

Prognostic Value of the ACTION ICU Score Compared to GRACE and TIMI Scores in Non-ST-Segment Elevation Acute Coronary Syndromes

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Abstract

Background: Non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) represent the primary manifestation of acute coronary syndromes, accounting for 60% to 70% of hospital admissions. Effective emergency department (ED) management relies on accurate risk stratification to guide triage. While established scores like GRACE and TIMI are widely used for long-term prognosis, they are not specifically validated to predict immediate in-hospital complications in the acute ED phase. This study evaluated the prognostic value of the ACTION ICU score compared to the performance of the GRACE and TIMI scores for short-term ED complications and 6-month major adverse cardiovascular events (MACE).

Methods: We conducted a retrospective observational analysis of a prospective registry at a regional hospital in Tunisia, over nine years (2014–2022). Inclusion of patients admitted for NSTEMI-ACS in the ED. Diagnostic performance was evaluated using Receiver Operating Characteristic (ROC) curves to identify optimal cut-off values for acute in-hospital complications (acute pulmonary edema, arrhythmias, death) and 6-month MACE.

Results: The cohort had a mean age of 60 ± 12 years with 59.3% males. In-hospital complications occurred in 6.3% of patients. For predicting these acute events, the ACTION ICU score significantly outperformed other models with an Area Under the Curve (AUC) of 0.88 (95% CI: 0.836–0.941), compared to 0.77 for GRACE and 0.59 for TIMI. An ACTION ICU cut-off value of >5.5 provided 80% sensitivity, 77.39% specificity, and a negative predictive value of 98.29%. Conversely, the GRACE score was the most accurate for 6-month MACE (AUC 0.707).

Conclusion The ACTION ICU score is an effective tool for immediate ED triage, providing high accuracy in predicting short-term complications. Its systematic implementation could optimize intensive care unit resource allocation in constrained healthcare settings without compromising patient safety.

Key-words: Score, Prognosis, Emergency Department, Acute Coronary Syndrome, NSTEMI, Mortality.

INTRODUCTION

Cardiovascular diseases are the leading cause of morbidity and mortality worldwide, with an increasing incidence in developing countries. Acute coronary syndromes (ACS) are the most

frequent cardiovascular manifestation of these diseases. Among them, non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) represent the primary manifestation, causing 60% to 70% of hospital admissions with a mortality rate of approximately 3.4% (1,2).

For frontline physicians, managing these patients is a daily challenge. While the management of ST-segment elevation myocardial infarction is well codified and relies on immediate coronary reperfusion, the emergency management of NSTEMI-ACS depends entirely on the risk stratification of cardiovascular complications and death.

To guide this risk stratification, medical societies have validated several scoring systems. The TIMI (Thrombolysis In Myocardial Infarction) score is a simple tool designed to stratify the medium-term risk of complications (3). The GRACE (Global Registry of Acute Coronary Events) score predicts both in-hospital and six-month mortality, and its use is currently recommended by the European Society of Cardiology to guide therapeutic decisions (4).

However, no specific score is used to predict the risk of in-hospital complications directly in the emergency department for NSTEMI-ACS patients.

To address this issue, the ACTION

ICU (Acute Coronary Treatment and Intervention Outcomes Network) score was first proposed in 2018 to predict the development of complications requiring intensive care unit admission during the initial phase of care (5).

Very few studies in international and national literature have focused on evaluating the ACTION ICU score. The aim of this study was to evaluate the short-term prognostic value of the ACTION ICU score by comparing it against the traditional GRACE and TIMI scores in the emergency department.

METHODS

Study Design and Setting

We conducted a retrospective observational analysis of a prospective monocentric registry of patients presenting with non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) during a nine-year period, from January 2014 to December 2022. Data were collected at

the Emergency Department of a regional hospital in Tunisia.

Patient Selection

We included adult patients of both sexes, who presented to the emergency department with clinical, electrocardiographic, and biological findings consistent with NSTEMI-ACS. We defined the diagnosis of NSTEMI-ACS using standard diagnostic criteria: symptoms suggestive of acute myocardial ischemia (chest pain, dyspnea, or epigastric discomfort), associated with electrocardiographic normal findings or ischemic changes (such as ST-segment depression, T-wave inversion or non-specific ST-T abnormalities), and the dynamic change of high-sensitivity cardiac troponin to distinguish between NSTEMI (rise or fall of troponin) and unstable angina (normal value).

Patients were excluded from the study if they met any of the following criteria:

Presentation with complications requiring immediate intensive care upon admission (cardiac arrest, cardiogenic shock, severe arrhythmias).

Presence of persistent ST-segment elevation on the initial ECG (STEMI).

Final diagnosis unrelated to NSTEMI-ACS (coronary angiography showing no significant lesions).

Missing contact information, leaving against medical advice, or being lost to follow-up.

Unavailable coronary angiography data.

The final diagnosis of ACS was confirmed either by ischemia tests conducted in outpatient cardiology clinics or by coronary angiography demonstrating a stenosis of more than 50% in a major coronary artery.

Data Collection and Definitions

For each included patient, data were retrospectively extracted from the registry using standardized medical records completed by the emergency physicians. We collected demographic characteristics, cardiovascular risk factors, and previous medical history.

Clinical presentation details included the characteristics of chest pain, time from symptom onset to first medical contact (FMC), vital signs (systolic and diastolic blood pressure, heart rate, respiratory rate, and oxygen saturation), Killip classification, and pain intensity using a visual analog scale.

A standard 17-lead ECG was performed within 10 minutes of FMC. Biological data obtained at admission included blood glucose, renal function, ionogram, complete blood count, and troponin levels. From 2016 onwards, high-sensitivity troponin assays were utilized following the 0/3h rule-out algorithm recommended by ESC guidelines (6).

Prognostic Risk Scores and Outcomes

Three prognostic risk scores were systematically calculated for each patient at admission based on clinical, biological, and electrical data:

TIMI Score (Thrombolysis In Myocardial Infarction).

GRACE Score (Global Registry of Acute Coronary Events).

ACTION ICU Score (Acute Coronary Treatment and Intervention Outcomes Network).

The primary short-term outcome was the occurrence of in-hospital complications during the emergency department stay. Complications were defined as acute pulmonary edema, cardiogenic shock, severe arrhythmias, conduction disorders, or death.

The long-term prognostic outcome was evaluated through telephonic follow-up at 6 months. We assessed the occurrence of Major Adverse Cardiovascular Events (MACE), defined as death, non-fatal myocardial infarction, recurrent angina, stroke, or the need for coronary artery bypass grafting (7).

Statistical Analysis

We performed data entry and statistical analyses were performed using SPSS software (version 23.0). Continuous variables were expressed as means $\pm$ standard deviations (SD) and compared using the Student's t-test or Analysis of Variance

(ANOVA). Categorical variables were expressed as frequencies and percentages and compared using Pearson's chi-squared test or Fisher's exact test when appropriate. A p-value of <0.05 was considered statistically significant.

To evaluate the predictive accuracy of the GRACE, TIMI, and ACTION ICU scores for short-term complications and 6-month MACE, we generated Receiver Operating Characteristic (ROC) curves. The Area Under the Curve (AUC) with 95% confidence intervals were calculated for each score. Optimal cut-off values were determined based on the highest combined sensitivity and specificity. Finally, AUCs were formally compared to establish statistical superiority among the models.

RESULTS

During the study period, out of the overall emergency department, 793 patients met the inclusion criteria and were managed for non-ST-segment elevation acute coronary syndromes. Figure 1 represents the inclusion flowchart.

The mean age was 60 ± 12 years. Men represented most of the cohort, accounting for 59.3% (n=470) of the patients.

The most prevalent cardiovascular risk factors were hypertension, present in 57.1% (n=453) of the cohort, followed by diabetes mellitus in 42.4% (n=336), active smoking in 30.1% (n=239), and dyslipidemia in 29.3% (n=232). A known history of coronary artery disease before admission

was present in 27.9% (n=221) of patients.

Clinically, chest pain was the cardinal symptom, motivating the emergency consultation in 92.4% (n=733) of cases. The median delay from symptom onset to first medical contact was 19.5 hours. Upon initial electrocardiographic (ECG) assessment, 48%

(n=381) of patients demonstrated ST-segment depression, 17.3% (n=137) showed isolated negative T waves, and 32.2% (n=256) had a normal initial ECG.

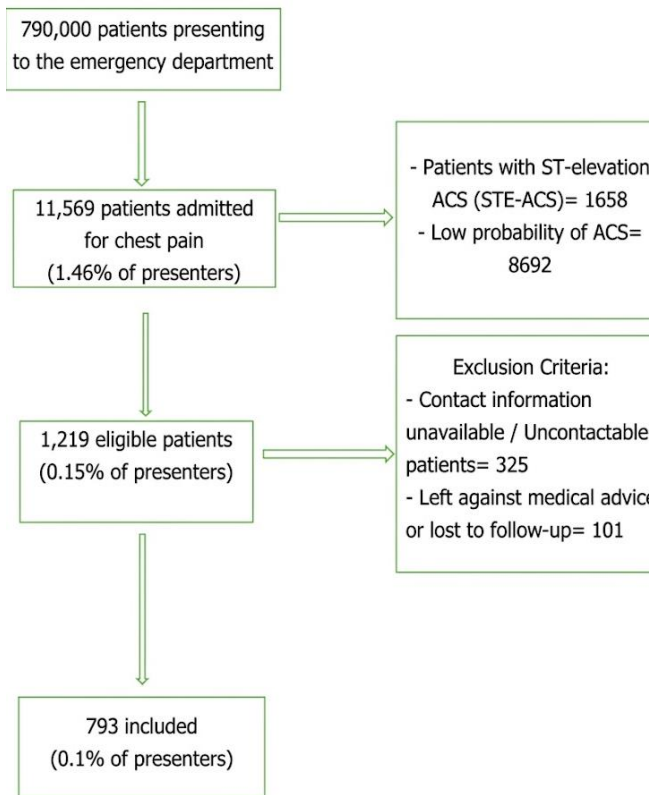


Figure 1: Patient inclusion flowchart in the study

The occurrence of complications during the emergency department stay was observed in 6.3% of patients (n=50). The most frequent complication was acute pulmonary edema (3.5%, n=28), followed by arrhythmias (1.9%, n=15) and conduction disorders (0.9%, n=7). In-hospital mortality occurred in 3 cases (0.37%). Table 1 highlights the significant clinical and biological differences between the stable group and the group that developed acute complications during their emergency department stay.

Receiver Operating Characteristic (ROC) curve analysis for short-term complications revealed that the ACTION ICU score demonstrated significant superiority over both the GRACE and TIMI scores (Fig 2). The ACTION ICU score yielded an Area Under the Curve (AUC) of 0.88 (95% CI: 0.836–0.941; $p < 0.01$). A cut-off value of 5.5 provided the best balance, with a sensitivity of 80% and a specificity of 77.39%. The GRACE score had an AUC of 0.777 (IC95%

(0,710-0,844)) with a cut-off of 110; sensitivity 76%, and specificity 57.32%, and the TIMI score an AUC of 0.599 (95% CI: 0.520–0.678) with a cut-off of 2.5; sensitivity 62% and specificity 52.32%.

Table 1: Comparative Analysis of Patients with and without In-Hospital Complications

Factor	Complications + (n=50)	Complications - (n=743)	p-value
Mean Age (years)	69.4 ± 12.6	60.1 ± 12.0	<0.001
Age > 65 years, n (%)	33 (66.0)	252 (33.9)	<0.001
Hypertension, n (%)	39 (78.0)	414 (55.7)	0.002
Diabetes, n (%)	30 (60.0)	306 (41.2)	0.009
Heart Rate (bpm)	102.4 ± 31.0	81.6 ± 15.5	<0.001
Respiratory Rate (c/min)	21.4 ± 7.3	16.6 ± 2.7	<0.001
Blood Glucose (mmol/l)	10.3 ± 5.0	8.4 ± 4.4	0.005
Creatinine (μmol/l)	119.2 ± 94.0	87.4 ± 69.0	0.002
ACTION ICU Score (mean)	9.0 ± 3.3	4.2 ± 1.9	<0.001
GRACE Score (mean)	141.2 ± 36.9	102.7 ± 35.0	<0.001
TIMI Score (mean)	3.0 ± 2.5	2.5 ± 1.4	0.016

At the six-month follow-up, 16% of the overall cohort (n=127) had experienced at least one Major Adverse Cardiovascular Event (MACE). Table 2 illustrates the variables that significantly influenced the occurrence of major adverse cardiovascular events at the six-month follow-up.

ROC curve analysis for predicting 6-month MACE showed that while all scores had

statistically significant predictive value, their overall accuracy was moderate compared to short-term predictions (Fig 3).

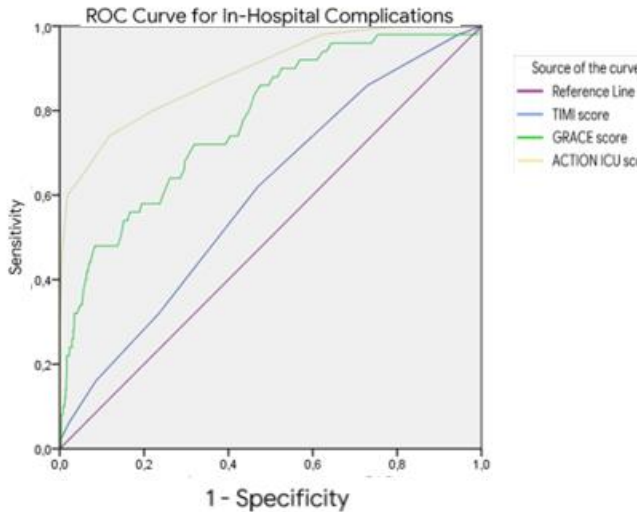


Figure 2: ROC Curves comparing the predictive accuracy of ACTION ICU, GRACE, and TIMI scores for in-hospital complications

The GRACE score performed slightly better for this long-term endpoint with an AUC of 0.707 (IC95% [0,659-0,756]) with a cut-off 114.5; sensitivity 62.7%, specificity 64.91%. The ACTION ICU score showed an AUC of 0.643 (IC95% [0,591-0,695]) with a cut-off 4.5 a sensitivity of 59.8%, and a specificity of 60.2%, and the TIMI score had an AUC of 0.624 (IC95% [0,576-0,672]). With a cut-off of 2.5, the sensitivity was 62%, and the specificity was 52.3%.

DISCUSSION

The aim of our study was to evaluate the prognostic value of the ACTION ICU score by comparing it against established baselines (GRACE and TIMI) in predicting ED complications and 6-month Major Adverse Cardiovascular Events (MACE) among patients presenting with non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS).

Table 2: Comparative analysis of factors associated with 6-month MACE

Factor	MACE +	MACE -	p-value
	(n=127)	(n=666)	
Mean Age (years)	64.6 ± 10.8	60.6 ± 11.7	<0.001
Male Gender, n (%)	88 (69.3)	201 (30)	<0.001
Heart Rate (bpm)	89.7 ± 24.1	81.7 ± 15.7	<0.001
Oxygen Saturation (SpO2 %)	96.4 ± 5.4	97.6 ± 2.1	<0.001
Negative T waves, n (%)	16 (12.6)	79 (12)	0.03
ST Amplitude (mm)	0.85 ± 0.8	0.5 ± 0.4	<0.001
ACTION ICU Score (mean)	5.5 ± 2.7	4.2 ± 2.8	<0.001
GRACE Score (mean)	127.9 ± 34.7	112.4 ± 33.8	<0.001
TIMI Score (mean)	3.0 ± 1.2	2.5 ± 1.4	<0.001

Our results demonstrate that while the GRACE score remains effective for predicting long-term MACE, the ACTION ICU score significantly outperforms both the GRACE and TIMI scores in identifying patients at high risk of immediate, in-hospital complications during their ED stay. With an Area Under the Curve (AUC) of 0.88 and an optimal cut-off value of 5.5, the ACTION ICU score presents as a highly sensitive and specific tool to guide acute triage and intensive care unit (ICU) admissions.

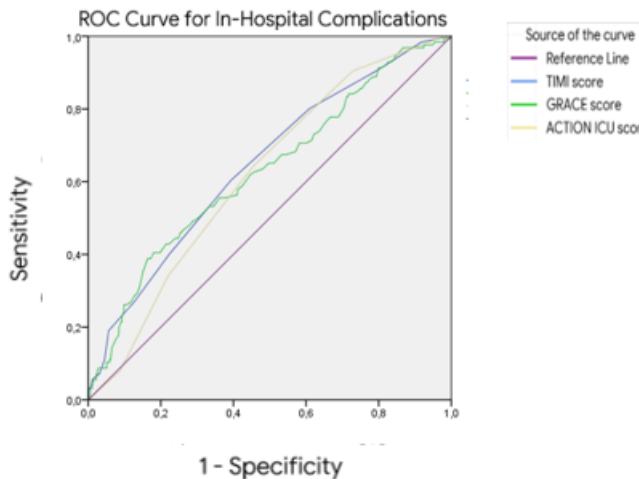


Figure 3: ROC Curves comparing the predictive accuracy of ACTION ICU, GRACE, and TIMI scores for Major Adverse Cardiovascular Events (MACE) at 6 months.

Baseline Demographic and Clinical Characteristics

Our cohort presented a mean age of 60 ± 12 years with a male predominance, which is comparable to data from the SCAAR (Swedish Coronary Angiography and Angioplasty Registry) registry (8). In comparison, data from an Egyptian registry reported a mean age of 62.6 years with a sex ratio of 1.17 (9). These metrics are consistent with a 2017 study conducted in our department, which reported a mean age of 61 years and a sex ratio of 1.46 (10). Conversely, Western populations typically present at an older age; statistics from the American Heart Association indicate the mean age for a first myocardial infarction is 65.6 years for men and 72 years for women (11). This earlier onset in our population may reflect different genetic predispositions or earlier exposure to unmanaged cardiovascular risk factors, notably hypertension, diabetes and smoking.

The high prevalence of hypertension in our study (57.1%) is consistent with international data. An analysis of the TIMI trials encompassing over 15,000 patients revealed an incidence of hypertension exceeding 70% among those with

coronary syndromes, while the SCAAR registry in Sweden observed hypertension in 63% of patients (8). Physiologically, chronic hypertension accelerates atherosclerosis through endothelial microtrauma and increased low-density lipoprotein (LDL) permeability, thereby increasing the vulnerability of coronary plaques (12).

During the initial ED management, 6.3% of our patients developed complications, the most frequent being acute pulmonary edema (3.5%). This complication rate is lower than some historical cohorts, such as the MOSCA-FRAIL study (13), which may be attributed to our exclusion of patients presenting initially with cardiogenic shock or cardiac arrest, as our goal was to evaluate initially stable patients requiring triage.

The central finding of our study is the superior performance of the ACTION ICU score in predicting these acute in-hospital events. With an AUC of 0.88, the score demonstrated excellent discriminatory power. This finding strongly corroborates recent international literature. A large Chinese cohort of 4,012 NSTEMI patients similarly reported the ACTION ICU score as the most accurate predictor of in-hospital mortality, with an AUC of 0.931 (14). Furthermore, a German study of 1,002 NSTEMI patients found the ACTION ICU score to outperform the GRACE model (AUC 0.87 vs. 0.84, respectively; $p=0.018$) for predicting in-hospital mortality (15).

In our analysis, a cut-off score of 5.5 provided a sensitivity of 80% and a specificity of 77.39%. This is clinically relevant. In the original derivation study by Fanaroff et al.(5), the score was designed to identify patients who genuinely required ICU care versus those who could be safely managed in step-down units. By demonstrating a high Negative Predictive Value (98.29%), our data suggests that an ACTION ICU score < 5.5 can reliably identify patients at low risk of acute deterioration, potentially

preventing unnecessary ICU admissions and optimizing resource allocation in constrained healthcare environments.

The GRACE score (AUC 0.77) and TIMI score (AUC 0.59) were less effective for immediate risk prediction. This is unsurprising, as the TIMI score was initially designed to predict events up to 14 days post-admission (16) while the GRACE score was primarily validated for in-hospital and 6-month mortality rather than acute procedural or hemodynamic complications in the immediate hours following ED presentation (17).

At the six-month follow-up, 16% of patients experienced MACE. For this long-term endpoint, the GRACE score demonstrated superior predictive performance (AUC 0.707) compared to ACTION ICU (AUC 0.643) and TIMI (AUC 0.624).

This validates the current European Society of Cardiology guidelines, which recommend the GRACE score (specifically GRACE 2.0) for long-term risk stratification (17).

Strengths and Limitations

This study benefits from a large, prospective data collection methodology over a nine-year period, allowing for a precise objective evaluation of NSTEMI-ACS epidemiology in an ED setting. Furthermore, conducting the study in a hospital without an integrated cardiology department necessitated meticulous clinical triage and prolonged ED observation, providing highly accurate data on acute in-hospital complications. However, we acknowledge several critical limitations. First, comparing the ACTION ICU score to the GRACE and TIMI scores introduces a comparability bias, as these tools were not designed for the same chronological endpoints or clinical purposes. Second, while baseline characteristics significantly differed between the complication + and complication- groups (Table 1), this does not constitute a true confounding bias. Instead, these differences naturally reflect the expected clinical predictors of acute events,

many of which are already partially integrated into the scoring systems being evaluated. Third, patient selection limits generalizability, as excluding patients with initial complications or missing angiographic data creates a selection bias. Finally, the retrospective monocentric design, reliance on telephone follow-ups, and the 2016 transition to high-sensitivity troponin assays carry inherent risks of reporting and methodological biases.

Clinical implications and perspectives

Our findings advocate for a dual-score strategy in the emergency department. While the GRACE score remains the gold standard for defining the long-term therapeutic strategy and timing of revascularization, the ACTION ICU score should be systematically integrated into the immediate triage process for NSTEMI-ACS patients. Implementing the ACTION ICU score in ED protocols could safely reduce unwarranted ICU admissions, thereby decreasing healthcare costs and freeing critical beds without additional risk to the patient particularly vital strategy in developing countries. . Prospective multicenter studies are strictly warranted to validate a triage algorithm utilizing this score before clinical implementation.

Non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) account for a substantial burden of cardiovascular hospitalizations, requiring precise risk stratification to optimize emergency department triage. This study demonstrates that while the GRACE score remains a robust tool for predicting long-term (6-month) Major Adverse Cardiovascular Events (MACE), the ACTION ICU offers superior accuracy for identifying immediate, in-hospital complications at the emergency department.

Specifically, the ACTION ICU score achieved an Area Under the Curve (AUC) of 0.88, significantly outperforming the GRACE (AUC:0.77) and TIMI (AUC:0.59). At an

optimal cut-off of 5.5, ACTION ICU score provided high sensitivity (80%) and specificity (77.39%), coupled with an excellent negative predictive value (98.29%), making it a highly reliable tool to rule out the need for immediate intensive care. These findings suggest that the ACTION ICU score can effectively guide emergency physicians in rationalizing intensive care unit admissions. Given the limitations of our retrospective design and potential population disparities, prospective multicenter validation is essential before integrating this score into routine clinical protocols.

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