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Glycemic Variability and Adverse Post-PCI Outcomes: A Retrospective Cohort Analysis

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Abstract

Background

Glycemic variability has emerged as an important metabolic determinant associated with oxidative stress, endothelial dysfunction, inflammatory activation, and myocardial injury. Although chronic hyperglycemia is a recognized cardiovascular risk factor, acute fluctuations in glucose concentration may independently contribute to adverse cardiovascular outcomes following percutaneous coronary intervention (PCI). The prognostic significance of post-procedural glycemic variability remains incompletely characterized in contemporary interventional cardiology populations.

Objective

The present study evaluated the relationship between glycemic variability and adverse short-term cardiovascular outcomes following PCI in a tertiary academic cardiovascular center.

Methods

A prospective observational cohort study was conducted involving 1,524 adult patients undergoing PCI during a recent multi-year study period. Serial glucose measurements were obtained during the first 72 hours following coronary intervention. Glycemic variability was assessed using coefficient of variation and mean amplitude of glycemic excursion. The primary endpoint consisted of 90-day major adverse cardiovascular events (MACE), including cardiovascular mortality, recurrent myocardial infarction, target vessel revascularization, acute heart failure hospitalization, ventricular arrhythmia, and cardiogenic shock. Multivariable Cox proportional hazards regression analysis was performed to identify independent predictors of adverse cardiovascular outcomes.

Results

Among the included population, 472 patients (31.0%) demonstrated elevated glycemic variability during the early post-procedural period. Patients with elevated glycemic variability experienced significantly higher rates of recurrent myocardial infarction, acute heart failure hospitalization, ventricular arrhythmia, cardiogenic shock, ICU admission, and cardiovascular mortality compared with patients demonstrating stable glucose profiles. Glycemic coefficient of variation greater than 25% independently predicted MACE (adjusted HR 3.11; 95% CI 2.14–4.66), together with peak glucose concentration greater than 240 mg/dL (adjusted HR 2.63; 95% CI 1.82–3.89), left ventricular ejection fraction below 40% (adjusted HR 2.28; 95% CI 1.53–3.42), and multivessel coronary artery disease (adjusted HR 1.92; 95% CI 1.29–2.81).

Conclusion

Elevated glycemic variability following PCI was strongly associated with adverse cardiovascular outcomes and increased short-term mortality. Early metabolic stabilization and integrated glucose monitoring may improve post-intervention cardiovascular risk stratification and facilitate targeted preventive strategies.

Introduction

Percutaneous coronary intervention (PCI) remains one of the most frequently performed cardiovascular procedures in contemporary interventional cardiology and has substantially improved survival among patients presenting with acute coronary syndrome and obstructive coronary artery disease (Anderson & Morrow, 2017; Bhatt et al., 2022). Despite major advancements in coronary stent technology, intravascular imaging, antithrombotic therapy, and cardiovascular critical care, adverse cardiovascular events following PCI continue to represent an important clinical challenge in modern cardiovascular practice.

Metabolic dysfunction has increasingly emerged as a major determinant of cardiovascular prognosis after coronary intervention. While chronic hyperglycemia and diabetes mellitus are well-established contributors to atherosclerotic progression and cardiovascular injury, accumulating evidence suggests that acute glycemic fluctuation may independently contribute to endothelial dysfunction, oxidative stress generation, inflammatory activation, platelet hyperreactivity, and myocardial injury (Ceriello, 1997; Monnier et al., 2006).

Experimental investigations have demonstrated that intermittent glucose oscillation may induce greater oxidative stress and endothelial injury than sustained chronic hyperglycemia alone (Monnier et al., 2006; Brownlee, 2005). Acute glycemic variability has additionally been associated with impaired nitric oxide bioavailability, mitochondrial dysfunction, inflammatory cytokine release, and coronary microvascular impairment, all of which may contribute to adverse cardiovascular recovery following myocardial ischemia and coronary reperfusion (Ceriello & Ihnat, 2010).

The early post-PCI period represents a physiologically vulnerable phase characterized by inflammatory activation, reperfusion injury, sympathetic neurohormonal stimulation, endothelial dysfunction, and transient myocardial instability. Consequently, acute metabolic fluctuation during this period may substantially influence myocardial recovery and subsequent cardiovascular prognosis. Previous investigations evaluating critically ill populations have demonstrated that elevated glycemic variability is associated with increased mortality, prolonged hospitalization, and multiorgan dysfunction (Egi et al., 2006; Krinsley, 2008). Similarly, studies involving acute coronary syndrome populations have identified stress hyperglycemia as a predictor of adverse cardiovascular outcomes independent of pre-existing diabetic status (Kosiborod et al., 2009).

Nevertheless, evidence specifically evaluating post-procedural glycemic variability following PCI remains relatively limited in contemporary interventional cardiology populations. Most previous studies have focused primarily on chronic diabetic control assessed using glycated hemoglobin rather than dynamic

glucose fluctuation occurring during the immediate post-intervention period. Furthermore, implementation of integrated metabolic monitoring strategies in routine post-PCI care remains inconsistent across cardiovascular centers.

The present study was therefore designed to evaluate the association between glycemic variability and adverse short-term cardiovascular outcomes among patients undergoing PCI in a tertiary academic cardiovascular center. We hypothesized that elevated glycemic variability during the early post-procedural phase would independently predict increased cardiovascular morbidity and mortality following coronary intervention.

Methods

Study Design and Setting

A prospective observational cohort study was conducted at a tertiary academic cardiovascular referral center during a recent multi-year study period. Consecutive adult patients undergoing PCI were prospectively enrolled and followed for short-term cardiovascular outcomes. Clinical information was extracted from institutional cardiovascular registries, coronary angiographic archives, echocardiographic databases, laboratory systems, and electronic medical records.

The study protocol was conducted according to the ethical principles outlined in the Declaration of Helsinki and contemporary recommendations for observational cardiovascular investigations (Thygesen et al., 2018; Garcia-Garcia et al., 2018).

Study Population

Adult patients aged ≥ 18 years undergoing PCI for ST-segment elevation myocardial infarction, non–ST-segment elevation myocardial infarction, unstable angina, or chronic coronary syndrome were screened for eligibility. PCI procedures were performed according to contemporary international cardiovascular guidelines and institutional interventional cardiology protocols (Ibanez et al., 2018; Byrne et al., 2023).

Patients were considered eligible if they underwent successful PCI and demonstrated complete serial glucose monitoring data during the first 72 hours following coronary intervention. In addition, all included patients were required to have complete coronary angiographic documentation, echocardiographic evaluation, and 90-day cardiovascular follow-up information available within the institutional cardiovascular registry.

Patients were excluded if they demonstrated diabetic ketoacidosis, hyperosmolar hyperglycemic state, severe systemic infection, advanced malignancy, end-stage liver disease, pregnancy, failed coronary intervention, or incomplete metabolic monitoring documentation. Patients with incomplete

echocardiographic or angiographic records were similarly excluded to preserve consistency of cardiovascular assessment across the study population.

Glycemic Variability Assessment

Serial glucose measurements were obtained every six hours during the first 72 hours following PCI. Glycemic variability was evaluated using glucose coefficient of variation, standard deviation of glucose concentration, and mean amplitude of glycemic excursion, consistent with previously published metabolic investigations (Nalysnyk et al., 2010; Su et al., 2011).

High glycemic variability was defined as coefficient of variation greater than 25% or mean amplitude of glycemic excursion exceeding 65 mg/dL. Peak glucose concentration and mean glucose levels were additionally recorded for all included patients.

Table 1
Glycemic Variability Parameters

Parameter	Definition
Coefficient of variation	Standard deviation divided by mean glucose concentration
Mean amplitude of glycemic excursion	Mean magnitude of glucose fluctuation
High variability threshold	CV > 25% or MAGE > 65 mg/dL
Monitoring duration	First 72 hours following PCI

Data Collection

Demographic characteristics, cardiovascular risk factors, laboratory biomarkers, procedural characteristics, coronary angiographic findings, inflammatory biomarkers, and clinical outcomes were prospectively collected.

Variables analyzed in the present study included age, sex, diabetes mellitus status, glycated hemoglobin concentration, serum creatinine concentration, inflammatory biomarkers, peak troponin concentration, left ventricular ejection fraction, coronary vessel involvement, multivessel coronary artery disease, procedural duration, ICU utilization, and recurrent cardiovascular hospitalization.

Primary Outcome

The primary endpoint consisted of 90-day major adverse cardiovascular events, including cardiovascular mortality, recurrent myocardial infarction, target vessel revascularization, acute heart failure hospitalization, ventricular arrhythmia, and cardiogenic shock. Composite cardiovascular endpoints were

defined according to previously established cardiovascular outcome definitions utilized in interventional cardiology trials (Garcia-Garcia et al., 2018; Stone et al., 2011).

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median with interquartile range according to distribution normality. Categorical variables were expressed as frequencies and percentages. Independent sample t-tests and chi-square tests were utilized for group comparisons.

Kaplan–Meier survival analysis was performed to compare short-term cardiovascular survival between patients with low and high glycemic variability. Multivariable Cox proportional hazards regression analysis was performed to identify independent predictors of major adverse cardiovascular events following adjustment for clinically relevant cardiovascular variables.

A p-value below 0.05 was considered statistically significant for all analyses.

Results

Patient Enrollment and Baseline Characteristics

During the study period, 1,684 patients undergoing PCI were screened for eligibility. Following exclusion of patients with incomplete glucose monitoring documentation, failed coronary intervention, severe systemic infection, end-stage hepatic dysfunction, and incomplete cardiovascular follow-up data, 1,524 patients were included in the final analysis.

Among the included population, 472 patients (31.0%) demonstrated elevated glycemic variability during the first 72 hours following PCI, whereas 1,052 patients (69.0%) demonstrated relatively stable glucose profiles.

Patients with elevated glycemic variability were significantly older and demonstrated higher prevalence of diabetes mellitus, chronic kidney disease, multivessel coronary artery disease, and impaired left ventricular systolic function. Mean glycated hemoglobin concentration was significantly higher among patients with elevated glycemic variability compared with the low-variability group.

Table 2
Baseline Characteristics of the Study Population

Variable	Low Variability Group (n = 1052)	High Variability Group (n = 472)	p-value
Mean age (years)	61.8 ± 10.6	67.1 ± 11.9	< 0.001
Male sex (%)	71.2	74.5	0.21
Diabetes mellitus (%)	39.2	74.5	< 0.001
Chronic kidney disease (%)	11.4	28.2	< 0.001
HbA1c (%)	6.9 ± 1.2	9.2 ± 1.8	< 0.001
Peak glucose (mg/dL)	176 ± 42	291 ± 73	< 0.001
LVEF (%)	49.1 ± 8.4	37.6 ± 10.2	< 0.001
Multivessel coronary disease (%)	34.6	61.3	< 0.001

Coronary Angiographic and Procedural Findings

Coronary angiographic evaluation demonstrated significantly greater cardiovascular complexity among patients with elevated glycemic variability. Multivessel coronary artery disease, proximal left anterior descending artery involvement, diffuse coronary atherosclerosis, and severe thrombotic burden were more frequently observed among patients demonstrating unstable glucose profiles.

TIMI 0 or TIMI 1 pre-intervention coronary flow was significantly more prevalent among patients with elevated glycemic variability, suggesting greater ischemic burden and impaired coronary perfusion before intervention. In addition, these patients required more extensive coronary intervention, including multivessel stenting, thrombus aspiration, prolonged procedural duration, and adjunctive hemodynamic support.

Patients with elevated glycemic variability additionally demonstrated significantly higher peak troponin concentrations and greater prevalence of impaired left ventricular systolic function, indicating more extensive myocardial injury and reduced ventricular reserve.

Table 3
Coronary Angiographic and Procedural Characteristics

Variable	Low Variability (%)	High Variability (%)	p-value
Multivessel coronary disease	34.6	61.3	< 0.001
Proximal LAD involvement	26.4	48.1	< 0.001
TIMI 0–1 flow pre-PCI	21.7	46.9	< 0.001
Severe thrombotic burden	18.9	39.7	< 0.001
Multivessel PCI	14.2	31.8	< 0.001
Mechanical circulatory support	2.7	11.4	< 0.001

Clinical Outcomes

Clinical outcome analysis demonstrated substantially higher cardiovascular morbidity and mortality among patients with elevated glycemic variability. Recurrent myocardial infarction, acute heart failure hospitalization, ventricular arrhythmia, cardiogenic shock, ICU admission, and cardiovascular mortality occurred significantly more frequently among patients demonstrating unstable metabolic profiles.

The composite MACE endpoint occurred in 39.6% of patients with elevated glycemic variability compared with 15.2% among patients with stable glucose profiles. Cardiovascular mortality reached 14.8% among patients with elevated glycemic variability versus 4.3% among patients demonstrating lower metabolic fluctuation.

Kaplan–Meier survival analysis demonstrated early divergence in cardiovascular survival probability within the first several weeks following PCI, with persistently lower short-term survival among patients demonstrating elevated glycemic variability.

Table 4
Clinical Outcomes and Major Adverse Cardiovascular Events

Outcome	Low Variability (%)	High Variability (%)	p-value
Recurrent myocardial infarction	6.1	17.8	< 0.001
Acute heart failure hospitalization	8.4	25.7	< 0.001
Ventricular arrhythmia	5.3	14.1	0.002
ICU admission	19.8	48.5	< 0.001
Cardiogenic shock	4.7	16.3	< 0.001
Cardiovascular mortality	4.3	14.8	< 0.001
Composite MACE	15.2	39.6	< 0.001

Multivariable Cox Regression Analysis

Multivariable Cox proportional hazards regression analysis demonstrated that elevated glycemic variability independently predicted major adverse cardiovascular events following adjustment for age, sex, diabetes mellitus status, coronary anatomy, inflammatory biomarkers, and left ventricular systolic function.

Glycemic coefficient of variation greater than 25% emerged as the strongest independent predictor of MACE. Peak glucose concentration exceeding 240 mg/dL, reduced left ventricular ejection fraction below 40%, multivessel coronary artery disease, and chronic kidney disease also remained independently associated with adverse cardiovascular outcomes.

Table 5
Independent Predictors of Major Adverse Cardiovascular Events

Predictor	Adjusted HR	95% CI	p-value
Glycemic CV > 25%	3.11	2.14–4.66	< 0.001
Peak glucose > 240 mg/dL	2.63	1.82–3.89	< 0.001
LVEF < 40%	2.28	1.53–3.42	< 0.001
Multivessel coronary disease	1.92	1.29–2.81	0.002
Chronic kidney disease	1.74	1.18–2.63	0.01

Discussion

The present study demonstrated a strong association between elevated glycemic variability and adverse cardiovascular outcomes among patients undergoing PCI in a contemporary interventional cardiology population. Patients demonstrating substantial glucose fluctuation during the early post-procedural period experienced significantly higher rates of recurrent myocardial infarction, acute heart failure hospitalization, ventricular arrhythmia, cardiogenic shock, ICU admission, and cardiovascular mortality compared with patients maintaining relatively stable glycemic profiles.

These findings reinforce the concept that acute metabolic instability may substantially influence cardiovascular prognosis independent of chronic glycemic control alone. While glycated hemoglobin remains an established marker of long-term metabolic status, increasing evidence suggests that dynamic glucose fluctuation may exert independent pathophysiological effects on endothelial integrity, oxidative stress generation, inflammatory activation, and myocardial recovery following coronary intervention.

One of the most important observations in the current analysis involved the strong prognostic significance of glycemic coefficient of variation greater than 25%, which emerged as the most powerful independent predictor of major adverse cardiovascular events after multivariable adjustment. Acute glycemic fluctuation has previously been associated with amplified oxidative stress, endothelial dysfunction, inflammatory cytokine release, platelet activation, and impaired coronary microvascular

function. These mechanisms may contribute directly to reperfusion injury, impaired myocardial healing, and increased susceptibility to recurrent ischemic events following PCI.

The present findings additionally demonstrated that elevated peak glucose concentration independently predicted adverse cardiovascular outcomes. Severe hyperglycemia during the early post-intervention phase may reflect both metabolic dysregulation and heightened physiologic stress response associated with extensive myocardial injury, neurohormonal activation, and systemic inflammatory burden. Previous investigations involving acute coronary syndrome populations have similarly demonstrated that stress hyperglycemia is associated with increased cardiovascular mortality independent of pre-existing diabetic status.

Reduced left ventricular ejection fraction also emerged as an independent predictor of adverse cardiovascular outcomes. Patients demonstrating impaired ventricular systolic function experienced significantly higher rates of recurrent ischemia, cardiogenic shock, ventricular arrhythmia, and cardiovascular mortality. Impaired myocardial reserve likely increases vulnerability to metabolic stress, endothelial dysfunction, and inflammatory activation during the early recovery phase following coronary reperfusion.

Another clinically important observation involved the significantly greater prevalence of multivessel coronary artery disease among patients demonstrating elevated glycemic variability. Extensive coronary atherosclerotic burden may contribute to diffuse myocardial ischemia, impaired coronary perfusion reserve, persistent inflammatory activation, and greater susceptibility to recurrent cardiovascular instability following intervention.

The present study additionally highlights the evolving role of integrated metabolic monitoring in contemporary interventional cardiology practice. Traditional PCI management strategies have primarily focused on coronary anatomy, procedural success, antithrombotic optimization, and revascularization completeness. However, the current findings suggest that acute metabolic assessment may provide equally important prognostic information capable of identifying high-risk patients vulnerable to adverse cardiovascular recovery following intervention.

Several limitations should be acknowledged. First, although the present investigation utilized prospective observational methodology, residual confounding may remain despite multivariable adjustment. Second, the study was conducted within a tertiary academic cardiovascular center, potentially limiting generalizability to smaller institutions and lower-resource healthcare settings. Third, long-term cardiovascular outcomes beyond 90 days were not comprehensively evaluated. Fourth, variability in insulin administration strategies and antihyperglycemic therapy may have influenced metabolic measurements and subsequent cardiovascular outcomes.

Despite these limitations, the present study provides clinically meaningful evidence supporting the prognostic significance of elevated glycemic variability following PCI. Future multicenter investigations incorporating continuous glucose monitoring, advanced metabolic profiling, and machine-learning-

assisted cardiovascular risk stratification may further improve post-intervention cardiovascular outcomes among high-risk coronary artery disease populations.

Conclusion

The present study demonstrated that elevated glycemic variability following PCI was strongly associated with increased cardiovascular morbidity and mortality in a contemporary interventional cardiology population. Patients demonstrating substantial glucose fluctuation during the early post-procedural period experienced significantly higher rates of recurrent myocardial infarction, acute heart failure hospitalization, ventricular arrhythmia, cardiogenic shock, ICU admission, and cardiovascular mortality compared with patients maintaining relatively stable glycemic profiles.

Importantly, the prognostic impact of glycemic variability remained significant even after adjustment for baseline cardiovascular risk factors, coronary anatomy, inflammatory biomarkers, and left ventricular systolic function, emphasizing that acute metabolic instability itself represents an important determinant of adverse cardiovascular recovery following coronary intervention.

The findings strongly support incorporation of integrated metabolic monitoring and glycemic stabilization strategies into routine post-PCI cardiovascular management pathways. Future multicenter prospective investigations incorporating continuous glucose monitoring systems and advanced metabolic surveillance may further reduce post-intervention cardiovascular complications and improve long-term survival among high-risk PCI populations.

Declarations

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Funding

No external funding was received for the present study.

Conflict of Interest

The authors declare that there are no conflicts of interest related to the present study.

Ethical Approval

The study protocol was conducted according to the ethical principles outlined in the Declaration of Helsinki and was approved by the institutional cardiovascular research ethics committee. Patient

confidentiality and data protection were maintained throughout all stages of data collection and analysis.

Informed Consent

Written informed consent was obtained from all participants or their legally authorized representatives prior to inclusion in the study.

Data Availability Statement

The datasets generated and analyzed during the current study are not publicly available because of institutional data protection policies but may be available from the corresponding author upon reasonable academic request and approval by the institutional ethics committee.

Author Contributions

Chen Jianye contributed to study conceptualization, methodology development, supervision of cardiovascular data interpretation, and critical revision of the manuscript. Qian Qi contributed to study design, procedural oversight, manuscript revision, and final approval of the submitted version. Ignasius Jappar contributed to data acquisition, cardiovascular outcome adjudication, and interpretation of clinical findings. Farozan Radjamin contributed to statistical analysis, manuscript drafting, literature review, and interpretation of study outcomes. All authors made substantial intellectual contributions to the manuscript, approved the final version prior to submission, and agreed to be accountable for all aspects of the work in accordance with the recommendations of the International Committee of Medical Journal Editors (ICMJE).

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