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Original Article

Validation of TIMI and CADILLAC Risk Scores Along with Other Variables in Predicting In-Hospital Mortality in Patients with STEMI Undergoing Primary Percutaneous Coronary Intervention

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Abstract

Objectives: Risk stratification in ST-elevation myocardial infarction (STEMI) is critical for predicting clinical outcomes and guiding treatment strategies. This study aims to evaluate the validity of the TIMI and CADILLAC risk scores in predicting in-hospital mortality in a Pakistani population undergoing primary percutaneous coronary intervention (PPCI).

Methodology: This cross-sectional study included all patients presenting to the emergency department of RIC with STEMI who underwent PPCI. The TIMI and CADILLAC risk scores were calculated, along with other key determinants of mortality. The primary endpoint was all cause in-hospital mortality.

Results: A total of 1,029 patients were included in the study. The presence of specific risk factors at presentation significantly increased the incidence of in-hospital mortality. These risk factors included ventricular arrhythmias (VT/VF) (OR 12.697, 95% CI 3.7-42.7), cardiogenic shock (OR 17.2, 95% CI 7.98-37.10), left ventricular failure (OR 11.64, 95% CI 5.1-26.6), and complete heart block (CHB) (OR 5.9, 95% CI 2.3-15.4). Diabetic patients (OR 2.19, 95% CI 1.116-4.318) and smokers (OR 0.314, 95% CI 0.121-0.815) were also at higher risk, along with females, who demonstrated increased mortality compared to males. The TIMI and CADILLAC risk scores had areas under the curve (AUC) of 0.729 and 0.701, respectively, indicating that both models were fair in predicting in-hospital mortality.

Conclusion: This study demonstrates that while the TIMI and CADILLAC risk scores provide moderate predictive value in the Pakistani population, their utility may be limited. The findings underscore the need for the development of new, region-specific risk models to improve the prediction of in-hospital mortality in STEMI patients undergoing PPCI.

Keywords: STEMI, Primary PCI, TIMI, CADILLAC

INTRODUCTION

Coronary heart disease (CHD) remains the leading cause of morbidity and mortality globally, with ST-elevation myocardial infarction (STEMI) contributing to over 15% of deaths annually [1]. Together, coronary artery disease and acute coronary syndrome (ACS) account for nearly 7 million deaths each year. While the incidence of STEMI has declined in developed nations, thanks to improved healthcare systems and public health interventions, rates continue to rise in developing regions such as South Asia, parts of Latin America, and Eastern Europe. ACS is a particularly significant cause of mortality in the Asia-Pacific region, contributing to nearly half of the global disease burden [1,2].

Over the past two decades, the management of STEMI has evolved dramatically with the broader availability of primary percutaneous coronary intervention (PPCI) and timely coronary revascularization. These advancements have contributed to significant reductions in STEMI-related morbidity and mortality. For instance, PPCI has been associated with a 37% reduction in the odds of 30-day mortality when compared to in-hospital fibrinolytic therapy [3,4].

Risk stratification in STEMI is crucial for optimizing treatment and ensuring that resource-intensive strategies are applied where they offer the greatest clinical benefit. This is particularly important in developing countries, where healthcare resources are often limited, and cardiovascular disease burden is disproportionately high. The Thrombolysis in Myocardial Infarction (TIMI) risk score is a widely used bedside tool designed to stratify STEMI patients eligible for reperfusion based on their mortality risk. Initially developed to predict mortality within one month to one year post-STEMI, the TIMI score is now also applied to predict short-term, in-hospital mortality [5]. Similarly, the CADILLAC risk score offers valuable prognostic insights, identifying high-risk STEMI patients. However, both risk scores were predominantly developed using data from Western populations [6].

The objective of this study is to identify the clinical and angiographic predictors of in-hospital mortality among patients with STEMI treated with PPCI. Previous studies have compared these risk scores in Western populations, but there is limited data on their performance in other populations. Our study aims not only to assess the applicability of these risk scores in our patient population but also to compare their individual parameters. This will help determine the validity of these scores in our setting and enhance risk stratification for patients in our region.

METHODOLOGY

Study Design: This cross-sectional study was conducted at the Rawalpindi Institute of Cardiology over a period of six months, from April 2022 to October 2022. The design aimed to provide a snapshot of the clinical outcomes associated with primary percutaneous coronary intervention (PPCI) in patients with ST-elevation myocardial infarction (STEMI) during this timeframe. The study was structured to collect data on various clinical, procedural, and outcome-related variables to assess their relationships and potential impact on in-hospital mortality.

Setting: The study was carried out at the Rawalpindi Institute of Cardiology, a specialized medical facility known for its expertise in cardiology and cardiac interventions. The institute follows rigorous standards and protocols for patient care and data management. The study adhered to these protocols to ensure the accuracy and reliability of the collected data. The setting provided a comprehensive environment for evaluating the outcomes of PPCI, given its established infrastructure and expertise in handling STEMI cases.

Participants: The study population consisted of patients of all age groups who were diagnosed with ST-elevation myocardial infarction (STEMI) and were undergoing primary percutaneous coronary intervention (PPCI) at the Rawalpindi Institute of Cardiology.

- **Inclusion criteria:** The study included patients diagnosed with ST-elevation myocardial infarction (STEMI), confirmed through clinical assessment and diagnostic testing, who underwent primary percutaneous coronary intervention (PPCI) as part of the standard treatment protocol at the Rawalpindi Institute of Cardiology. This inclusion criterion ensured that the focus was on evaluating the outcomes of PPCI in a consistent and defined patient population.
- **Exclusion criteria:** Patients with a prior history of coronary artery bypass grafting (CABG) were excluded to avoid confounding effects related to previous cardiac surgeries. This criterion was set

to ensure a more homogeneous study group and to isolate the impact of PPCI on the outcomes of interest.

Data Sources/Measurement: Data collection in this study was conducted through a combination of patient interviews and a review of medical records. Demographic profiles, including age, gender, and comorbidities, were gathered through direct patient interaction and electronic medical records, ensuring comprehensive data for each participant. Clinical variables such as vital signs, including blood pressure and heart rate, were documented at the time of admission. Angiographic reports provided detailed insights into the procedural aspects of primary percutaneous coronary intervention (PPCI), including angiographic findings, complications during the procedure, and technical details of the intervention. Additionally, hospital records were meticulously reviewed to document critical outcomes, such as mortality and major adverse cardiac events (MACE), which occurred during the hospital stay. These sources of data provided a holistic view of each patient's condition and allowed for accurate outcome analysis.

Bias: To ensure the reliability and validity of the findings, several measures were implemented to minimize bias throughout the study. The use of clear inclusion and exclusion criteria, such as excluding patients with a prior history of coronary artery bypass grafting (CABG), helped to define a consistent patient population. Standardized data collection procedures were followed, ensuring uniformity in how variables were measured and recorded. Ethical approval was obtained from the hospital's ethical committee before initiating the study, and written informed consent was acquired from all patients, which safeguarded patient autonomy and ensured data accuracy. By adhering to these rigorous methods, the study aimed to reduce potential sources of bias and maintain the integrity of the data.

Quantitative Variables: Several key quantitative variables were analyzed to understand their relationship with patient outcomes. These included age, the duration of chest pain before hospital admission, and the door-to-balloon time. For each of these variables, the mean and standard deviations were calculated to provide an understanding of the central tendencies and dispersion within the study population. In addition, independent sample t-tests were performed to assess whether there were statistically significant differences in these variables between patients who survived and those who experienced mortality. This helped to identify which quantitative factors might have the greatest impact on patient outcomes.

Statistical Methods: Data analysis was performed using SPSS version 26, a widely recognized statistical software package. The analysis began with frequency analysis for qualitative variables, such as gender, comorbidities (e.g., diabetes, hypertension), and angiographic findings, to summarize the distribution of these variables in the study population. Chi-square tests were employed to determine the association between these qualitative variables and in-hospital mortality, identifying which factors were most strongly linked to adverse outcomes.

For variables that were significantly associated with mortality, odds ratios were calculated to quantify the strength of these associations. This provided a clearer understanding of the risk factors for mortality among patients undergoing PPCI. Furthermore, receiver operating characteristic (ROC) curve analysis was conducted to evaluate the sensitivity of the TIMI and CADILLAC risk scores in predicting in-hospital mortality. This analysis assessed the ability of these scores to correctly identify patients at higher risk of death. Statistical significance was set at a p-value of less than 0.05, ensuring that the results were robust and that any observed associations were unlikely to have occurred by chance.

RESULTS

Participants: A total of 1,029 patients diagnosed with ST-elevation myocardial infarction (STEMI) were included in this study. Of these, 856 (83.2%) were males and 173 (16.8%) were females, reflecting the higher prevalence of STEMI in males. The mean age of the study population was 55 ± 10 years. Patients who underwent primary percutaneous coronary intervention (PPCI) at the Rawalpindi Institute of Cardiology during the study period were included.

Outcome Data: The in-hospital mortality rate in this cohort was significantly influenced by several clinical factors. The mean age of patients who died during their hospital stay was 60 ± 13.2 years, while the mean age of survivors was 55 ± 10.63 years (p=0.046). The duration of chest pain and door-to-balloon time

did not show significant associations with mortality, with p-values of 0.421 and 0.341, respectively.

Patients with diabetes had a higher mortality rate (5.4%, p=0.020), and smokers also demonstrated a significant association with mortality (1.4%, p=0.012). Interestingly, hypertension, despite being prevalent in 44% of the cohort, did not have a statistically significant impact on in-hospital death (p=0.626). Additionally, patients with LVF (p<0.001), cardiogenic shock (p<0.001), tachycardia with heart rates greater than 100 bpm (p=0.002), and those requiring temporary pacing due to complete heart block (p<0.001) had significantly higher mortality rates.

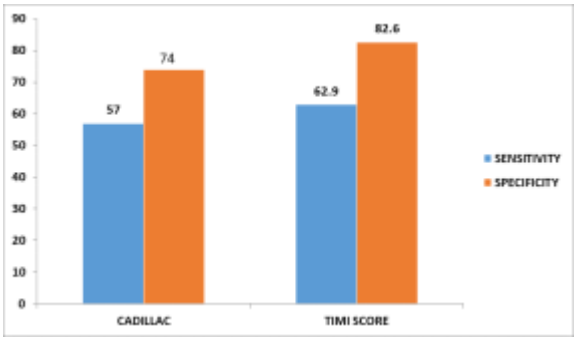
Table 1: demonstrates baseline and clinical characteristics of patients associated with mortality

	Total	Survival Status		P value
		Dead	Alive	
Gender				
Male	856 (83.2%)	22 (2.6%)	834 (97.4%)	0.001
Female	173 (16.8%)	13 (7.5%)	160 (92.5%)	
Age Mean ± SD	1029 (100%)	60 ±13.2	55±10.63	0.046
Duration of chest pain in hours	1029 (100%)	6.2±4.7	5.1±4.4	0.421
Door to balloon time (minutes)	1029 (100%)	58±23	62±26	0.341
Diabetes	316 (30.7%)	17 (5.4%)	299 (94.6%)	0.200
Hypertension	453 (44%)	14 (3.1%)	439 (96.9%)	0.626
Smoker	350 (34%)	5 (1.4%)	345 (98.6%)	0.012
Family History	19 (1.4%)	0 (0%)	19 (100%)	0.409
Obesity	6 (0.6%)	0 (0%)	6 (100%)	0.645
Previous history of IHD	78 (7.6%)	5 (6.4%)	73 (93.6%)	0.127
Left ventricular dysfunction	43 (4.2%)	10 (23.3%)	33 (76.7%)	<0.001
Cardiogenic shock	46 (4.5%)	13 (28.3%)	33 (71.7%)	<0.001
Tachycardia (HR>100 bpm)	90 (8.7%)	8 (8.9%)	82 (91.1%)	0.002
Complete heart block	43 (4.2%)	6 (14%)	37 (86%)	<0.001
Type of MI				
Anterior	516 (50.1%)	23 (4.5%)	493 (95.5%)	0.251
Inferior	497 (48%)	13 (2.6%)	484 (97.4%)	
High Lateral	14 (1.4%)	0 (0%)	14 (100%)	
Posterior	3 (0.3%)	0 (0%)	3 (100%)	
Ejection fraction <30%	57 (5.5%)	8 (14%)	49 (86%)	<0.001

Table 2: demonstrates various angiographic findings associated with mortality

	Total	Survival Status		P value
		Dead	Alive	
Number of vessels involved				
Single vessel	480 (46.4%)	12 (2.5%)	468 (97.5%)	0.236
Double vessel	342 (33.2%)	6 (1.8%)	326 (98.2%)	
Triple vessels	207 (20.1%)	7 (3.4%)	200 (96.6%)	
Stent thrombosis	32 (3.1%)	5 (15.6%)	27 (84.4%)	<0.001
Coronary dissection	12 (1.2%)	2 (16.7%)	10 (83.3%)	0.011
Coronary perforation	2 (0.2%)	0 (0%)	2 (100%)	0.791
Ventricular arrhythmias	14 (1.4%)	4 (28.6%)	10 (71.4%)	<0.001
Intra-aortic balloon pump used	15 (1.5%)	5 (33.3%)	10 (66.7%)	<0.001
Slow flow	301 (29.3%)	13 (4.3%)	288 (95.7%)	0.296
Treatment				
Stent	746 (72.5%)	21 (2.8%)	725 (97.2%)	0.163
Plain old balloon angioplasty (POBA) and thrombus aspiration	18 (1.8%)	5 (27.8%)	13 (72.2%)	
POBA	109 (10.6%)	7 (6.4%)	102 (93.6%)	
Drug coted balloon	91 (8.8%)	2 (2.2%)	89 (97.8%)	
Future revascularization				
Percutaneous coronary intervention	174 (17%)	4 (2.3%)	170 (97.7%)	0.016
Coronary artery bypass grafting	82 (8%)	4 (4.9%)	78 (95.1%)	
Med treatment	727 (70.7%)	25 (3.4%)	702 (96.6%)	
Myocardial perfusion imaging stress for residual disease	37 (3.6%)	0 (0%)	37 (100%)	

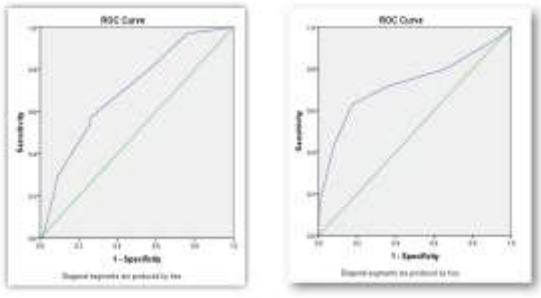
Figure 1: showing sensitivity and specificity of both risk scores



Main Results: The independent sample t-test revealed that while the duration of chest pain and door-to-balloon time were not significantly associated with mortality, patient age played a critical role, with older patients having a higher likelihood of death. Patients presenting with LVF and cardiogenic shock had some of the highest in-hospital mortality rates at 23.3% and 28.3%, respectively.

Additionally, patients who developed ventricular arrhythmias (ventricular tachycardia or ventricular fibrillation) were at a significantly higher risk of death (OR 12.697, 95% CI 3.7-42.7), while those with cardiogenic shock had an OR of 17.2 (95% CI 7.98-37.10), and those with LVF had an OR of 11.64 (95% CI 5.1-26.6). Patients requiring temporary pacing for complete heart block were also at elevated risk, with an OR of 5.9 (95% CI 2.3-15.4). Female patients and those with diabetes or a smoking history also had higher odds of mortality compared to the rest of the population (OR 2.19, 95% CI 1.116-4.318 and OR 0.314, 95% CI 0.121-0.815, respectively).

Figure 2: showing ROC curve analysis of both CADILLAC and TIMI risk scores



Area under the curve (AUC) of CADILLAC = 0.701, TIMI = 0.729

On angiography, 46.6% of patients had single-vessel coronary artery disease (SVCAD), and among those who had stent thrombosis (3.1%) or coronary dissection (1.2%), both complications had a significant association with mortality ($p<0.001$ and $p=0.011$, respectively). The use of intra-aortic balloon pumps (IABP) was associated with a mortality rate of 33.3% in the 15 patients who required this intervention.

Risk Score Analysis: ROC curve analysis was performed to evaluate the predictive sensitivity of the CADILLAC and TIMI risk scores for in-hospital mortality. The area under the curve (AUC) for the CADILLAC score was 0.701 (95% CI 0.618-0.784, $p=0.000$), and for the TIMI score, it was 0.729 (95% CI 0.622-0.836, $p=0.000$), indicating that both scores are fair predictors of in-hospital mortality. A CADILLAC score greater than 4.5 had a sensitivity of 57% and a specificity of 74%, while a TIMI score greater than 3.5 had a sensitivity of 62.9% and a specificity of 82.6% for predicting mortality during hospital stay.

DISCUSSION

In our study, we identified several risk factors associated with in-hospital mortality that are not always included in existing risk scoring systems. Notably, female patients exhibited significantly higher mortality rates post-primary PCI compared to males, a finding consistent with prior studies. This gender difference may be attributed to less aggressive treatment options and a higher burden of comorbidities in females [7]. Age also emerged as a strong predictor, with patients over 60 years showing a significant association with mortality. This aligns with data showing that patients over 65 represent 60% of ACS hospitalizations [8].

Diabetes and smoking were significantly associated with higher mortality rates, whereas hypertension, although part of the TIMI risk score, was not. Interestingly, we found that the type of myocardial infarction (MI), whether anterior or inferior, did not significantly affect mortality outcomes. Tachycardia, defined as a heart rate greater than 100 beats per minute, is a well-established predictor of mortality included in the TIMI score. However, our study also found that patients with complete heart block faced a higher risk of in-hospital death, an association not captured by current scoring systems.

Cardiogenic shock (CS) remains one of the most significant causes of mortality in STEMI patients, even with advancements in reperfusion therapies like PPCI.

In our study, 28.3% of patients with CS died, a lower rate than international studies, likely due to delayed access to PPCI facilities in our population [9]. Although CADILLAC and TIMI scores account for various risk factors, we found that certain variables, such as an ejection fraction (EF) below 30%, carried a significant mortality risk. In contrast, CADILLAC considers EF under 40% as a critical marker, and neither scoring system includes EF values below 30% [9]. Additionally, we observed that multi-vessel disease, while considered a negative prognostic factor in CADILLAC, was not significantly associated with mortality in our cohort.

Stent thrombosis was another significant predictor of mortality in our study, with 15.6% of affected patients dying in the hospital. Previous clinical trials have reported mortality rates as high as 50% for early stent thrombosis [10]. Life-threatening arrhythmias (LTA), a known complication of PPCI, occurred in 28.6% of our study population, also contributing to a higher mortality rate. Despite their impact, neither stent thrombosis nor LTA is included in most risk scores, underscoring a gap in current risk stratification methods.

Our comparison of the TIMI and CADILLAC scores revealed that both are fair predictors of in-hospital mortality, though TIMI slightly outperformed CADILLAC in our cohort. TIMI demonstrated a sensitivity of 62.9% and specificity of 82.6%, figures slightly lower than the 88% sensitivity reported in earlier studies involving European and American populations [11]. This difference may reflect the unique cardiovascular risk factors present in our Asian population, including genetic predispositions, dietary habits, and lifestyle choices like physical activity, and smoking [12].

The CADILLAC score, while considered effective in predicting short- and long-term mortality in patients undergoing PPCI, had a lower predictive accuracy in our population, with an AUC of 0.72. This is lower than the AUC of 0.82 reported in other studies, suggesting that the score may be less applicable in high-risk patients or in non-Western populations [13]. Importantly, CADILLAC does not account for key variables that significantly impacted mortality in our study, including gender, heart rate, cardiogenic shock, arrhythmias, and stent thrombosis [14]. Similarly, the TIMI score does not include low EF, complete heart block, or stent thrombosis, all of which were significant predictors in our population [15].

Given that no single risk score comprehensively accounts for all the predictors identified in our study, there is a clear need for the development of more tailored scoring systems, particularly for Asian populations. Such models should include additional variables like arrhythmias, gender differences, stent thrombosis, and EF levels below 30%, to improve the accuracy of in-hospital mortality predictions.

Limitations

This study was conducted at a single center, and the patients were only followed until hospital discharge. As a result, our findings may not fully capture long-term outcomes or mortality trends. To better assess and validate risk scores for long-term prognosis, future studies should involve multi-center trials with extended follow-up periods. This would provide more robust data for refining predictive models and tailoring them to diverse populations.

CONCLUSION

In our study population, both the TIMI and CADILLAC scores were fair predictors of in-hospital mortality for patients undergoing primary PCI for STEMI, with the TIMI score demonstrating slightly better sensitivity and specificity. Key individual predictors of mortality included female gender, comorbidities such as diabetes and smoking, as well as the development of arrhythmias, complete heart block, cardiogenic shock, stent thrombosis, coronary dissection, and low ejection fraction. Notably, no existing risk score incorporates all of these critical variables, underscoring the need for the development of more comprehensive scoring systems. Such models should include these predictors to improve risk stratification, particularly in patients of Asian ethnicity, who may have distinct risk profiles when undergoing primary PCI for STEMI.

AUTHORS' CONTRIBUTION

AS, MK, AJ, SA, and MASA: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AS, MK, AJ, SA, and MASA: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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