specificity	PPV	NPV	p value
TIMI	0.631	0.55 – 0.71	25.5	71.4	24	73.1	0.681
PURSUIT	0.592	0.50 – 0.67	34	58.7	22.5	71	0.372
GRACE	0.602	0.52 – 0.69	46.8	51.3	25.3	73.1	0.801

AUC – Area under the curve, 95% CI – 95% confidence interval, PPV – Positive predictive value, NPV – Negative predictive value.

Table 11: Sub group analysis of those patients with syntax looking at 30 day mortality

Scores	AUC	95% CI
Syntax	0.885	0.781 – 0.989
TIMI	0.527	0.117 – 0.876
PURSUIT	0.842	0.693 – 0.990
GRACE	0.696	0.300 – 1.00

AUC – Area under the curve, 95% CI – 95% confidence interval.

Table 12: Sub group analysis of those patients with syntax score looking at 1 year mortality

Scores	AUC	95% CI
Syntax	0.840	0.638 – 1.000
TIMI	0.576	0.371 – 0.781
PURSUIT	0.775	0.634 – 0.915
GRACE	0.813	0.671 – 0.955

AUC – Area under the curve, 95% CI – 95% confidence interval.

A subgroup analysis (Table 11 and Table 12) of patients who underwent coronary angiogram in the same centre was done using their syntax score, comparing them to Grace, pursuit and TIMI risk scores. Syntax had a better predictability for shorterm and long-term mortality when compared to the other scores. This subgroup is not a random sample and hence may not represent the cohort as a whole.

Discussion

Patients with non ST elevation myocardial infarction are a very heterogenous population, with varying risks of early and long-term adverse events. Early risk stratification at admission seems to be essential for planning therapeutic strategy. The major benefit of early invasive therapy is largely restricted to those at high-risk as assessed by one of the commonly used risk scoring systems [9]. The three risk scores were initially validated for early events and mortality that is 14 days for TIMI RS, 30 days for PURSUIT RS and in hospital for Grace Rs [1,2,4]. Later various studies have validated these risk scores to predict long-term events and mortality [10].

The cardiac in hospitalmortality was 2.82%, 30 day mortality was 5.5% and the 1 year mortality was 15%. In this study we have compared the three risk scores in a single centre Indian cohort with NSTEMI for prediction of short and long-term events and mortality. For in hospital mortality GRACE risk score was good (AUC – 0.890 CI: 0.77 – 0.99) as compared to TIMI (Fair – AUC – 0.778) and pursuit (good – AUC – 0.865) in predicting mortality. This goes with the fact that this risk score was primarily designed for in hospital events and mortality [4]. This score has also been validated for Indian patients for in hospital mortality and found to have good correlation [10,11].

Shorterm mortality at 30 days was again predicted better with GRACE risk score with good AUC (0.824), as compared to fair results with TIMI (AUC – 0.687) and PURSUIT (AUC – 0.790). Forlong-term (1 year) mortality all the risk scores have a good discriminative accuracy and were similar with AUC of 0.7 [5,6,7]. When events and mortality were combined, the predictive and discriminative accuracy dropped to low levels with AUC of 0.5, hence in our cohort of patients these risk scores were better in predicting mortality.

A subgroup analysis of patients who underwent coronary angiogram in the same centre was done using their syntax score. This included 29% of patients only and it is not based on the risk scores as decision of angiogram is based on multiple financial and social factors. Hence this random group does not represent a sample of the cohort.

Comparing their Grace, pursuit and TIMI risk scores to syntax score showed that the Syntax score had a better predictability for shorterm and long-term mortality when compared to the other scores with AUC of 0.8 [12].

Univariate predictors of early mortality included low systolic (p – 0.010), low diastolic blood pressures (p – 0.048) and patient with CCS Class IV at admission (p – 0.019). Predictors of early events and mortality include low systolic blood pressure (p – 0.018) and level of 6 hour troponin I (p – 0.002). The same parameters showed significant predictors of early mortality after logistic regression. All of these parameters have been validated in the three risk scores except diastolic blood pressure.

Univariate predictors of long-term (1 year) mortality includes age (p - 0.000), low systolic (p - 0.030) and low diastolic (p - 0.001) blood pressure, low ejection fraction (p - 0.002), low hemoglobin (p - 0.004), high serum creatinine (p - 0.009), prior history of cerebrovascular accident or presence of peripheral vascular disease and cardiac failure during hospital stay (p - 0.022). The same parameters showed significant predictors of long term mortality after logistic regression. All of these parameters have been validated in the three risk scores except diastolic BP and hemoglobin.

Diastolic blood pressure has shown significant mortality prediction for shorterm (p value - 0.048) and long-term (p value - 0.001) duration [13]. This parameter has not been validated for, in any of the risk scores. Hemoglobin at admission was also found to significantly predict long-term risk (p value - 0.004) in our cohort [14,15]. Hemoglobin is not part of these three risk scores.

Conclusion

In an Indian cohort of NSTEMI, GRACE risk score was better than TIMI and PURSUIT risk scores in discriminative and predictive accuracy for in hospital and shorterm (30 days) mortality. The three risk scores were similar in predicting long-term mortality. Low hemoglobin and diastolic blood pressure are not part of these scores but were independently associated with long term mortality in our cohort. In a small subgroup analysis the syntax score was better than Grace, TIMI and PURSUIT risk scores for shorterm and long-term mortality prediction but the group was not random and hence the results have to be checked in a large group of representative cohort.

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