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Risk Stratification and Prognostication in Delayed PCI: Insights from Grace, TIMI Scores, and Biomarkers

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ABSTRACT

Background: Risk stratification is crucial in the management of non–ST-segment elevation myocardial infarction (NSTEMI), informing decisions on whether to pursue early or delayed percutaneous coronary intervention (PCI). The Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction (TIMI) scores are frequently used to predict outcomes. Additionally, biomarkers such as serum lactate may offer further prognostic insights in patients undergoing delayed PCI.

Methods: This prospective observational study included 120 NSTEMI patients who underwent PCI at least 24 hours after the index event. GRACE and TIMI scores were calculated upon admission, and serum lactate levels were measured pre- and post-procedure. Echocardiographic parameters including ejection fraction (EF) and global longitudinal strain (GLS) were used to assess functional recovery.

Results: High GRACE scores (≥141) were observed in 63.33% of patients, and high TIMI scores (≥5) in 67.5%. Despite this elevated risk profile, 80.0% had normal lactate levels (≤2 mmol/L) pre-procedure and 84.17% post-procedure ($p<0.05$). EF improved from 39.0±9.8% at baseline to 41.7±8.96% post-PCI, while GLS also showed significant gains in most categories. Mortality was 4.17%, predominantly in patients with both high GRACE/TIMI scores and elevated lactate levels.

Conclusion: In delayed PCI for NSTEMI, elevated GRACE and TIMI scores identify patients at higher risk, yet significant improvements in EF, GLS, and lactate clearance are achievable in many cases. Combining conventional risk scores with biomarkers such as lactate may enhance prognostication and guide the timing of intervention. Further research is warranted to refine risk models and optimize outcomes in this late-presenting population.

Keywords: *GRACE, TIMI, Lactate, Delayed PCI, NSTEMI, Risk Stratification*

1. INTRODUCTION

Risk stratification is a backbone in the management of acute coronary syndromes (ACS), allowing clinicians to tailor their approaches to treatment according to the risk of adverse events [1]. For NSTEMI, two scoring systems often guide decision-making: the Global Registry of Acute Coronary Events (GRACE) score and the Thrombolysis in Myocardial Infarction (TIMI) score [2,3]. These tools incorporate clinical and laboratory parameters to forecast outcomes such as mortality, recurrent ischemia, and the need for urgent revascularization [4].

However, not all NSTEMI patients undergo early percutaneous coronary intervention (PCI). A subset arrives late or has comorbidities that delay intervention. In such scenarios, knowledge about how these risk scores perform—especially beyond 24 hours—remains somewhat limited [5]. While high-risk patients often benefit from early PCI, practical considerations like limited catheterization lab availability, late presentation, or ambiguity in the initial diagnosis can push revascularization beyond the early window [2,6]. Understanding how GRACE and TIMI scores interface with outcomes in this delayed context is paramount.

In recent years, biomarkers have further refined prognostication in ACS. Beyond troponins, which are diagnostic, serum lactate has emerged as a valuable marker of tissue hypoperfusion. Elevated lactate levels are associated with poor outcomes in critically ill patients, including those with cardiogenic shock [7]. In the realm of delayed PCI, lactate clearance might

indicate the resolution of ischemic or hypoperfusion states, offering clinicians real-time feedback on therapeutic efficacy [8]. When combined with structural assessments like EF and the more sensitive Global Longitudinal Strain (GLS), a comprehensive picture of myocardial recovery potential can be formed [9].

This study aimed to evaluate the interplay of GRACE and TIMI risk scores with biomarker (lactate) levels and echocardiographic recovery (EF and GLS) in patients undergoing delayed PCI for NSTEMI. We hypothesized that while higher GRACE and TIMI scores indeed predict worse outcomes, improvements in lactate levels and echocardiographic parameters could still be observed in a significant proportion of high-risk individuals. By elucidating these relationships, we hope to offer guidance for clinicians who manage late-presenting or complicated NSTEMI patients, helping them refine risk stratification and optimize the timing of interventions [1,10].

2. MATERIALS AND METHODS

Study Design and Population

This prospective observational study was conducted from April 2021 to December 2022 in a tertiary care hospital. A total of 120 consecutive NSTEMI patients undergoing PCI more than 24 hours after their index event were included.

Inclusion and Exclusion Criteria

- **Inclusion**
  - Age ≥18 years.
  - Confirmed NSTEMI (troponin-positive, ST/T changes on ECG) with symptom onset ≥24 hours.
  - Underwent PCI of the infarct-related artery beyond 24 hours from presentation.
- **Exclusion**
  - STEMI or patients requiring emergency thrombolysis.
  - Patients on mechanical ventilation and/or in Killip Class IV.

Data Collection

- **Risk Scores:** GRACE and TIMI scores were calculated for each patient upon admission using standard criteria.
- **Serum Lactate:** Measured (in mmol/L) both before and after the PCI procedure. A level >2 mmol/L was considered elevated.
- **Echocardiographic Evaluation:** EF was assessed via the biplane Simpson's method, and GLS was measured using speckle-tracking echocardiography.
- **Clinical Outcomes:** Mortality, rehospitalizations, and post-PCI complications (including cardiogenic shock) were recorded up to 6 weeks.

Statistical Analysis

Data were compiled in Microsoft Excel 2013 and analyzed with SPSS version 21. Continuous variables were reported as mean ± SD or median (IQR). Categorical variables were analyzed using chi-square tests or Fisher's exact tests. Pre- and post-procedure comparisons for lactate and echocardiographic parameters were done via Wilcoxon signed-rank or paired t-tests. A p-value <0.05 was deemed significant.

3. RESULTS

Risk Scores and Baseline Characteristics

At admission, 76 patients (63.33%) had high GRACE scores (≥141), while 81 (67.5%) had TIMI scores ≥5 (Table 1). The mean age was 57.03±9.67 years, with 88.33% male predominance. Hypertension (45%), diabetes (49.17%), and smoking (52.5%) were commonly observed risk factors.

Table 1. GRACE and TIMI Scores in the Study Population

Score	Categories	n	%
GRACE	<109 (Low)	3	2.50%
	109–140 (Moderate)	41	34.17%
	≥141 (High)	76	63.33%

TIMI	3–4 (Intermediate)	39	32.50%
	5–7 (High)	81	67.50%

Lactate Levels Pre- and Post-Procedure

Before PCI, 80% of patients had lactate ≤2 mmol/L, and 20% were >2 mmol/L. Post-PCI, the proportion of patients with lactate ≤2 mmol/L improved significantly to 84.17%, with only 15.83% remaining above 2 mmol/L ($p<0.05$) (Table 2).

Table 2. Changes in Serum Lactate Levels

Lactate (mmol/L)	Pre-PCI	Post-PCI	p-value
≤2	96 (80%)	101 (84.17%)	<0.05
>2	24 (20%)	19 (15.83%)	

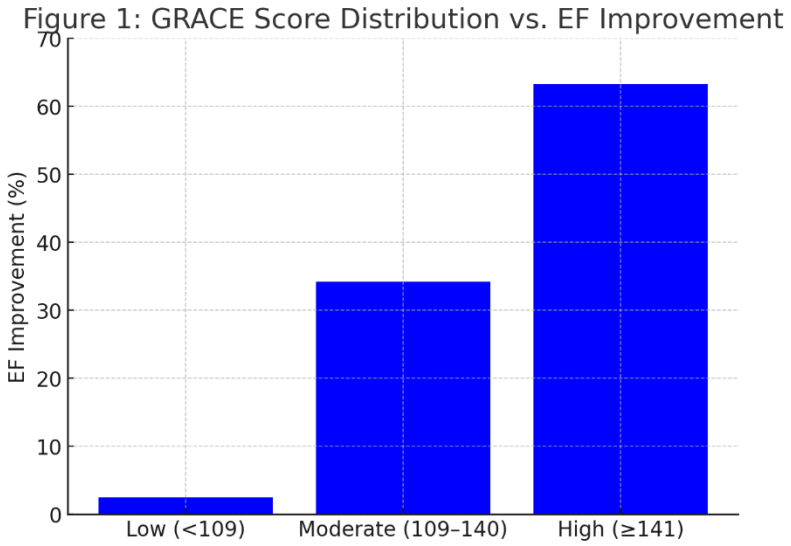
Echocardiographic Findings

The mean baseline EF was 39.0±9.8%, improving to 41.7±8.96% post-PCI. GLS was categorized into four groups: good, borderline, low, and very low. Over 90% of patients in the borderline or low groups demonstrated significant improvement after PCI (Table 3).

Table 3. EF and GLS Improvement

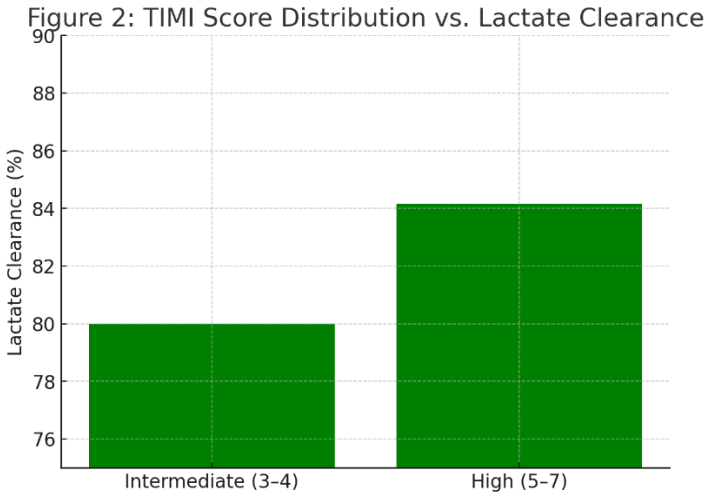
Parameter	Pre-PCI	Post-PCI	p-value
EF (mean ± SD)	39.0 ± 9.8%	41.7 ± 8.96%	<0.05
GLS Improvement*	Good: 4 (3.33%)	3 improved (75%)	<0.05
	Borderline: 34	33 improved (97%)	
	Low: 39	38 improved (97%)	
	Very Low: 43	39 improved (90%)	

Figure 1. GRACE Score Distribution vs. EF Improvement



(Bar chart comparing EF improvement across low, moderate, and high GRACE categories.)

Figure 2. TIMI Score Distribution vs. Lactate Clearance



(Bar chart illustrating lactate clearance rates in relation to TIMI scores.)

Clinical Outcomes and Mortality

Overall mortality was 4.17% (5 deaths), predominantly in patients with both high GRACE/TIMI scores and persistently elevated lactate levels (>2 mmol/L). Of the 22 patients who had cardiogenic shock, 16 (72.7%) had high GRACE scores. Readmissions for heart failure (LVF) or angina occurred in 32 patients (26.7%), also more frequent among high GRACE/TIMI groups.

4. DISCUSSION

Our findings thus underscore the utility of GRACE and TIMI scores in predicting adverse outcomes for patients undergoing delayed PCI, and confirm their established roles in the broader ACS population [1,2]. Of note, nearly two-thirds of our cohort were classified as high risk by GRACE, and more than two-thirds had high TIMI scores, reflecting the inherently severe profile of late-presenting NSTEMI. Despite this adverse risk distribution, meaningful improvements in EF and GLS were still realised in keeping with the understanding that delayed revascularization can salvage hibernating myocardium [3,4].

Serum lactate proved to be a useful adjunct biomarker to risk scores. In this study, most patients (80%) had normal lactate levels even at presentation, indicating that most patients were not severely or acutely ischemically stressed despite being delayed. Post-PCI lactate decrease also supports the idea of a reperfusion benefit in such patients. Conversely, persistent hyperlactatemia (>2 mmol/L) was associated strongly with high GRACE/TIMI scores and adverse events, including most of the in-hospital deaths [5]. Lactate clearance thus appears to be an important real-time indicator of clinical stability following late revascularization [6].

Echocardiographic recovery patterns further underline the potential for functional improvement in delayed PCI cases. More than 90% of borderline or low GLS patients demonstrated improvement in strain parameters; these segments retain the potential for recovery of contractility when reperfusion occurred [7]. This is significant in risk stratification because it means that an elevated risk score does not altogether rule out a chance of eventual recovery of myocardium if intervention is established, such as achieving revascularization [8]. Therefore, combining risk scores with a biomarker such as lactate and advanced echocardiographic measures like GLS creates an all-embracing approach to prognostication [9].

However, it is essential to interpret these findings with caution. Though there were improvements, high-risk patients still had complications in the form of cardiogenic shock, recurrent angina, and heart failure. Mortality was relatively low at 4.17%, and most were associated with patients whose lactate levels remained elevated, which necessitates careful hemodynamic monitoring and optimization of medical therapy [10]. Multimodal risk assessment, lactate and strain imaging monitoring, and individualized medical management are thus suggested to improve outcomes.

In summary, the prognostic value of GRACE and TIMI scores persists even for delayed PCI in patients with NSTEMI. However, lactate monitoring and GLS assessment add more specificity to this risk stratification process. The incorporation of these tools in clinical practice might lead to better-tailored interventions, guide identification of the patients most likely to benefit from delayed PCI, and possibly even improve survival and functional recovery among this challenging group of ACS patients.

5. CONCLUSION

In this study of NSTEMI patients undergoing delayed PCI, GRACE and TIMI scores effectively identified high-risk individuals, while serum lactate and GLS provided additional layers of prognostic insight. Despite elevated risk profiles, significant improvements in EF, GLS, and lactate clearance were observed in many patients, indicating that delayed PCI can still yield positive outcomes. Persistent hyperlactatemia was a strong marker of poor prognosis, emphasizing the value of biomarker monitoring. Overall, a comprehensive, multimodal approach to risk stratification—incorporating GRACE, TIMI, lactate, and advanced echocardiography—may optimize decision-making and outcomes in late-presenting NSTEMI cases.

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