Correlation of In-Hospital Grace Risk Score with Severity of Coronary Artery Disease by Syntax Score in Patients with Non-St Segment Elevation Myocardial Infarction (NSTEMI)

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ABSTRACT

Background: The GRACE score predicts NSTEMI risk, while the SYNTAX score assesses coronary complexity. This study evaluated their association in NSTEMI patients.
Methods: This prospective observational diagnostic-correlation cohort included 120 consecutive adults with NSTEMI undergoing coronary angiography within 48 hours at a tertiary cardiac center in Pakistan. GRACE scores were calculated at admission, while two interventional cardiologists independently assessed SYNTAX scores. Pearson correlation, ROC analysis, and multivariable logistic regression evaluated associations and discrimination for SYNTAX ≥23 and ≥33. SYNTAX inter-rater reliability was assessed using ICC and Bland-Altman analysis.
Results: The mean age was 60.9 ± 10.6 years, and 91 (75.8%) participants were male. The GRACE score demonstrated a strong positive correlation with the SYNTAX score (r = 0.781, 95% CI 0.699-0.842; p < 0.001). ROC analysis showed excellent discrimination for SYNTAX ≥23 (area under the curve [AUC] 0.890, 95% CI 0.828-0.952; p < 0.001), with an optimal GRACE cutoff of 107 yielding 83.2% sensitivity and 84.2% specificity. For SYNTAX ≥33, the AUC was 0.798 (95% CI 0.716-0.879; p < 0.001), with an optimal GRACE cutoff of 126, providing 69.6% sensitivity and 81.3% specificity. After multivariable adjustment, each 10-point increase in GRACE score was independently associated with higher odds of SYNTAX ≥23 (adjusted odds ratio [aOR] 2.88, 95% CI 1.57-5.29; p < 0.001) and SYNTAX ≥33 (aOR 1.86, 95% CI 1.38-2.50; p < 0.001). Inter-rater agreement for SYNTAX scoring was excellent (ICC 0.933, 95% CI 0.905-0.952).
Conclusion: In NSTEMI patients, higher GRACE scores were associated with greater coronary complexity and effectively identified SYNTAX ≥23, supporting pre-angiographic risk stratification, pending external validation.

Keywords: NSTEMI; GRACE score; SYNTAX score; coronary artery disease; risk stratification; ROC curve; angiographic complexity.

INTRODUCTION

A seizure is an abrupt alteration of cerebral function resulting Acute coronary syndromes (ACS), including non-ST-segment elevation myocardial infarction (NSTEMI), are a major cause of cardiovascular morbidity and mortality globally and demand prompt risk-stratified management.[1] Clinical risk scores, such as the GRACE (Global Registry of Acute Coronary Events) model, estimate short-term (in-hospital and 6-month) mortality and guide decisions about the timing of invasive strategies in NSTEMI.[2] Conversely, angiographic scoring systems, such as the SYNTAX score, quantify anatomical complexity and are widely used to guide the mode of revascularization (PCI vs. CABG) and to predict procedural risk.[3,4]

Across international and regional studies, the association between bedside clinical risk (GRACE) and angiographic complexity (SYNTAX) is consistently positive but heterogeneous in magnitude, with reported correlation coefficients ranging from small/moderate (r ≈ 0.23–0.508) in larger registries[5–7], to very large (r ≈ 0.64–0.87) in some smaller or selected samples[8,9]. Larger and more recent cohorts also showed the reproducible but modest predictive performance of GRACE for severe coronary anatomy.[10] However, available studies differ in patient selection (ACS vs. NSTEMI only), sample size, timing of angiography, SYNTAX thresholds, and local practice patterns. Furthermore, few studies have reported rigorous inter-rater reliability for SYNTAX scoring or prospective reproducibility checks for GRACE calculation.[7]Because the GRACE score is calculated at the bedside and the SYNTAX score requires invasive angiography, demonstrating a reliable correlation would allow for earlier risk-based triage and targeted heart-team planning before angiography in NSTEMI patients, thereby improving efficiency and potentially outcomes. Existing evidence points to a consistent but heterogeneous association that requires replication in prospectively collected, well-characterized NSTEMI cohorts with explicit quality control for score calculations and blinded angiographic reading. This study will therefore prospectively evaluate the in-hospital GRACE–SYNTAX relationship in a contemporary NSTEMI population and seeks to confirm whether

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GRACE-based triage can reliably optimize healthcare utilization and stratification strategies to improve patient outcomes and inform future multicenter validation and pathway implementation.

METHODOLOGY

This was a prospective, observational, diagnostic-correlation cohort study conducted at the catheterization laboratory of Faisalabad Institute of Cardiology, Faisalabad, Pakistan, from January 1, 2021, to December 31, 2021. Ethical approval for this study was obtained from the Ethical Review Committee of Faisalabad Institute of Cardiology, Faisalabad (Approval No. 06/DME/FIC/FSD; dated December 23, 2020). The sample size was calculated to be 120 patients (to account for 10-20% exclusions/missing data) with a minimum required sample size of 107 based on an expected correlation coefficient of 0.36 (α = 0.05, power = 95%) using Fisher's z-transformation. A consecutive sampling technique was employed to enroll patients meeting the ESC criteria for NSTEMI. Inclusion criteria included adult patients (≥18 years) diagnosed with NSTEMI, undergoing coronary angiography within 48 hours of index hospitalization, and providing written informed consent. Exclusion criteria encompassed prior CABG, severe contrast allergy, hemodynamic instability, inadequate angiographic views, or inability to provide consent. All participants provided informed consent following Institutional Review Board approval. The GRACE score was calculated upon admission using the MDCalc tool, and a 10% random sample of GRACE calculations were rechecked by a second clinician for reproducibility. SYNTAX scores were computed by two independent interventional cardiologists, with discrepancies >5 points or >10% resolved by a third expert. Data were collected via a prespecified CRF, with quality control measures including double data entry and periodic audits.

Statistical Analysis

Data analysis was performed using SPSS v27.0 (IBM). Two-sided tests were used, with α = 0.05. Continuous variables were examined for normality using histograms and the Shapiro–Wilk test; descriptive statistics (mean ± SD or median (IQR)) were reported accordingly. Primary analysis involved correlation between GRACE and SYNTAX scores, with Pearson's correlation coefficient (r) and 95% CI. Secondary analyses included ROC curve analysis for diagnostic performance, with AUC, sensitivity, specificity, and predictive values calculated for SYNTAX thresholds. Multivariable linear regression was used to assess the impact of GRACE score on SYNTAX, adjusting for confounders. Inter-rater reliability for SYNTAX scoring was assessed using the intraclass correlation coefficient (ICC) with 95% CI. Sensitivity analyses included subgroup evaluations by age, diabetes status, sex, and time to angiography. Statistical significance was considered for $p < 0.05$.

RESULTS

A total of 120 consecutive patients with NSTEMI who underwent coronary angiography were included in the analysis. The mean age was 60.9 ± 10.6 years, and 91 (75.8%) were male. Based on the SYNTAX category, 19 (15.8%) had low complexity, 45 (37.5%) had intermediate complexity, and 56 (46.6%) had high complexity. Patients with higher SYNTAX categories were significantly older, had higher rates of diabetes and hypertension, and had significantly higher GRACE scores. **Table 1** summarizes baseline characteristics by SYNTAX group (SYNTAX < 23 vs. SYNTAX ≥ 23). Continuous variables are shown as mean ± SD or median (IQR) where appropriate; categorical variables are n (%). P-values compare groups using t-tests/Mann–Whitney and χ^2/Fisher exact tests as appropriate.

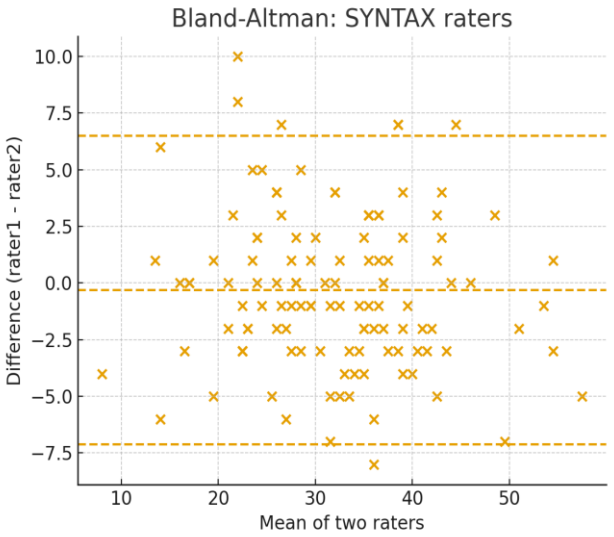
Table 1: Baseline characteristics by SYNTAX group.

Variable	SYNTAX <23	SYNTAX ≥23	p-value
Age, years	52.78 ± 8.59	62.33 ± 10.30	0.00
GRACE score	93.50 (IQR 19.50)	123.50 (IQR 32.75)	0.00
BMI, kg/m²	25.80 ± 5.44	26.99 ± 5.27	0.399
Systolic BP, mmHg	146.72 ± 16.92	134.39 ± 21.29	0.011
Heart rate, bpm	72.89 ± 19.92	85.20 ± 16.49	0.022
SYNTAX score	18.50 (IQR 4.75)	33.00 (IQR 10.00)	0.00
Male, n (%)	11 (61.1%)	80 (78.4%)	0.199
Diabetes mellitus, n (%)	6 (33.3%)	42 (41.2%)	0.715
Hypertension, n (%)	11 (61.1%)	61 (59.8%)	1.00
Current smoking, n (%)	7 (38.9%)	48 (47.1%)	0.469

IQR = Interquartile Range

As per the study protocol, inter-rater reliability for the SYNTAX score was assessed between the two primary independent cardiologists (on variables SYNTAX A and SYNTAX B) using a two-way mixed-effects model for absolute agreement. The analysis demonstrated excellent reliability, with an intraclass correlation coefficient (ICC) of 0.933 (95% CI 0.905-0.952, $p<0.001$), indicating excellent agreement. Bland–Altman analysis showed a mean difference of −0.31 (95% limits of agreement −7.11 to 6.49), indicating no substantial systematic bias between readers. The Bland–Altman plot is embedded below in **Figure 1**.

Figure 1: Bland–Altman plot for SYNTAX raters (A vs B).



We found a strong, positive, and statistically highly significant correlation between the GRACE Total Score and the SYNTAX Adjudicated Final Score (Pearson r = 0.78, p-value < 0.001, 95% CI for r = 0.70-0.84) **(Figure 2)**.

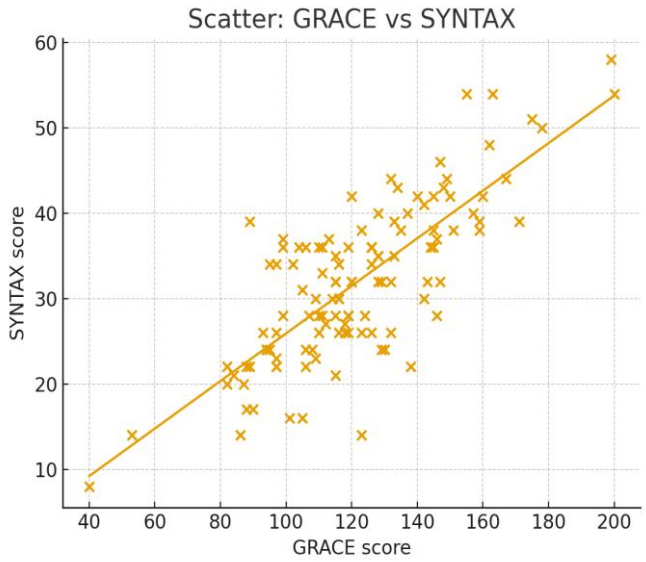
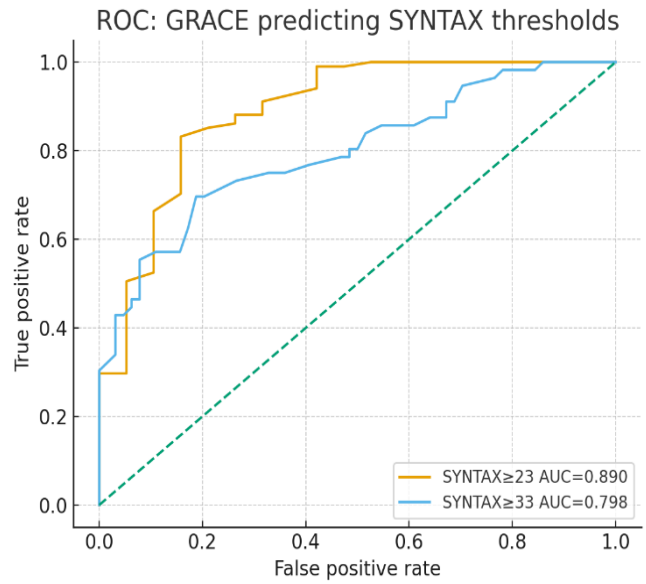


Figure 2: Scatter plot of GRACE vs SYNTAX with fitted regression line.

Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate the ability of the GRACE score to discriminate between patients with high and non-high anatomical complexity, using two common SYNTAX score thresholds: ≥23 and ≥33.

The GRACE score demonstrated excellent discriminatory power for identifying patients with a SYNTAX score of ≤ 23; the area under the ROC curve (AUC) was 0.890 (95% CI 0.828-0.952, p vs 0.5 < 0.001). The optimal GRACE score cut-off, determined by the Youden index, was 107. At this threshold, the sensitivity was 83.2% and the specificity was 84.2%. For predicting a SYNTAX score ≥33, the GRACE score demonstrated good discriminatory power. The area under the ROC curve (AUC) was 0.798 (95% CI 0.716-0.879, p vs 0.5 < 0.001). The optimal GRACE score cut-off, determined by the Youden index, was 126. At this threshold, the sensitivity was 69.6% and the specificity was 81.3% **(Figure 3)**.

Figure 3: ROC curves for GRACE predicting SYNTAX thresholds.



Linear regression (adjusted for age, sex, diabetes, hypertension, smoking, and BMI) indicated that GRACE (per 10-point increase) was independently associated with an increase of approximately 2.41 SYNTAX points **(Tables 2a and 2b)**.

Table 2a: Multivariable Logistic Regression for Predictors of SYNTAX Score ≥23.

Variable	Adjusted OR	95% CI	p-value
Intercept	9.05×10^{-7}	3.26×10^{-10} – 0.0025	0.0006
GRACE (per 10-point increase)	**2.88**	**1.57 – 5.29**	**0.0007**
Age (per year)	1.04	0.94 – 1.14	0.463
Male sex	2.25	0.49 – 10.42	0.299
Diabetes mellitus	1.04	0.23 – 4.66	0.958
Hypertension	0.83	0.19 – 3.53	0.799
Smoking (Former)	1.28	0.22 – 7.37	0.782
Smoking (Never)	**8.56**	**1.55 – 47.33**	**0.014**
Body Mass Index (per kg/m²)	1.03	0.90 – 1.19	0.642

OR = odds ratio; CI = confidence interval; BMI = body mass index.

Table 2b: Multivariable Logistic Regression for Predictors of SYNTAX Score ≥33.

Variable	Adjusted OR	95% CI	p-Value
Intercept (Constant)	0.0004	0.00001 – 0.027	<0.001
GRACE (per 10 points)	**1.86**	**1.38 – 2.50**	**<0.001**
Age (years)	1.01	0.96 – 1.07	0.71
Male sex	0.98	0.34 – 2.83	0.97
Diabetes mellitus	0.53	0.20 – 1.38	0.19
Hypertension	0.67	0.26 – 1.73	0.41
Smoking – Former	0.97	0.26 – 3.56	0.96
Smoking – Never	2.74	0.94 – 7.98	0.065
Body-mass index (kg/m²)	0.98	0.90 – 1.07	0.71

OR = odds ratio; CI = confidence interval; BMI = body mass index.

The strong positive correlation between GRACE and SYNTAX scores remained consistent and statistically significant across key subgroups (**Table 3**). Sensitivity analyses using the two raw rater SYNTAX scores produced similar results; the ICC between raters was high (~0.93).

Table 3: Subgroup correlations (age, diabetes, sex).

Variables		N	Spearman ρ	95%CI
Age	< 65 years	80	0.60	0.41-0.75
	> 65 years	40	0.74	0.52-0.87
Diabetes	Yes	48	0.68	0.42-0.85

	No	72	0.74	0.59-0.86
Gender	Male	91	0.69	0.52-0.81
	Female	29	0.82	0.60-0.92

DISCUSSION

Acute medical assessment of new-onset seizures in adults is In this prospective, NSTEMI-specific cohort of 120 consecutive patients, we observed a robust, positive association between the in-hospital GRACE score and angiographic complexity as measured by the total SYNTAX score. The primary correlation was strong (Pearson r = 0.78, 95% CI 0.70–0.84, p < 0.001), and the GRACE score showed excellent discrimination for anatomic complexity at conventional thresholds, area under the curve (AUC) 0.890 for SYNTAX ≥23 and AUC 0.798 for SYNTAX ≥33. The association remained statistically significant after multivariable adjustment [adjusted ORs (aOR) per 10-point GRACE increment: ≈2.9 for SYNTAX ≥23 and ≈1.9 for SYNTAX ≥33] and was supported by high inter-rater reliability for SYNTAX scoring (ICC 0.933).

Although our findings contrast sharply with the weak-to-moderate correlations (r = 0.23–0.508) reported in several large, international, and heterogeneous acute coronary syndrome (ACS) registries,[5–7] our results align with the upper range of associations reported in smaller, more focused, or regional single-center studies, such as those reported by Namazi et al. and Ali et al. in mixed ACS cohorts.[8,9] The literature review posited that heterogeneity in patient selection (mixed ACS vs. NSTEMI-only) and variable scoring reproducibility were key unresolved issues. Our study was designed to address these gaps directly. By restricting enrollment to a well-characterized, prospective NSTEMI-only cohort and enforcing rigorous, blinded SYNTAX scoring with proven excellent inter-rater reliability (ICC = 0.933), we likely minimized the measurement variance and population heterogeneity that may have attenuated the correlation in broader ACS studies.

The GRACE score aggregates age, hemodynamic status, markers of cardiac injury, and renal function, and thus captures multiple clinical dimensions that commonly track with a high atherosclerotic burden and more extensive or complex coronary anatomy.[17] Patients with advanced age, higher Killip class, hypotension/tachycardia, greater biomarker rise, and renal dysfunction are more likely to harbor multivessel and complex lesions that increase SYNTAX and the associated adverse outcomes.[13,14] However, GRACE remains a clinical mortality instrument rather than an anatomical score;[15] the strong correlation we observed likely reflects substantial overlap between clinical severity and lesion burden in our cohort rather than a direct mapping of individual clinical variables to specific lesion morphologies. The stronger correlation in this study may also reflect local case mix (high prevalence of complex disease), the NSTEMI-only design, and rigorous quality control for SYNTAX adjudication (pre-study calibration, blinded duplicate reads, and an adjudication plan).[18]

The clinical implications of our secondary findings are particularly noteworthy. The optimal GRACE score cut-off of 107 for predicting a SYNTAX score ≥23 yielded a sensitivity of 83.2% and a specificity of 84.2%. This discriminatory power is substantially greater than that reported by Doğan et al. and Rahmani et al., who found a sensitivity of 73.5% and a specificity of only 60% at a similar threshold.[19,5] Moreover, our AUC of 0.798 for predicting a SYNTAX score ≥33 markedly improves upon the modest AUC of 0.66 reported by Sofidis et al.[10] for the same high-complexity endpoint. This demonstrates that the GRACE score may serve not only as a prognostic tool for mortality but also as a potential diagnostic adjunct for anatomical severity in the NSTEMI population. After multivariable adjustment, the GRACE score remained a powerful independent predictor for both SYNTAX ≥23 (aOR 2.88 per 10-point increase) and SYNTAX ≥33 (aOR 1.86 per 10-point increase).[20]

This study has several strengths. Its prospective design, strict focus on an NSTEMI-only population, and pre-specified methodology for blinded, dual-reader SYNTAX scoring with high reported ICC directly address key limitations identified in the existing literature. We also confirmed the robustness of the primary correlation across pre-specified subgroups based on age, sex, and diabetes status.

Nonetheless, our study has important limitations. First, as a single-center study conducted at a tertiary cardiac referral hospital, our findings may not be generalizable to other settings, such as community hospitals or different healthcare systems with distinct referral patterns and patient demographics. This single-center context, as noted by Namazi et al.,[8] might contribute to the observed high correlation. Second, our sample size of 120 patients, while powered for the primary correlation analysis, provides less stable estimates for the multivariable logistic regression models, as evidenced by some wide confidence intervals.[21] Third, using SYNTAX as the anatomical endpoint has known limitations (it emphasizes morphological lesion features but does not capture some functional or microvascular elements relevant to prognosis). Finally, our empirically derived GRACE cut-points require external validation before use in clinical pathways; thresholds and operating characteristics may differ across populations and practice settings. These aspects should temper immediate changes in guideline recommendations.

Key next steps are external validation in larger, multicenter, and internationally diverse NSTEMI cohorts to (1) confirm the observed correlation magnitude, (2) validate GRACE cut-points for predicting high SYNTAX, and (3) evaluate whether GRACE-guided triage strategies (for example, accelerated transfer to PCI centers or pre-angiography heart-team notification) improve process measures and patient-centered outcomes in randomized or stepped-wedge implementation studies. Additionally, integrating GRACE with rapid bedside imaging (e.g., focused coronary CT or echocardiographic markers) or biomarkers might further improve pre-angiography discrimination and should be explored. Finally, formal decision-analytic modelling could quantify the resource and outcome trade-offs of GRACE-directed pathways in low-resource settings where cath lab capacity is limited.

CONCLUSION

We identified a strong, positive, and clinically significant correlation between the bedside in-hospital GRACE score and angiographic coronary complexity measured by the SYNTAX score. The GRACE score demonstrated excellent diagnostic accuracy for identifying patients with high anatomical disease burden, with a score ≥ 107 serving as a reliable threshold for predicting a SYNTAX score ≥ 23. These findings strongly support the use of the GRACE score as an immediate, non-invasive triage tool to enhance risk stratification, optimize resource allocation, and expedite heart-team planning before invasive assessment. The robust association observed in our well-characterized cohort warrants urgent multicenter validation to confirm its

generalizability and support its formal integration into regional and national NSTEMI clinical pathways.

Ethical Approval

Ethical approval for this study was obtained from the Ethical Review Committee of Faisalabad Institute of Cardiology, Faisalabad (Approval No. 06/DME/FIC/FSD; dated December 23, 2020). Written informed consent was obtained from all participants or their legal guardians prior to inclusion. All data were de-identified and stored in password-protected files accessible only to the investigators to ensure participant confidentiality.

Data Availability

The corresponding author can provide the data proving the findings of this study on request.

Author Contributions

Conceptualization: Tariq Saleem, Asifa Tariq
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Data Collection: Asifa Tariq, Muhammad Ahsan Fareed, Maham Riaz, Momina Arshad
Formal Analysis: Tariq Saleem, Muhammad Ayaz Arshad, Muhammad Sultan Bashir
Writing–Original Draft: Tariq Saleem, Asifa Tariq, Momina Arshad
Writing–Review & Editing: Muhammad Ayaz Arshad, Muhammad Sultan Bashir, Momina Arshad, All authors
All authors read and approved the final version of the manuscript.

Informed Consent

Written informed consent was obtained from all participants before enrollment in the study.

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Conflict of Interest

The authors declare no conflicts of interest regarding this manuscript.

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Declaration of AI-Assisted Language Editing

No AI used.

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