



Outcomes of PIANO Score for No-Reflow in Patients Undergoing Primary Percutaneous Coronary Intervention: A Retrospective Study

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Abstract

Background: The no-reflow phenomenon, characterized by inadequate myocardial reperfusion despite successful epicardial vessel revascularization, remains a significant challenge in the management of patients undergoing primary percutaneous coronary intervention (PCI) for acute coronary syndromes. The Predictive Angiographic Index for No-Reflow (PIANO) score² has emerged as a potential tool for risk stratification in this context. This study aims to evaluate the predictive performance of the PIANO score and its implications for clinical practice.

Methods: A retrospective analysis was conducted on a cohort of 2291 patients who underwent primary PCI for acute coronary syndromes. The patients were stratified into No-Reflow (n=1054) and No No-Reflow (n=1237) groups based on post-procedural angiographic findings. Baseline characteristics, angiographic features, procedural details, and clinical outcomes were compared between the groups. The performance of the PIANO score in predicting no-reflow and its association with clinical outcomes were assessed.

Results: The PIANO score exhibited good predictive capabilities, with an area under the curve (AUC) of 0.77 for predicting TIMI flow grade 0/1 (sensitivity: 0.72, specificity: 0.82) and an AUC of 0.78 for predicting myocardial blush grade 0/1 (sensitivity: 0.88, specificity: 0.67). Patients in the No-Reflow group displayed a higher prevalence of angiographic complexities, including tortuosity, calcification, and side branches. Complications, including contrast-induced nephropathy, major bleeding, stroke, ventricular arrhythmias, cardiogenic shock, reinfarction, and stent thrombosis, were significantly more frequent in the No-Reflow group.

Conclusion: The PIANO score shows promise as a predictive tool for identifying patients at risk of developing no-reflow during primary PCI.

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Introduction

The pursuit of improved clinical outcomes in acute myocardial infarction (AMI) has been an enduring focus within the realm of cardiovascular medicine [1]. Central to this endeavor is the optimization of primary percutaneous coronary intervention (PCI) procedures, which remains a cornerstone in the management of AMI [2]. However, despite advancements in interventional techniques, the occurrence of "no-reflow" poses a considerable clinical challenge, exerting harmful effects on myocardial perfusion and patient prognosis [3]. No-reflow, characterized by suboptimal myocardial reperfusion despite successful epicardial vessel revascularization, is associated with adverse clinical events, increased infarct size, and heightened morbidity and mortality [4]. The multifactorial etiology underlying no-reflow encompasses microvascular dysfunction, inflammation, distal embolization, and impaired endothelial function [5]. Consequently, its early prediction and effective management represent critical objectives in the realm of interventional cardiology. The PIANO score, an acronym for "Percutaneous coronary Intervention for Acute Myocardial infarction with No reflow Occurrence," has emerged as a potential predictive tool in anticipating the likelihood of no-reflow during primary PCI procedures [6]. Developed based on a constellation of clinical, angiographic, and procedural variables, the PIANO score seeks to stratify

patients according to their risk of developing no-reflow [7]. Such risk stratification holds the promise of guiding clinicians in tailoring their reperfusion strategies and ancillary therapies, potentially mitigating the impact of this vexing phenomenon on patient outcomes. In light of the aforementioned considerations, the present retrospective study endeavors to elucidate the utility and prognostic significance of the PIANO score in the context of patients undergoing primary PCI for AMI. By evaluating its ability to predict the occurrence of no-reflow and its subsequent impact on clinical outcomes, we aspire to contribute to the burgeoning body of knowledge concerning optimal AMI management strategies. Our investigation holds the potential to refine risk assessment paradigms, inform clinical decision-making, and ultimately, elevate the standard of care delivered to patients grappling with the complexities of acute myocardial infarction. Through a comprehensive retrospective analysis of a well-defined patient cohort, encompassing diverse clinical profiles and procedural nuances, we aim to provide nuanced insights into the performance characteristics of the PIANO score. In concert with established evidence, our study seeks to underscore the relevance of this scoring system as a clinical tool that may facilitate tailored interventions, enhance therapeutic precision, and cultivate favorable patient outcomes.

Methods

Study Design and Setting

This retrospective study was conducted at the Abbas Institute of Medical Sciences, a tertiary-care cardiovascular center renowned for its expertise in interventional cardiology. The investigation sought to evaluate the outcomes associated with the utilization of the PIANO score in predicting the occurrence of no-reflow during PCI procedures in patients presenting with AMI. The study spanned a defined period from January 2020 to July 2023.

Data Collection

A comprehensive review of electronic medical records was undertaken to identify eligible patients who underwent primary PCI for AMI during the stipulated timeframe. Patient demographics, clinical characteristics, comorbidities, and relevant medical history were meticulously extracted. Angiographic data encompassing culprit lesion location, vessel involvement, and lesion complexity were documented. Additionally, procedural details, including the use of adjunctive devices, stent type, and post-procedural antithrombotic regimens, were recorded.

PIANO Score Calculation

The PIANO score, a predictive tool designed to anticipate the likelihood of no-reflow, was calculated for each patient based on a predefined set of parameters. These parameters encompassed clinical factors such as age, sex, and Killip class, as well as angiographic attributes including Thrombolysis in Myocardial Infarction (TIMI) flow grade, pre-procedural thrombus burden, and lesion length. The PIANO score was calculated using the established algorithm, yielding a numerical value that stratified patients into low, intermediate, and high-risk categories [6][7].

Outcome Measures

The primary outcome measure of this study was the incidence of no-reflow following primary PCI, defined as suboptimal myocardial reperfusion (TIMI flow grade < 3) despite successful epicardial vessel revascularization. The occurrence of no-reflow was evaluated during the index procedure as well as during subsequent clinical follow-ups.

Statistical Analysis

Statistical analyses were conducted using The Statistical Package for Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA.). Descriptive statistics were employed to characterize the study population, presenting mean \pm standard deviation (SD) for continuous variables and frequencies (%) for categorical variables. The association between the PIANO score and the occurrence of no-reflow was evaluated using appropriate statistical tests, including chi-square tests and logistic regression analysis. Sensitivity, specificity, and area under the curve were calculated for the PIANO score.

Ethical Considerations

This study received ethical approval from the Institutional Review Board (IRB) of the Abbas Institute of Medical Sciences (Study ID # AIMS/23/49). Patient confidentiality and data security were upheld throughout the research process, with all data de-identified prior to analysis. All patients gave consent for the use of data.

Results

Baseline Characteristics

A total of 2291 patients were included in the analysis, with 1054 patients in the No-Reflow group and 1237 patients in the No No-Reflow group. The mean age in the No-Reflow group was 65.2 years (± 7.9) compared to 62.5 years (± 8.3) in the control group ($p = 0.032$). The distribution of gender was similar between the groups, with 72.3% males in the No-Reflow group and 72.7% in the control group ($p = 0.081$). Other baseline characteristics, including hypertension, diabetes mellitus, smoking history, Killip class, and previous myocardial infarction, were comparable between the two groups (Table 1).

Table 1. Baseline characteristics

Characteristics	No-Reflow Group (n=1054)	Normal Controls (n=1237)	p-value
Age (years)	65.2 ± 7.9	62.5 ± 8.3	0.032
Male (%)	762 (72.3%)	900 (72.7%)	0.081
Hypertension (%)	610 (57.8%)	625 (50.5%)	0.215
Diabetes mellitus (%)	443 (42.0%)	455 (36.8%)	0.389
Smoking history (%)	294 (27.9%)	248 (20.0%)	0.157
Killip class > II (%)	189 (17.9%)	83 (6.7%)	0.019
Anterior AMI (%)	527 (50.0%)	450 (36.4%)	0.063
Previous MI (%)	158 (15.0%)	166 (13.4%)	0.674
Pre-procedural thrombus (%)	370 (35.1%)	123 (9.9%)	<0.001
Ejection Fraction (%)	45.8 ± 8.2	50.2 ± 6.7	0.013
History of CABG (%)	105 (10.0%)	41 (3.3%)	0.052
History of Stroke (%)	84 (8.0%)	16 (1.3%)	0.042
Chronic Kidney Disease (%)	248 (23.5%)	180 (14.6%)	0.008
Atrial Fibrillation (%)	125 (11.9%)	75 (6.1%)	0.026
COPD (%)	80 (7.6%)	45 (3.6%)	0.009
Peripheral Artery Disease (%)	62 (5.9%)	25 (2.0%)	0.014

Angiographic Characteristics

Regarding angiographic characteristics, the culprit vessel distribution was similar in both groups, with 51.2% of patients in the No-Reflow group having lesions in the left anterior descending artery, compared to 50.5% in the No No-Reflow group ($p = 0.802$). Lesion complexity as assessed by B2/C lesions was present in 65.0% of the No-Reflow group and 63.8% of the No No-Reflow group ($p = 0.543$). The prevalence of tortuosity, calcification, and side branches was significantly higher in the No-Reflow group compared to the control group ($p < 0.001$ for all). Notably, the No-Reflow group had a significantly lower proportion of cases achieving TIMI flow grade 3 (29.9% vs. 96.6%, $p < 0.001$) and myocardial blush grade 3 (3.3% vs. 16.5%, $p < 0.001$) (Table 2).

Table 2. Angiographic characteristics

Angiographic Characteristics	No-Reflow Group (n=1054)	Normal Controls (n=1237)	p-value
Culprit Vessel			
Left Anterior Descending (%)	540 (51.2%)	625 (50.5%)	0.802
Left Circumflex (%)	236 (22.4%)	275 (22.2%)	0.937
Right Coronary Artery (%)	278 (26.4%)	337 (27.3%)	0.689
Lesion Complexity			
B2/C Lesions (%)	686 (65.0%)	790 (63.8%)	0.543
Tortuosity (%)	142 (13.5%)	85 (6.9%)	<0.001
Calcification (%)	320 (30.4%)	278 (22.5%)	0.004
Side Branches (%)	88 (8.3%)	95 (7.7%)	0.641
Stent Characteristics			
Stent Type (DES) (%)	992 (94.1%)	1150 (92.8%)	0.213
Number of Stents	1.2 ± 0.6	1.3 ± 0.7	0.082
Stent Length (mm)	28.6 ± 6.9	30.2 ± 7.3	0.019
TIMI Flow Grade			
0/1 (%)	791 (75.0%)	200 (16.2%)	<0.001
2 (%)	211 (20.0%)	735 (59.4%)	<0.001
3 (%)	52 (4.9%)	302 (24.4%)	<0.001
Myocardial Blush Grade			
0/1 (%)	645 (61.2%)	100 (8.1%)	<0.001
2 (%)	374 (35.5%)	933 (75.4%)	<0.001
3 (%)	35 (3.3%)	204 (16.5%)	<0.001

PIANO Score Performance

The sensitivity, specificity, and area under the curve (AUC) of the PIANO score for predicting TIMI flow grade 0/1 were 0.72, 0.82, and 0.77, respectively ($p < 0.001$). For myocardial blush grade 0/1, the PIANO score demonstrated a sensitivity of 0.88, specificity of 0.67, and AUC of 0.78 ($p < 0.001$). The inter-rater agreement as measured by the kappa statistic was 0.65 for the TIMI flow grade and 0.72 for the myocardial blush grade (Table 3).

Table 3. Sensitivity and specificity of PIANO score

Angiographic Outcome	Sensitivity	95% CI (Sensitivity)	Specificity	95% CI (Specificity)	Area Under the Curve (AUC)	Kappa	p-value
TIMI Flow Grade 0/1	0.72	(0.69 - 0.75)	0.82	(0.80 - 0.84)	0.77	0.65	<0.001
Myocardial Blush Grade 0/1	0.88	(0.85 - 0.91)	0.67	(0.64 - 0.70)	0.78	0.72	<0.001

Complications

In terms of complications, the No-Reflow group exhibited a higher incidence of contrast-induced nephropathy (4.3% vs. 2.1%, $p = 0.023$), major bleeding (2.7% vs. 1.2%, $p = 0.091$), stroke (1.0% vs. 0.2%, $p = 0.042$), ventricular arrhythmias

(3.6% vs. 1.0%, $p = 0.008$), cardiogenic shock (4.9% vs. 0.6%, $p < 0.001$), reinfarction (2.2% vs. 0.8%, $p = 0.032$), and stent thrombosis (1.7% vs. 0.4%, $p = 0.018$). Additionally, the mean hospital stay was significantly longer in the No-Reflow group compared to the control group (6.8 ± 3.1 days vs. 4.9 ± 2.5 days, $p < 0.001$) (Table 4).

Table 4. Complications in no-reflow vs. control group

Complications	No-Reflow Group (n=1054)	No No-Reflow Group (n=1237)	p-value
Contrast-Induced Nephropathy (%)	45 (4.3%)	26 (2.1%)	0.023
Major Bleeding (%)	28 (2.7%)	15 (1.2%)	0.091
Stroke (%)	10 (1.0%)	3 (0.2%)	0.042
Ventricular Arrhythmias (%)	38 (3.6%)	12 (1.0%)	0.008
Cardiogenic Shock (%)	52 (4.9%)	8 (0.6%)	<0.001
Reinfarction (%)	23 (2.2%)	10 (0.8%)	0.032
Stent Thrombosis (%)	18 (1.7%)	5 (0.4%)	0.018
Hospital Stay (days, mean \pm SD)	6.8 ± 3.1	4.9 ± 2.5	<0.001

Discussion

The findings of our retrospective study provide insights into the potential applicability of the PIANO score as a predictive tool in the complex context of no-reflow phenomenon during PPCI. Our investigation not only contributes to the growing body of literature on risk stratification but also sheds light on the mechanisms underlying no-reflow, a multifactorial phenomenon that poses challenges in acute coronary syndrome management. The PIANO score's predictive performance in identifying patients at risk of developing no-reflow, as indicated by an area under the curve (AUC) of 0.77 for predicting TIMI flow grade 0/1, demonstrates its ability to discriminate between individuals with compromised coronary blood flow post-PCI. Our findings resonate with the intricate interplay of factors contributing to no-reflow, including distal embolization of thrombotic and atheromatous material, microvascular spasm, inflammation, and endothelial dysfunction. The high sensitivity (0.72) and specificity (0.82) of the PIANO score suggest its potential to capture this multifaceted phenomenon effectively. Of particular interest is the PIANO score's performance in predicting myocardial blush grade 0/1, with an elevated AUC of 0.78 and sensitivity of 0.88. This aligns with the evolving understanding of no-reflow as not solely a macrovascular issue but rather a microvascular one. Microvascular dysfunction, stemming from microembolization and endothelial injury, can contribute significantly to impaired myocardial perfusion. The PIANO score's capacity to predict microvascular impairment reinforces its potential in identifying patients who might be predisposed to this aspect of no-reflow. Our exploration of angiographic characteristics accentuates the mechanistic complexity underlying no-reflow. The No-Reflow group exhibited a higher prevalence of tortuosity, calcification, and side branches. These features, which the PIANO score takes into account, reflect technical hurdles often encountered during PCI. The association between these characteristics and no-reflow resonates with the mechanical obstruction and distal embolization mechanisms that contribute to diminished coronary flow. Importantly, the disparate rates of achieving optimal coronary flow (TIMI flow grade 3) and myocardial perfusion (myocardial blush grade 3) further substantiate the role of the PIANO score in capturing the

complexity of no-reflow mechanisms. The score's potential to identify patients at risk of failing to achieve these crucial angiographic endpoints underscores its potential in guiding therapeutic strategies to mitigate the phenomenon's impact. In the clinical realm, our study highlights the importance of accurately predicting and managing no-reflow. The observed higher incidence of complications in the No-Reflow group mirrors previous research illustrating the correlation between no-reflow and adverse clinical outcomes. Beyond the immediate procedural implications, the prolonged hospital stay observed in the No-Reflow group underscores the clinical challenges in managing these patients. Early identification through the PIANO score may enable proactive measures to address complications, potentially improving patient outcomes and resource utilization.

One study by Dai et al. evaluated the prognostic value and clinical usefulness of the PIANO score in their population^[7]. Patients with AMI undergoing primary PCI were consecutively enrolled and followed up in this registry. The endpoint of interest was all-cause mortality at 2 years after the procedure. The clinical benefits of thrombus aspiration (TA) during primary PCI in certain subgroups were also evaluated as exploratory analyses. A total of 2100 patients were identified, and 54.3% had a high (≥ 8) PIANO score. After 2 years of follow-up, patients with a high PIANO score had a higher risk of all-cause mortality after adjustment for propensity score (6.7% vs. 3.1%, adjusted hazard ratio = 2.11 [1.21-3.68], $p = 0.008$), especially in the first month (adjusted hazard ratio = 2.33 [1.17-4.65], $p = 0.017$). Restricted cubic spline analysis indicated a linear association between the PIANO score and 2-year all-cause mortality (nonlinear $p = 0.556$).

Similarly, another study by Dai et al. developed and validated a score system to predict angiographic no-reflow in primary PCI^[6]. Angiographic no-reflow occurred in 362 (17.8%) of 2036 patients. Age ≥ 70 years, absence of pre-infarction angina, total ischaemic time ≥ 4 h, left anterior descending artery as the culprit artery, pre-PCI TIMI flow grade ≤ 1 , and pre-PCI TIMI thrombus score ≥ 4 were independent predictors of angiographic no-reflow. The PIANO score ranged from 0 to 14 points, yielding a concordance index of 0.857 (95% confidence interval: 0.833 to 0.880), with good calibration. In the high-risk (≥ 8 points) group, the probability of the angiographic no-reflow phenomenon was 38.7%, while it was only 4.8% in the low-risk (< 8 points) group.

The no-reflow phenomenon, also known as inadequate reperfusion or slow reflow, refers to a condition where, despite successful revascularization of a coronary artery, there is insufficient blood flow to the myocardial tissue downstream^[8]. This phenomenon can occur following procedures such as PCI or thrombolytic therapy. The mechanisms underlying no-reflow are complex and often involve a combination of factors. While the exact cause may vary from case to case, several contributing mechanisms have been identified^[9]. During revascularization procedures, particularly in the setting of AMI, there's a risk of dislodging thrombotic material or atheromatous debris from the treated lesion^[10]. These emboli can migrate downstream, causing microvascular obstruction and impairing blood flow. The microcirculation within the myocardium can undergo spasm as a result of various factors, including the release of vasoconstrictor substances like endothelin and thromboxane A₂^[11]. This spasm can reduce blood flow through the microvessels and contribute to the no-reflow phenomenon. The inflammatory response triggered by ischemia-reperfusion injury can lead to endothelial dysfunction, disrupting the normal function of the coronary microvasculature^[12]. This dysfunction impairs vasodilation and contributes to reduced blood flow. Paradoxically, the restoration of blood flow can itself cause damage to the myocardium. Reperfusion injury involves a cascade of events, including the generation of reactive oxygen species and the activation of

inflammatory pathways, which can further compromise microvascular function. Blood elements such as platelets and leukocytes can adhere to the endothelial surface in areas of injury [4]. This can lead to capillary plugging, reducing blood flow through the microvasculature and contributing to no-reflow. Myocardial edema, ischemic myocardium is prone to develop edema upon reperfusion due to altered cell membrane permeability. Myocardial edema can increase interstitial pressure, compressing the microvasculature and hindering blood flow [5]. Reperfusion can result in an excessive generation of reactive oxygen species, which cause oxidative stress and damage to cellular structures, including endothelial cells [4]. This oxidative stress can impair vasodilation and promote vasoconstriction. Despite successful revascularization, residual thrombus or platelet aggregation within the microvasculature can persist, impairing blood flow and causing microvascular thrombosis [3].

Limitations

Several limitations should be acknowledged when interpreting the findings of this study. First, the retrospective nature of our investigation introduces inherent limitations, including the potential for selection bias and confounding variables that might influence the results. The reliance on medical records and historical data may result in incomplete or inconsistent information, leading to potential inaccuracies in patient profiles and outcomes. Secondly, the study was conducted at a single center, which could limit the generalizability of our findings to a broader patient population. Variations in patient demographics, procedural techniques, and local practices among different centers may impact the applicability of the PIANO score's predictive performance in diverse clinical settings. Additionally, as with any observational study, the presence of unmeasured or unknown confounders could influence the relationships observed in our analyses. Despite our efforts to adjust for relevant covariates, residual confounding cannot be completely ruled out. Moreover, the relatively short follow-up duration in our study limits the assessment of long-term clinical outcomes beyond the hospitalization period. The long-term implications of the PIANO score's predictive value for no-reflow and its influence on patient prognosis remain to be elucidated through prospective, longer-term studies. Finally, the evolving nature of interventional cardiology practices and advancements in treatment modalities may impact the applicability of the PIANO score to contemporary patient cohorts. Therefore, while our study offers valuable insights into the predictive utility of the PIANO score, these limitations underscore the need for further research involving larger, multicenter, prospective cohorts with extended follow-up periods to provide a more comprehensive understanding of its clinical validity and generalizability.

Conclusion

In conclusion, our study contributes valuable insights into the predictive capabilities of the PIANO score in identifying patients at risk of no-reflow during primary PCI. The score's discriminative ability and potential clinical implications for risk stratification and timely intervention make it a promising tool in the clinical setting. Understanding the angiographic characteristics associated with no-reflow and their impact on clinical outcomes is pivotal in optimizing patient care during primary PCI. Further prospective research is warranted to validate our findings and refine the clinical utility of the PIANO

score in real-world practice.

Statements and Declarations

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Conflict of interest

The authors declare no conflict of interest.

Ethical statement

This study received ethical approval from the Institutional Review Board (IRB) of the Abbas Institute of Medical Sciences (Study ID # AIMS/23/49). Patient confidentiality and data security were upheld throughout the research process, with all data de-identified prior to analysis. All patients gave consent for the use of data.

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