

# Clinical Application of Grace Risk Score in Patients with Acute Coronary Syndrome

Samar Firdous,<sup>1</sup> Uzma Malik<sup>2</sup>

## Abstract

**Objectives:** To determine clinical application of GRACE risk score in patients with acute coronary syndrome (ACS).

**Patients and Methods:** It was an observational analytical study conducted in the Cardiology ward of Mayo hospital, Lahore from April to July 2015. Patients with Acute STEMI, NSTEMI or Unstable angina (UA) were selected on the basis of typical chest pain, ECG changes or cardiac biomarkers. For all eligible cases, at presentation GRS was calculated using online calculator. Also, GRACE risk categories and predicted in-hospital mortality were determined. Patients with previous episodes of STEMI/ NSTEMI, old Left Bundle Branch Block (LBBB), stable angina pectoris, acute pericarditis, myocarditis, acute rheumatic fever or pulmonary embolism were excluded. Data was analyzed on SPSS 20 and the R project for statistical computing. Individual components of GRS were compared among discharged and expired cases using t-test. A p-value of <0.05 was considered significant.

**Results:** A total of 165 patients with STEMI and ACS were included. The mean GRS among males and

females was  $137.4 \pm 39$  and  $151.5 \pm 50.6$ . The observed in-hospital mortality was 12.12% with 60% patients of STEMI. Among expired cases, 90% patients had high GRS, predominantly from STEMI group. Important determinants of adverse outcome were advanced age, tachycardia, low systolic blood pressure and presence of cardiac failure.

**Conclusion:** STEMI was the major acute cardiac event. The mean GRS of expired patients was significantly higher than discharged group. GRS accurately identified low risk cases with low probability of in-hospital death. GRS over estimate probability of in-hospital death among STEMI high risk cases that had higher scores and discharged uneventfully. Grace Risk Score is a reliable predictor of risk category and adverse outcomes and its use by clinicians should be strongly recommended.

## Introduction

Atherosclerotic cardiovascular disease is the foremost cause of morbidity and mortality worldwide. Although its prevalence varies according to the ethnic origin, with high risk population being blacks and Asians, but no race is virtually free of this global pandemic. The reason behind this alarming threat is stressful life style, dietary habits, sedentary personalities and obesity. Controlling the modifiable risk factors can help preventing the deadly consequences.<sup>1</sup>

Acute coronary syndrome (ACS) commonly presents with sudden onset typical central chest pain. The word ACS is an umbrella for similar ischaemic cardiac conditions like unstable angina, sub-endocardial infarction and transmural infarction<sup>2</sup>. Unstable angina (UA) is characterized by reduction in blood supply to heart due to atherosclerotic narrowing of coronary arteries. Whereas, in non-ST segment elevation myocardial

<sup>1</sup> Assistant Professor of Medicine, KEMU/Mayo Hospital, Lahore

<sup>2</sup> Assistant Professor of Medicine, KEMU/Mayo Hospital, Lahore

Date of Submission: 13-05-2017

Date of 1<sup>st</sup> Revision Received: 17-05-2017

Date of Acceptance for Publication: 20-06-2017

Conflict of Interest: None

Funding Source: None

## Contribution

All Authors have contributed in Study Design, Data Collection, Data Analysis, Data Interpretation, Manuscript Writing and Approval.

infarction (NSTEMI) there is infarction of sub-endocardium only. In ST segment elevation myocardial infarction (STEMI) there is transmural involvement.<sup>3</sup>

The extent of cardiac damage following an episode of ACS is determined using various scoring systems. GRACE risk score is one of the valid tools for application following ACS. It helps clinicians to determine overall cardiac risk and mortality from cardiac events. Thus, patients are categorized into high, moderate or low risk categories and urgent referral to cardiologist for intervention can be planned according to the risk category.<sup>4</sup>

The rationale of this study was to determine the clinical application of GRACE risk score among patients with ACS. The timely assessment of patients by using this clinical tool provides sufficient help to highlight high risk cases so that interventions can be performed without any delay.

## Patients and Methods

After approval from Institutional Review Board, this observational analytical study was conducted in the Cardiology department of Mayo Hospital, Lahore from April to July 2015. Data of cardiac patients who presented with typical chest pain and suffered acute coronary syndrome was collected. Subjects with old STEMI/NSTEMI, old Left Bundle Branch Block (LBBB), stable angina pectoris, acute pericarditis, myocarditis, acute rheumatic fever or pulmonary embolism were excluded. Blood samples for necessary baseline investigations were taken from selected cases. Online GRACE score calculator<sup>5</sup> was applied on all selected patients and they were categorized as high, moderate or low risk cases. Outcomes in the form of patient's discharge from hospital, death during hospital stay or any other complication were noted in each subject's record.

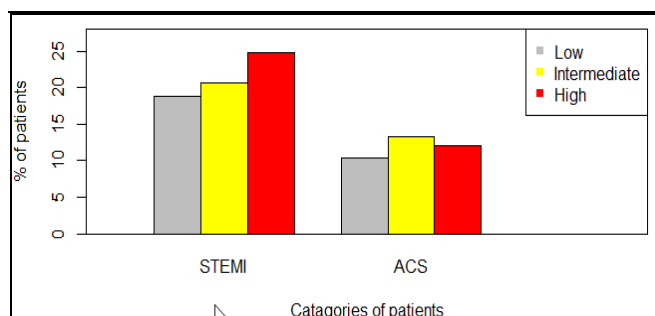
According to GRACE risk score STEMI patients were categorized as low risk (GRS  $\leq$  108), intermediate risk (GRS 108 – 140), and high risk (GRS  $\geq$  141). In addition, patients with ACS (NSTEMI/UA) were categorized as low risk (GRS  $\leq$  125), intermediate risk (GRS 126 – 154), and high risk (GRS  $\geq$  155).

Data were analyzed on SPSS version 20. Qualitative variables were presented as percentages along with frequencies. Quantitative data were in the form of mean  $\pm$  SD. In addition, individual components of GRS were compared among discharged and expired cases using t-test. A p-value of  $< 0.05$  was considered significant.

## Results

This study was conducted on 165 patients with ACS. The male to female ratio was 3:2. The mean age of study population was 53 years. Table 1 shows baseline characteristics of discharged and expired cases. The overall mean age of all cases was same in STEMI and ACS patient groups. Comparing mean age of discharged and expired cases, the later had higher mean age (p value 0.003). It indicates that advanced age was associated with adverse outcome. Although most of the patients were male, there was equal proportion of both genders in STEMI and ACS group. Comparing discharged and expired cases among both genders, the females exhibited a higher mortality as compared to males who were mostly discharged (15.6% vs. 9.9%).

Figure 1 showed the percentages of the admitted and expired patients in different risk categories of STEMI and ACS groups. There were 106 (64.2%) patients of STEMI and 59 (35.75%) patients with ACS. Most of the deaths in both groups were seen in high risk category of GRS.



**Fig. 1:** Distribution of STEMI & ACS patients in different GRS groups.

STEMI was the major cardiac event (64.2%). The mean heart rate was  $82.2 \pm 15.8$ . The mean heart rate was similar in STEMI, ACS and discharged patient groups. This is in contrast to expired cases that had relatively higher heart rate, although it was not statistically significant (p-value 0.26).

The overall mean systolic BP was  $117.7 \pm 24.7$ . Figure 2 shows comparison of systolic blood pressure among discharged and expired cases. The expired patients had lower systolic BP than discharged cases (p-value 0.004) as shown in table 1. It focuses on the importance of systolic BP as one of the major determinant of survival following ACS.

Presence of cardiac failure was another important

component of GRACE risk score which determined chances of death following ACS. There were 80% cases in Killip class I and 95% of them were discharged uneventfully. Among 9.1% cases in Killip class IV, the proportion of expired cases was significantly higher 53.3%. Most of the class II and III patients were also discharged uneventfully.

Mean serum creatinine level was  $1.31 \pm 1.03$ mg/dl which was similar among discharged and expired cases. Similarly other components of GRACE risk score like cardiac biomarkers, ECG changes and cardiac arrest at presentation were significantly different among discharged and expired patient groups. Among the discharged cases 86.1% had absence of cardiac arrest at first presentation.

The overall mean GRS was  $142.8 \pm 44.28$ . The mean GRS among males and females was  $137.4 \pm 39$  and  $151.5 \pm 50.6$  respectively. Comparing GRACE risk score of discharged and expired cases, the later had significantly higher score (p-value < 0.0001). The main reasons were low systolic blood pressure and higher mean heart rate among expired patients contributing to a higher GRS leading to mortality. Another significant factor was advanced age among expired

cases (p-value 0.002). It was evident that as the risk category increased, GRS also increased. This finding was important as no death was seen in the low risk category of either group. It stresses on importance of GRACE risk score as an excellent tool for differentiating high risk cases from low risk. The main determinants affecting a higher GRS among expired patients were higher mean age, relatively high mean heart rate, lower systolic BP, and advanced Killip class of heart failure.

The overall observed in-hospital mortality was 12.12%. Sixty percent of expired patients belonged to STEMI group, rest of them had ACS. The GRACE risk score of 90% expired cases revealed higher figures (11 had STEMI and 7 with ACS) indicating them to be at high risk of early cardiac death.

GRACE risk score was used to determine the predicted in-hospital mortality at presentation among all selected patients. This probability of in-hospital death was compared with the actual observed mortality as shown in figure-3. GRS very accurately pointed out high risk individuals with increased probability of in-hospital death, which later expired during hospitalization. All except two expired cases had low probability

**Table 1:** Mean Baseline Characteristics of Discharged and Expired Patients.

Characteristics	Total	Discharged Cases	Expired Cases	Comparison of Discharged & Expired Cases (p-value)
Age (years)	53.16 ± 11.17	52.09 ± 10.78	60.95 ± 11.07	0.003
Gender (Male)	101 (61.2%)	91 (90.1%)	10 (9.9%)	-
Gender (Female)	64 (38.8%)	54 (84.4%)	10 (15.6%)	-
Heart rate (beats/ min)	82.24 ± 15.87	81.31 ± 12.89	89 ± 29.32	0.26
Systolic BP (mmHg)	117.7 ± 24.7	120.07 ± 23.6	100.5 ± 26.2	0.004
Diastolic BP mm Hg	75.97 ± 14.57	77.07 ± 13.81	68 ± 17.65	0.03
Killip class I	134 (81.2%)	127 (94.7%)	7 (5.2%)	-
Killip class II	10 (6.1%)	7 (70%)	3 (30%)	-
Killip class III	6 (3.6%)	4 (66.6%)	2 (33.3%)	-
Killip class IV	15 (9.1%)	7 (46.6%)	8 (53.3%)	-
Serum creatinine (mg/dl)	1.31 ± 1.03	1.32 ± 1.09	1.23 ± 0.41	0.51
ST deviation present (%)	150 (90.9%)	130 (78.8%)	20 (12.1%)	-
Cardiac arrest absent at presentation (%)	159 (96.4%)	142 (86.1%)	17 (10.3%)	-
Raised cardiac markers (%)	114 (69.1%)	96 (58.2%)	18 (10.1%)	-
Mean GRS	142.8 ± 44.28	133.8 ± 36.1	208.4 ± 43.1	< 0.0001

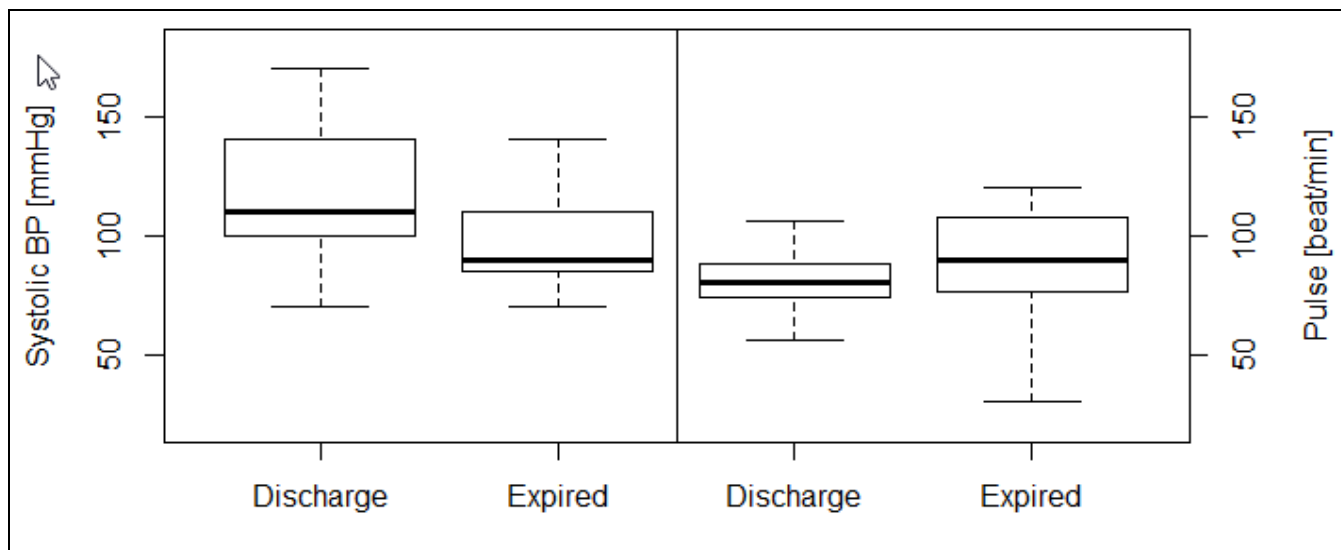


Fig. 2: Median/IQR Systolic BP & Pulse Rate among Discharged and Expired Cases.

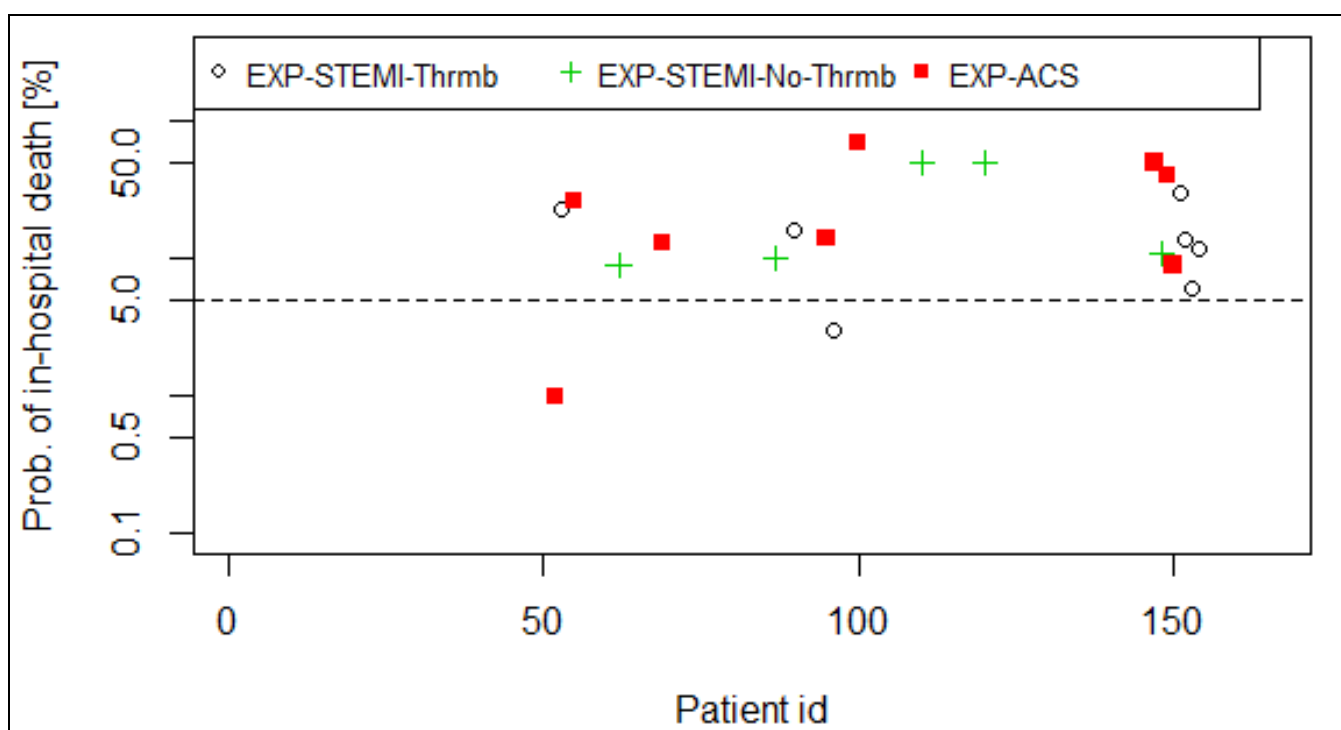
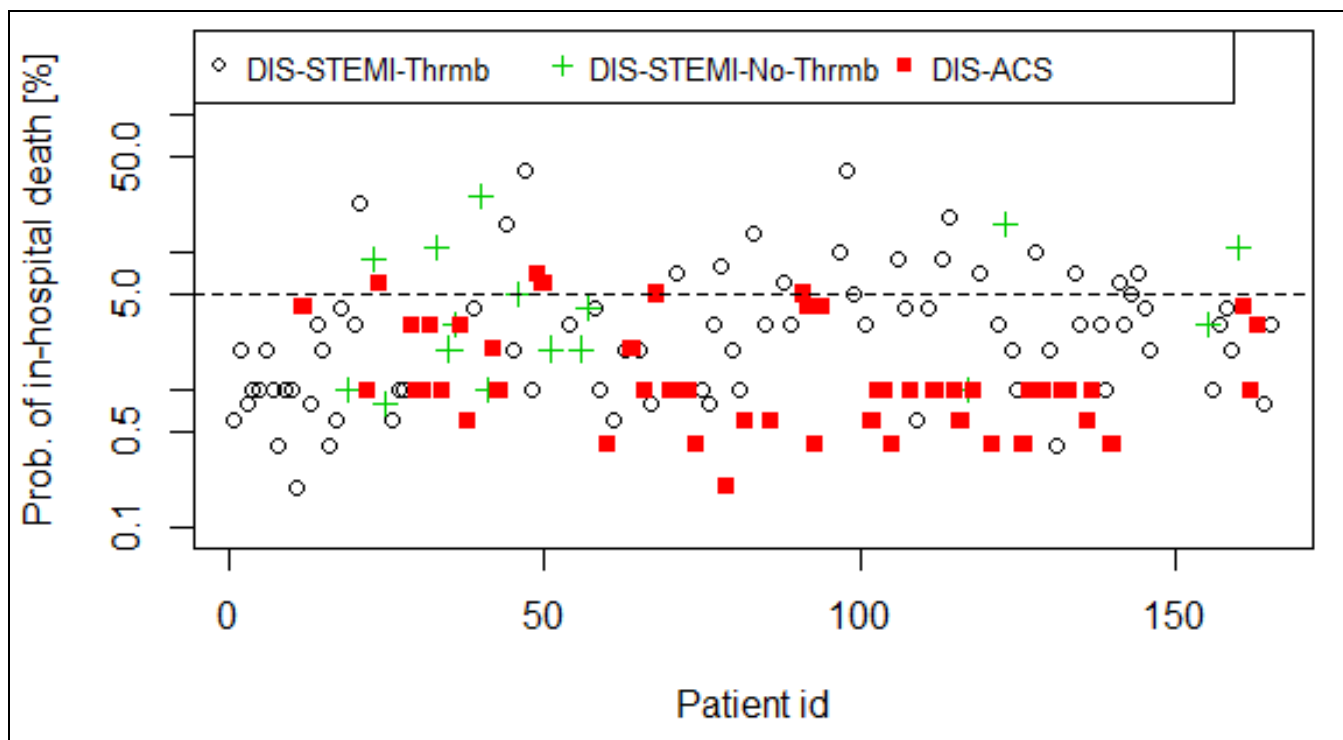


Fig. 3: Predicted In Hospital Mortality (According to GRS) among Expired ACS and STEMI Thrombolysed vs. STEMI Non-thrombolysed Patients [y-axis=log].

of in-hospital death. It pointed towards accuracy of GRS calculator as a strong tool to predict the course of events after an acute cardiac insult. Mostly expired STEMI patients received thrombolytic therapy except few patients who did not fulfill the criteria for thrombolysis.

Next, a comparison was done regarding predicted in-hospital mortality among discharged patients of ACS, STEMI cases who received thrombolytic therapy and patients who could not be thrombolysed due to any reason (Figure 4). The discharged cases of STEMI exhibited a wide range in probability of in-hospital



**Fig. 4:** Predicted In-Hospital Mortality (According to GRS at Presentation) among Discharged ACS and STEMI Thrombolysed vs. STEMI Non-thrombolysed Patients [y-axis=log].

death according to GRS at presentation. Many thrombolysed STEMI cases with high probability of death within 7 days were discharged uneventfully. This result highlights that even though Grace Risk Score is a reliable predictor of in-hospital mortality; however, it also over predicts in some cases and needs a fine tuning for our local population. The STEMI patients who did not receive thrombolytic therapy also had a diverse range of predicted in-hospital death, with most cases of low probability (< 5%). The discharged cases of ACS had predicted deaths < 5% at presentation and they did not had complicated course of events during hospital stay. In general, this supports the effectiveness of GRS as a powerful judgment tool.

**Discussion**

STEMI was the main cardiac event among patients with ACS. The analysis of individual components of GRACE risk score showed multiple factors determining the outcome of patients following ACS. This predictive tool makes use of eight parameters including patient’s age, gender, systolic blood pressure, heart rate, ST – segment changes, presence of cardiac arrest

at presentation, elevated cardiac biomarkers and serum creatinine. It is vital to identify high risk patients at an earlier stage of presentation such that risk factor stratification along with timely intervention can bedoneto reduce morbidity and mortality.<sup>6</sup> GRACE risk score is a predictive tool, designed by the largest multinational registry to estimate in-hospital as well as 6 months mortality and to segregate patients at high and intermediate risk of cardiac death after acute STEMI or ACS from low risk patients.<sup>7</sup>

The presence of tachycardia after ACS is one of the major determinants of poor prognosis. Our results show relatively higher heart rate among expired cases than discharged ones. Therefore authorities recommend controlling heart rate with beta blockers to reduce further ischaemia. This carries negative inotropic effect by reducing heart rate and myocardial oxygen demand.<sup>8</sup>

Hypotension is another important component of GRACE risk score and a major determinant of poor prognosis and early death following ACS<sup>9</sup>. Our results show relatively lower systolic blood pressure among expired patients. This along with presence of pulmonary edema indicates that patient is in cardiogenic

shock. Our results showed most of the discharged cases did not have any evidence of heart failure. Whereas among expired cases, presence of advanced Killip class indicated presence of cardiogenic shock leading to mortality.

Baseem Elbarouni et al., conducted a study in Canada on 12242 patients with ACS to determine validation of GRACE score for predicting in-hospital mortality. They stressed on excellent capacity of GRACE risk score for stratifying patients into low or high risk. The prediction of probability of in-hospital death was relatively less accurate, rather it relatively over-estimated the predicted mortality, especially among low-risk patients.<sup>10</sup> This result is highly consistent with our study as it was seen that many high risk cases with significant probability of in-hospital death following an acute cardiac event were safely discharged. However, the expired cases had significantly higher probability of in-hospital death according to GRS at presentation. In-hospital mortality was 3.4% (in-contrast to 12.2% in our study). The difference in results is related to different ethnic origins of two study populations, furthermore difference of health care systems may also contribute.

A Pakistani study was conducted by Sheikh MK et al., in Karachi on 530 patients with NSTEMI and USA. The mean GRS was  $131.87 \pm 41.5$ . In-hospital mortality was 3.6% with 8.4% high risk cases. They validated GRACE risk score as it was found to be a good predictor of poor outcomes. The in-hospital mortality increased as GRACE score category increased.<sup>11</sup>

The routine use of GRACE risk score is highly recommended for all physicians working in emergency department. This application of GRACE risk score among patients of acute chest pain and diagnosis of ACS helps to categorize them into low, intermediate or high risk groups. It helps to plan urgent intervention in high risk groups without time lapse and also avoiding aggressive management of low risk cases.<sup>12,13</sup>

This study had few limitations. First, there was no data to look into long term mortality according to the risk category. Further it was a single centre study. In future, large scale, multicentre studies with longer follow-up would help in determining long term predictive ability of GRACE risk score.

## Conclusion

GRACE risk score is an excellent clinical tool to differentiate between low and high risk cases of ACS. It is

strongly recommended that clinicians should routinely use it for patient management. It helps to highlight risk of poor outcomes among high risk cases and intervention can be prioritized according to risk category.

## References

1. Am Heart Association. Heart Disease and Stroke Statistics—2009 Update. Dallas, Tex: American Heart Association. 2009.
2. Abu-Assi E, Ferreira-González I, Ribera A, Marsal JR, Cascant P, Heras M, et al. "Do GRACE (Global Registry of Acute Coronary events) risk scores still maintain their performance for predicting mortality in the era of contemporary management of acute coronary syndromes?" *Am Heart J.* 2010;160:826-4.
3. Iqbal MW, Fayyaz A, Hanif A frequency of left ventricular thrombus after anterior wall ST-segment elevation acute Myocardial infarction. *Annals of King Edward Medical Uni.* 2014;20 (1):68-75.
4. Chan MY1, Shah BR, Gao F, Sim LL, Chua T, Tan HC, et al. Recalibration of the Global Registry of Acute Coronary Events risk score in a multiethnic Asian population. *Am Heart J.* 2011;162:291-9.
5. Calculator Online (Cited 2013 Dec 13). Available from URL: [http://www.outcomes-umassmed.org/grace/acs\\_risk/acs\\_risk\\_content.html](http://www.outcomes-umassmed.org/grace/acs_risk/acs_risk_content.html).
6. Eggers KM, Kempf T, Venge P, Wallentin L, Wollert KC, Lindahl B. Improving long-term risk prediction in patients with acute chest pain: the Global Registry of Acute Coronary Events (GRACE) risk score is enhanced by selected non-necrosis biomarkers *Am Heart J.* 2010;160:88-94.
7. Mehta SR, Granger CB, Boden WE, Steg PG, Bassand JP, Faxon DP. et al. Early versus delayed invasive intervention in acute coronary syndromes. *N Engl J Med.* 2009;360:2165–2175.
8. Brindle P, Beswick A, Fahey T, Ebrahim S. Accuracy and impact of risk assessment in the primary prevention of cardiovascular disease: a systematic review. *Heart.* 2006;92:1752-9.
9. Yan AT, Yan RT, Huynh T. Understanding physicians' risk stratification of acute coronary syndromes: insights from the Canadian ACS 2 Registry. *Arch Intern Med.* 2009;169:372-8.
10. Elbarouni B, Goodman SG, Yan RT. Validation of the Global Registry of Acute Coronary Event (GRACE) Risk Score for In-hospital Mortality in Patients with Acute Coronary Syndrome in Canada. *Am Heart J.* 2009;158(3):392-399.
11. Shaikh MK, Hanif B, Shaikh K, Khan W, Parkash J. Validation of grace risk score in predicting in-hospital mortality in patients with non ST-elevation myocardial infarction and unstable angina. *JPMA.* 2014;64(7): 807-11.

12. Cooney MT, Dudina AL, Graham IM. Value and limitations of existing scores for the assessment of cardiovascular risk: a review for clinicians. *J Am Coll Cardiol.* 2009;54:1209-27.
13. Emad A, José M GA, Carlos PG, José R. G. Validation of the GRACE Risk Score for Predicting Death Within 6 Months of Follow-Up in a Contemporary Cohort of Patients With Acute Coronary Syndrome. *Rev Esp Cardiol.* 2010;63:640-8.