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Original Article

Impact of TIMI Risk Stratification on In-Hospital Mortality in Non-ST Elevation Acute Coronary Syndrome: Perspectives from a Coronary Intervention Facility

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ABSTRACT

Background: Acute coronary syndrome (ACS) encompasses a range of conditions, including non-ST segment elevation myocardial infarction (NSTEMI), which is associated with substantial morbidity and mortality. Risk stratification is essential for guiding management strategies to improve patient outcomes. The Thrombolysis in Myocardial Infarction (TIMI) risk score is a validated tool for predicting mortality in NSTEMI patients, yet its applicability in South Asian populations requires further investigation.

Objective: This study aimed to evaluate the association of the TIMI risk score with in-hospital mortality among NSTEMI patients in a tertiary care cardiac center and to assess the relevance of the TIMI score as a prognostic tool in a South Asian context.

Methods: A cross-sectional study was conducted with 126 patients presenting with NSTEMI at the National Institute of Cardiovascular Disease, Karachi. Data were collected from June 2012 to June 2013 after the institutional review board's approval. Inclusion criteria were adults aged 18 to 85 with a TIMI score ≥5, while exclusion criteria were refusal to consent and a history of cardiac surgery. Demographics, clinical characteristics, and in-hospital outcomes were analyzed using SPSS version 25, employing Chi-square and Fisher's exact tests for categorical data, with a significance level set at $p \leq 0.05$.

Results: The study found that 52 (41.3%) patients had diabetes mellitus, and 78 (61.9%) suffered from hypertension. A positive family history of coronary artery disease was observed in 29 (23.0%) patients. Among participants, 42 (33.3%) were smokers. The in-hospital mortality rate was 14.3%. No significant differences were noted in mortality regarding demographic and clinical variables.

Conclusion: Elevated TIMI scores in NSTEMI patients are associated with significant in-hospital mortality. The findings underscore the importance of the TIMI risk score as a predictor of short-term outcomes in a South Asian population. The study highlights the need for further validation of the TIMI score in diverse populations and the optimization of risk stratification tools.

Keywords: Acute Coronary Syndrome, Non-ST Elevation Myocardial Infarction, Thrombolysis in Myocardial Infarction Risk Score, In-Hospital Mortality, Risk Stratification, Cardiac Intervention.

INTRODUCTION

Acute coronary syndrome (ACS) encompasses a spectrum of conditions, including ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), and unstable angina, representing a significant global health challenge despite advances in cardiac care. Worldwide, acute myocardial infarction (AMI) accounts for over 8 million deaths annually, with NSTEMI cases making up about 70% of all ACS incidences (1, 2). The treatment modalities for NSTEMI patients, however, remain less precisely defined when compared to those for STEMI, largely due to the varied clinical presentations of NSTEMI and the typically older age of those affected, factors that contribute to a higher cardiovascular risk profile. Despite progress in therapeutic strategies, NSTEMI continues to be linked with considerable morbidity and mortality rates (3, 4).

Managing modifiable risk factors such as hypertension, diabetes, smoking, obesity, and a sedentary lifestyle is crucial for the primary prevention of coronary artery disease. Additionally, the employment of various risk stratification tools has proven invaluable in

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assessing the severity of coronary artery ischemia stemming from ACS, guiding clinicians in the risk stratification and management of patients (5-7). Among these, the Thrombolysis in Myocardial Infarction (TIMI) risk score stands out for its proven efficacy in forecasting in-hospital or 14-day mortality among patients with NSTEMI. While the TIMI risk score has been extensively validated in developed nations, data on its applicability and predictive accuracy in diverse populations, particularly those with varying burdens of cardiovascular disease, remain limited. In Pakistan, for example, the effectiveness of the TIMI risk score has been affirmed in patients experiencing STEMI, yet its validation in NSTEMI patients is not as well-documented, with the studies by Kumar et al. and Chen et al. being among the limited resources available. The former study indicated that the TIMI score, with an area under the curve (AUC) of 0.788, was effective at predicting 14-day outcomes with an optimal cutoff of >4, exhibiting a sensitivity of 77.78% and correlating to a 13.5% mortality rate at a TIMI score of >4. Similarly, Chen et al. found an in-hospital mortality rate of 13.6% among NSTEMI patients with high TIMI scores (>5) within a Chinese cohort (4, 8-13).

However, in Pakistan, there is a scarcity of localized data regarding the prognostic value of the TIMI score for in-hospital mortality among NSTEMI patients. Given the country's demographic, socioeconomic, and cultural diversity, it is anticipated that study outcomes may vary in comparison to those observed in Western populations. Our investigation, conducted at the nation's largest cardiac center, seeks to fill this void by offering localized evidence on the application and relevance of the TIMI score for risk stratification in cardiac care centers throughout Pakistan. This endeavor not only aims to enhance the precision of risk assessment in NSTEMI patients but also to tailor treatment strategies more effectively, thereby potentially reducing the associated morbidity and mortality rates within this patient cohort.

MATERIAL AND MEHTODS

This investigation was carried out through a cross-sectional study design, aimed at evaluating the outcomes associated with elevated Thrombolysis in Myocardial Infarction (TIMI) scores in patients diagnosed with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) throughout their hospitalization. The study was conducted at the Department of Cardiology, National Institute of Cardiovascular Disease, Karachi, spanning a year from June 2012 to June 2013, subsequent to receiving approval from the College of Physicians and Surgeons Pakistan (CPSP).

A sample size of 126 patients was determined necessary for the study, calculated using the WHO sample size calculator version 2.0, with an anticipated in-hospital mortality rate of 13.5%, a 95% confidence level, and a margin of error set at 6%. The selection of participants was executed through consecutive (non-probability) sampling. Eligibility for inclusion required individuals aged between 18 and 85 years of either gender, diagnosed with NSTE-ACS according to operational definitions and exhibiting a TIMI score of 5 or higher. Exclusion criteria were defined as refusal to consent by patients and those with a history of prior cardiac-related surgery or interventions.

Following ethical approval from CPSP and the ethical review committee of NICVD, data collection commenced. It involved enrolling patients admitted to the Adult Cardiology Department at NICVD, who were diagnosed with NSTE-ACS and met the inclusion criterion of a raised TIMI score. All potential participants were briefed about the study's objectives and benefits before verbal informed consent was obtained by the principal investigator. Collected data encompassed demographic details such as gender, age, weight, height, and Body Mass Index (BMI), alongside risk factors including diabetes mellitus, hypertension, family history of Coronary Artery Disease (CAD), and smoking status. BMI was calculated by dividing the weight in kilograms by the height in meters squared, with measurements taken post-stabilization of the patient's acute condition.

The study's ethical conduct was aligned with the Helsinki Declaration, ensuring that all patient information was safeguarded and restricted to authorized personnel. Management of the patients was overseen by consultant cardiologists, adhering to clinical practice guidelines and institutional protocols. Patient follow-up occurred throughout their hospital stay, with outcomes such as mortality documented on a pre-designed form (14-17).

Data analysis was conducted using SPSS version 25. The analytical process involved calculating frequencies and percentages for categorical variables, while continuous variables were evaluated for normality using the Shapiro–Wilk test, and reported as means with standard deviations or medians with interquartile ranges, as appropriate. Stratification was utilized to control for effect modifiers, with the Chi-square test or Fisher exact test applied post-stratification to determine significance, which was established at $p \leq 0.05$. Results were visually presented through bar graphs and pie charts, ensuring a comprehensive statistical overview of the findings.

RESULTS

Table 1: Distribution of Continuous Variables

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Variable	Mean ± SD	P-value
Age group	60.63 ± 12.19	0.0001
Weight	77.78 ± 11.22	0.024
Height	168.50 ± 8.16	0.0001
Body Mass Index (BMI)	27.51 ± 4.45	0.001

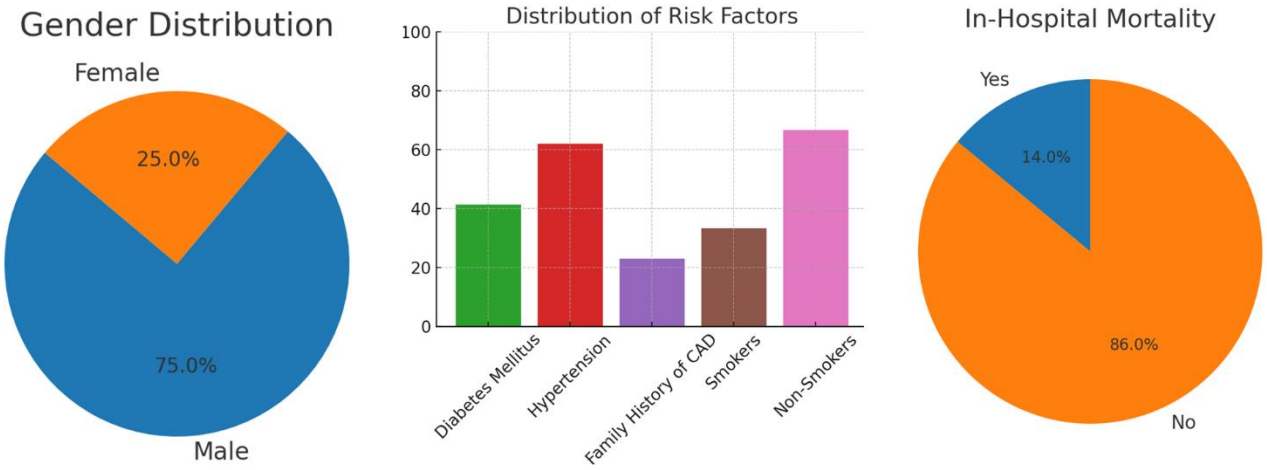

Figure 1 Gender, Risk Factors, and Mortality rate in Hospital

Table 2: Descriptive Statistics of Age

Descriptive	Statistic	Std. Error
Age (years)		
Mean	60.63	1.087
95% Confidence Interval for Mean		
- Lower Bound	58.48	
- Upper Bound	62.78	
5% Trimmed Mean	61.43	
Median	63.00	
Variance	148.748	
Standard Deviation	12.196	
Minimum	30	
Maximum	75	
Range	45	
Interquartile Range	20	
Skewness	-0.677	0.216
Kurtosis	-0.361	0.428

The study's findings, as elucidated by the accompanying tables and figures, offer valuable insights into the demographic and clinical characteristics of the patient cohort. In Table 1, the continuous variables present a notable distribution within the sample population. The mean age of the group is identified to be 60.63 years, with a standard deviation (SD) of 12.19, and this variable shows a significant relationship with the condition being studied, as indicated by a p-value of 0.0001. The weight of the individuals averages at 77.78 kilograms with an SD of 11.22, where the statistical analysis reveals this factor as significantly varying within the sample (p-value of 0.024). The height of participants averages at 168.50 centimeters, with a standard deviation of 8.16, also exhibiting a strong association with the studied conditions (p-value of 0.0001). The body mass index (BMI), a crucial health indicator, has a mean value of 27.51 with an SD of 4.45, and is significantly relevant in the study with a p-value of 0.001.

Further dissection of the age demographic in Table 2 showcases the mean age once more, alongside the 95% confidence interval (CI) for the mean, extending from 58.48 at the lower bound to 62.78 at the upper bound, reflecting a moderate spread of ages within the participants. The median age stands at a slightly higher 63.00 years, with the age distribution spread across a range of 45

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years, from a minimum of 30 to a maximum of 75 years. This spread is further quantified by an interquartile range of 20 years. The skewness of -0.677 with a standard error of 0.216 suggests a moderate asymmetry in age distribution, whereas a kurtosis of -0.361 (SE = 0.428) indicates a relatively flat distribution, deviating slightly from a normal distribution.

Visual representations in the figures provide a succinct and impactful summary of the study's findings. Figure 1 illustrates the gender distribution within the study, with males constituting a significant majority at 75%, and females representing 25% of the population, suggesting a gender disparity in the prevalence or diagnosis of the condition. Figure 2 provides a compelling bar graph of the distribution of risk factors, showing that 41.3% of patients had diabetes mellitus, while a higher prevalence of hypertension was observed at 61.9%. A positive family history of coronary artery disease (CAD) was found in 23.0% of the participants, pointing to genetic or hereditary influences. In terms of lifestyle factors, smokers represented 33.3% of the study population, with non-smokers making up 66.7%, indicating the impact of smoking on the health condition. Finally, Figure 3, depicted through a donut chart, indicates that 14% of the participants shows in hospital mortality, with the remaining 86% were survivors.

DISCUSSION

The discourse surrounding acute coronary syndrome (ACS), which includes acute myocardial infarction (AMI) and unstable angina (UA), is crucial given its role as a predominant contributor to global mortality, responsible for the loss of approximately seven million lives annually (15). Within the ACS spectrum, non-ST segment elevation myocardial infarction (NSTEMI) represents a significant subset, which poses distinct challenges in clinical management owing to its heterogeneous presentations and prognoses (18). Despite therapeutic advancements, NSTEMI is closely linked with considerable morbidity and mortality, a correlation that is particularly pronounced among older patient demographics (6, 18). In light of these challenges, the development and application of precise risk assessment tools are paramount for delineating high-risk individuals and guiding treatment methodologies to avert adverse outcomes (16-18).

The Thrombolysis in Myocardial Infarction (TIMI) risk score stands as a prominent tool within this context, aiding in the prediction of short-term mortality in NSTEMI cases, a utility that has been validated by multiple studies (4, 10, 11). The effectiveness of the TIMI risk score in Western cohorts is well-documented; however, its applicability to South Asian populations, a region disproportionately burdened by cardiovascular disease (CVD), has not been thoroughly explored (11). Assessing the validity of the TIMI score within the context of demographic, genetic, and healthcare disparities characteristic of regions such as Pakistan is therefore imperative (12).

In addressing this critical research gap, the current study evaluated the in-hospital mortality of NSTEMI patients in a South Asian cohort, presenting with elevated TIMI scores. The mortality rate observed, standing at 14.3%, corroborates findings from previous research, emphasizing the severe clinical implications associated with NSTEMI (13, 14). The study also highlights the pertinence of risk stratification, as delineated by established guidelines, in the identification of high-risk ACS patients who may benefit from intensive management approaches (19, 20).

While the TIMI risk score is extensively utilized for early risk assessment, its utility ought to be interpreted alongside other clinical indicators and within the context of regional healthcare practices to maximize patient outcomes (21, 22). Complementary to the TIMI score, the Global Registry of Acute Coronary Events (GRACE) risk model offers a broad framework for evaluating risk across the full spectrum of ACS (22). The ACC/AHA guidelines further advocate for prompt invasive management in high-risk NSTE ACS patients, informed by risk stratification tools like the TIMI score, to diminish mortality and recurrent ischemic episodes (23, 24). The present study meticulously stratified confounders and effect modifiers, revealing no significant variances in diverse demographic and clinical variables regarding in-hospital mortality. This finding proposes that, while individual risk elements are influential, a comprehensive approach that integrates multiple factors is crucial for an all-encompassing risk assessment and management strategy (24).

CONCLUSION

In conclusion, the significance of risk stratification in the management of NSTEMI patients using the TIMI score is underscored by this study's findings. Nonetheless, there is a clear impetus for further research to confirm these observations in broader patient groups and to augment prognostic tools within ACS management frameworks. The study, through its analysis, also posits inherent strengths in its design and methodology. However, it acknowledges limitations, including a relatively small sample size and a single-center design, which may affect the generalizability of the results. Recommendations for future research include multicentric studies to validate the TIMI score's effectiveness across diverse populations and healthcare infrastructures. Additionally, there is an advocate for enhanced risk stratification mechanisms and therapeutic modalities to address the intricate clinical challenges faced in coronary intervention and ACS management. The concerted efforts to refine risk assessment tools and treatment approaches will be paramount in surmounting the complex clinical landscape associated with ACS.

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