



Metabolic predictors of no-reflow in diabetic STEMI patients undergoing primary percutaneous coronary intervention

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Abstract

Objectives: The aim of the work was to examine the link between selected metabolic risk factors and the incidence of the no-reflow phenomenon in diabetic individuals undergoing primary percutaneous coronary intervention (PPCI) for acute myocardial infarction (AMI).

Methods: This prospective cross-sectional investigation was conducted on 120 diabetic participants aged 18 or older, of both sexes, who presented with ST-elevation myocardial infarction (STEMI) and underwent PPCI. Two groups were formed based on participant characteristics: Group I (normal-reflow), defined by thrombolysis in myocardial infarction (TIMI) grade 3 flow, and Group II (no-reflow), characterized by TIMI flow ≤ 2 , which is not attributed to dissection, residual vessel narrowing, or vasospasm.

Results: Results from univariate regression indicated that age, hypertension, and dyslipidemia were significantly linked to the development of the no-reflow phenomenon ($P < 0.05$). In addition, systolic blood pressure (SBP), diastolic blood pressure, platelet count, high-density lipoprotein, triglycerides, serum urea, uric acid, and glomerular filtration rate (GFR) were significant predictors of no-reflow ($P < 0.05$). After a regression model incorporating multiple variables indicated that SBP and platelet count independently predicted no-reflow ($P < 0.05$). Regarding clinical outcomes, the incidence of heart failure and atrial fibrillation was significantly higher in the no-reflow group ($P < 0.05$).

Conclusions: No-reflow is a common adverse event observed in diabetic individuals presenting with STEMI who undergo PPCI. It is influenced by a combination of clinical and biochemical risk factors, including advanced age, smoking, hypertension, dyslipidemia, impaired renal function, elevated serum uric acid, and reduced GFR.

Keywords

No-Reflow, Primary Percutaneous Coronary Intervention, ST-Elevation Myocardial Infarction, Diabetes, Metabolic Profile

Rezumat

Obiective: Scopul lucrării a fost de a examina legătura dintre factorii de risc metabolici selectați și incidența fenomenului de no-reflow la persoanele diabetice supuse intervenției coronariene percutanate primare (ICPP) pentru IMA.

Metode: Această investigație transversală prospectivă a fost efectuată pe 120 de participanți diabetici cu vârsta de 18 ani sau peste, de ambele sexe, care au prezentat infarct miocardic cu supradenivelare ST (STEMI) și au fost supuși ICPP. Au fost formate două grupuri pe baza caracteristicilor participanților: Grupul I (normal-reflow), definit prin flux de gradul 3 conform trombolizei în infarctul miocardic (TIMI), și Grupul II (no-reflow), caracterizat prin flux TIMI ≤ 2 , care nu este atribuit disecției, stenozei reziduale coronariene sau vasospasmului.

Rezultate: Rezultatele regresiei univariate au indicat că vârsta, hipertensiunea arterială și dislipidemia au fost semnificativ legate de dezvoltarea fenomenului de no-reflow ($P < 0,05$). În plus, tensiunea arterială sistolică (TAS), tensiunea arterială diastolică, numărul de trombocite, lipoproteinele cu densitate mare, trigliceridele, ureea serică, acidul uric și rata de filtrare glomerulară (GFR) au fost predictorii semnificativi ai fenomenului de no-reflow ($P < 0,05$). Un model de regresie care încorporează mai multe variabile, a indicat faptul că TAS și numărul de trombocite au prezis independent fenomenul de no-reflow ($P < 0,05$). În ceea ce privește rezultatele clinice, incidența insuficienței cardiace și a fibrilației atriale a fost semnificativ mai mare în grupul cu no-reflow ($P < 0,05$).

Concluzii: Fenomenul de no-reflow este un eveniment advers frecvent observat la persoanele diabetice care prezintă STEMI și care sunt supuse intervenției coronariene percutanate (PPCI). Este influențat de o combinație de factori de risc clinici și biochimici, inclusiv vârsta înaintată, fumatul, hipertensiunea arterială, dislipidemia, funcția renală afectată, acidul uric seric crescut și RFG redus.

Cuvinte cheie

no-reflow, intervenție coronariană percutanată primară, infarct miocardic cu supradenivelare de segment ST, diabet, profil metabolic

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Introduction

Acute myocardial infarction (AMI) and its related complications continue to represent major contributors to global morbidity and mortality [1]. No-reflow is a serious complication that adversely affects both functional and clinical outcomes in AMI individuals [2].

This multifactorial phenomenon is thought to arise from the interplay of four principal underlying pathophysiological mechanisms, including distal embolization of atherothrombotic material, myocardial injury due to ischemia, reperfusion-induced damage, and impaired function of the coronary microvasculature [3]. Therefore, implementing suitable interventions to reduce the risk or mitigate these underlying mechanisms is essential for improving patient outcomes [2, 3].

Metabolic syndrome, defined by the co-occurrence of multiple recognized risk determinants such as central obesity, hypertension, diabetes mellitus (DM), and dyslipidemia, is firmly related to an elevated probability of cardiovascular events [4]. In diabetic patients, the magnitude of coronary heart disease (CHD) risk is influenced by the intensity of specific risk factors, with hypertension, high low-density lipoprotein (LDL) cholesterol levels, tobacco use, metabolic syndrome, poor glycemic control, and the presence of microalbuminuria serving as key determinants of cardiovascular events [5].

Although many investigations have demonstrated the correlation between metabolic risk determinants and the severity or extent of myocardial infarction (MI), data specifically addressing the relationship between these factors and the incidence of the no-reflow phenomenon among patients with STEMI remain limited. Timely detection of high-risk individuals during PCI initiation is essential for tailoring management strategies and enhancing clinical outcomes.

This research was conducted to investigate the association between multiple metabolic risk factors and the occurrence of no-reflow in diabetic individuals with AMI undergoing PPCI.

Methods

This prospective cross-sectional research included 120 diabetic patients (aged ≥ 18 years, of both sexes) who presented with STEMI and underwent treatment with PPCI.

Prior to enrollment, the study was approved by the Ethics Committee of Assiut University Hospitals, and written informed consent was obtained from all participants. The study was conducted between October 1, 2022, and November 30, 2023.

Exclusion criteria included patients with advanced hepatic or renal disease, preceding coronary artery bypass grafting (CABG), significant valvular heart disease or cardiomyopathy, coronary dissection or vasospasm, and contraindications to anticoagulant therapy. Such contraindications comprised uncontrolled internal bleeding, a history of hemorrhagic stroke or ischemic stroke (including transient ischemic attacks) within the past six months, aortic dissection, and hematologic disorders associated with coagulopathy.

Following PPCI, patients were stratified on the basis of post-procedural TIMI flow grade. Group I (normal-reflow) included individuals who achieved TIMI grade 3 flow, whereas Group II (no-reflow) comprised patients with TIMI flow ≤ 2 , not attributed to dissection, residual vessel narrowing, or vasospasm.

All patients underwent comprehensive data collection and clinical evaluation. This included a detailed medical history and demographic profiling—covering age, sex, weight, height, and body mass index (BMI) as well as documentation of prior MI, CABG, or PPCI.

Routine laboratory assessments included a complete blood count (CBC), kidney function tests, serum uric acid, and electrolyte levels (Na^+ , K^+). A lipid profile was obtained, measuring LDL, HDL, triglycerides, and total cholesterol. Preoperative blood glucose levels, HbA1c levels, and cardiac biomarkers such as troponin, CK, and CK-MB. Additionally, all patients underwent electrocardiography (ECG) and Echocardiography study for ejection fraction (M-mode), LV dimensions segmental wall motion abnormality (SWMA), and complications, coronary angiography to evaluate the infarct-related artery (IRA), lesion location, degree of occlusion, culprit lesion length, vessel diameter, TIMI flow grade, myocardial blush grade (MBG), and thrombus burden.

Regarding the PCI protocol, all individuals were administered an initial dose of 300 mg aspirin and an ADP antagonist (180 mg ticagrelor) prior to the procedure. Unfractionated heparin (10,000 units) was administered intravenously as a bolus to all participants at a dosage of 70–100 U/kg, to achieve an activated clotting time (ACT) of approximately 250 seconds. Using standard catheterization techniques, baseline coronary angiography was completed. During PCI, direct stenting was the preferred strategy when anatomically feasible, while balloon pre-dilatation was employed when necessary. The use of adjunctive techniques and devices—including balloon pre- and post-dilatation, drug-eluting stents (DES), glycoprotein IIb/IIIa inhibitors such as tirofiban, and thrombus aspiration was determined at the discretion of the attending interventional cardiologist.

No-reflow definition and TIMI flow grading

Two experienced interventional cardiologists assessed the no-reflow phenomenon. It was defined as persistent myocardial hypoperfusion regardless of the successful outcome of mechanical revascularization of the IRA following PCI, excluding cases caused by coronary dissection or vasospasm.

Coronary perfusion after the intervention was evaluated using the TIMI flow grading system. TIMI grade 0 indicated total lack of antegrade circulation beyond the obstruction, while grade 1 reflected minimal forward flow with incomplete distal vessel opacification. Grade 2 signified full distal vessel opacification with delayed flow, and grade 3 represented normal flow with complete distal perfusion. No-reflow was operationally defined as a TIMI flow ≤ 2 post-PCI, indicating suboptimal myocardial reperfusion despite successful epicardial revascularization.

Angiographic thrombus severity was classified based on visual assessment. Grade 0 indicated no detectable thrombus; grade 1

included subtle angiographic signs suggestive of thrombus, such as blurred contrast filling or uneven outlines. A thrombus occupying under 50% of the vessel diameter was classified as grade 2; grade 3 denoted a thrombus larger than 50% but smaller than two vessel diameters; grade 4 referred to a thrombus exceeding two vessel diameters; and grade 5 indicated total occlusion by thrombus. In cases presenting with grade 5 thrombus, additional interventional measures were undertaken to reestablish antegrade flow, enabling subsequent reassessment and reclassification of thrombus grade.

In-hospital follow-up

Participants were carefully monitored for clinical outcomes until discharge during hospitalization (about 7 days) for the development of major adverse cardiac events (MACE), including recurrent chest pain, HF, arrhythmias, mortality, and the need for reintervention. HF was defined based on clinical symptoms such as dyspnea, ankle swelling, and physical examination findings, including elevated jugular venous pressure, pulmonary rales, and a laterally displaced apical impulse.

All patients received drug-eluting stents (DES) during PCI, and additional therapeutic measures, such as glycoprotein IIb/IIIa inhibitors (e.g., tirofiban, eptifibatide) and aspiration thrombectomy, were utilized based on thrombus burden and physician discretion.

Sample size calculation

Sample size calculation was performed using StatCalc (Epi Info version 7.2), assuming a 30% prevalence of no-reflow following MI recanalization procedures, with a 7% margin of error and a 90% confidence level, yielding a minimum required sample size of 120 patients.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics version 27 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was evaluated using the Shapiro-Wilk test in conjunction with visual assessment of histograms. Continuous data with a normal distribution were summarized as mean $\pm$ SD and compared using an independent-samples t-test. For non-normally distributed data, results were reported as median and interquartile range (IQR), and the Mann-Whitney U test was applied for analysis. Categorical variables were described using counts and percentages, with statistical comparisons made via the Chi-square test or Fisher's exact test, depending on expected frequency counts.

Independent factors associated with the no-reflow phenomenon were determined through logistic regression analysis. Univariate analysis was first conducted to assess the influence of each independent factor and the outcome of interest. Variables demonstrating statistical significance were then incorporated into

a multivariate logistic regression model to account for possible confounders and identify independent predictors. All statistical tests were two-sided, with a P-value below 0.05 considered significant.

Results

The study cohort was comprised of 120 diabetic patients presenting with STEMI who underwent PPCI. Among them, 37 patients exhibited the no-reflow phenomenon (defined as TIMI flow grade ≤ 2), while 83 patients achieved normal coronary reperfusion (TIMI grade 3 flow).

A number of clinical, laboratory, and angiographic variables differed significantly between the no-reflow and normal-reflow groups. Individuals in the no-reflow group were older and exhibited higher BMI than those in the normal-reflow group. Additionally, the prevalence of hypertension and dyslipidemia was greater among no-reflow patients. The Killip classification was notably elevated in the no-reflow group, indicating worse clinical status on presentation ($P < 0.001$). In contrast, systolic and diastolic blood pressures were notably lower in the no-reflow group. No meaningful variation was found between the groups concerning sex, smoking history, or prior CAD. **Table 1**

Regarding laboratory findings, the no-reflow group demonstrated significantly elevated levels of platelets, triglycerides (TGs), serum creatinine, serum urea, and uric acid. Conversely, levels of high-density lipoprotein (HDL) and estimated GFR were markedly reduced in the no-reflow group ($P < 0.001$ and $P = 0.038$, respectively). There was no meaningful difference between the groups with respect to hemoglobin levels, white blood cell count (WBC), total cholesterol, LDL, random blood glucose (RBG), glycated hemoglobin (HbA1c), serum sodium (Na^+), or potassium (K^+). **Table 2**

ECG findings showed no marked variation among the groups. However, echocardiographic assessment revealed that the LV end-systolic diameter (LVESD) was significantly elevated in patients who experienced the no-reflow phenomenon, while LV end-diastolic diameter (LVEDD) and LVEF were significantly lower in patients who experienced the no-reflow phenomenon ($P < 0.001$). **Table 3**

Angiographic findings further highlighted differences between the two groups. Individuals with the no-reflow group possess markedly higher thrombus grades relative to those in the normal-reflow group ($P < 0.001$); these patients had a greater number of affected coronary vessels ($P = 0.021$). However, despite the culprit vessel involvement, no significant variation was observed between the two groups. Conversely, post-intervention TIMI grade, lower thrombus grade, and MBG were markedly elevated in the normal-reflow group compared to the no-reflow group ($P < 0.001$), indicating better post-procedural perfusion outcomes. **Table 4**

With respect to clinical outcomes, the occurrence of HF and AF was significantly elevated in the no-reflow group ($P < 0.001$ and $P = 0.002$, respectively). In contrast, no marked differences were observed among the groups in the rates of cardiogenic shock, cardiac arrest, or in-hospital mortality. **Table 5**

Table 1 - Comparison between normal reflow and no reflow according to demographic data, associated diseases/risk factors, blood pressure vessels and laboratory data.

		Normal reflow (n=83)	With no reflow (n=37)	P
Age (years)		50.1 ± 5.8	54.9 ± 5.2	<0.001*
Sex	Female	58 (69.9)	25 (67.6)	0.800
	Male	25 (30.1)	12 (32.4)	
BMI (kg/m ²)		26.76 ± 0.83	27.6 ± 0.85	<0.001*
Diseases/risk factors				
HTN		19 (22.9%)	16 (43.2%)	0.024*
History of dyslipidemia		16 (19.3%)	14 (37.8%)	0.030*
Smoking		41 (49.4%)	25 (67.6%)	0.065
History of CAD		31 (37.4%)	15 (40.5%)	0.740
Blood pressure				
SBP (mmHg)		121.3 ± 5.7	111.43 ± 8.14	<0.001*
DBP (mmHg)		74.04 ± 3.8	71.5 ± 6.7	0.038*
Killip classification				
1		76 (91.6%)	3 (8.1%)	<0.001*
2		4 (4.8%)	5 (13.5%)	
3		2 (2.4%)	18 (48.7%)	
4		1 (1.2%)	11 (29.7%)	

Data are presented as mean ± SD or frequency (%). * Significant P value <0.05, HTN: Hypertension, CAD: Coronary Artery Disease, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

Table 2 - Comparison between normal reflow and no reflow according to laboratory data, risk assessment, and outcomes.

		Normal reflow (n=83)	With no reflow (n=37)	P
Hemoglobin (gm/dl)		11.7 ± 0.5	11.6 ± 1.1	0.599
Platelets (x103/fl)		231.02 ± 31.7	268.03 ± 33.95	>0.001*
WBCs (x103/fl)		8.35 ± 0.73	8.21 ± 0.82	0.361
Cholesterol (mg/dl)		201.2 ± 11.3	204.4 ± 10.2	0.145
LDL (mg/dl)		159.96 ± 11.62	157.54 ± 9.3	0.227
HDL (mg/dl)		45.4 ± 4.02	37 ± 3.7	>0.001*
TGs (mg/dl)		147.9 ± 13.7	212.2 ± 27.04	>0.001*
RBG (mg/dl)		136.6 ± 11.8	134.14 ± 11.22	0.296
HbA1C (%)		7.5 ± 0.3	7.5 ± 0.4	0.894
Serum creatinine (mg/dl)		0.8 ± 0.1	1.22 ± 0.14	>0.001*
Serum urea (mg/dl)		17.33 ± 3.6	25.97 ± 4.11	>0.001*
Uric Acid (mg/dl)		8.7 ± 0.99	13.51 ± 1.3	>0.001*
Serum Na (Meq/L)		137.7 ± 2.3	138.1 ± 1.97	0.412
Serum K (Meq/L)		4.53 ± 0.3	4.63 ± 0.34	0.106
GFR (ml/hr/1.73 m ²)		78.5 ± 6.42	58.8 ± 5.53	>0.001*

Data are presented as mean ± SD. * Significant P value <0.05, LDL: Low density lipoprotein, WBCs: white blood cells, HDL: High density lipoprotein, TGs: triglycerids, RBG: Random blood sugar, HbA1C: Glycated hemoglobin, GFR: Glomerular Filtration rate.

Table 3 - Comparison between the two study groups categorized by reflow status according to echocardiography.

		Normal Reflow (n=83)	With No Reflow (n=37)	P
LVESD (mm)		34.29 ± 1.30	35.27 ± 1.50	<0.001*
LVEDD (mm)		55.57 ± 2.52	47.65 ± 1.89	<0.001*
LVEF (M-mode) (%)		47.63 ± 3.30	40.97 ± 3.58	<0.001*

Data are presented as mean ± SD. * Significant P value <0.05, LVESD: LV end-systolic diameter, LVEDD: LV end-diastolic diameter.

Table 4 - Comparison between the two study groups categorized by reflow status according to risk assessment, number of affected vessels, and culprit vessels.

	Normal reflow (n=83)	With no reflow (n=37)	P
Initial TIMI flow grades pre-PCI			
TIMI 0	65 (78.3%)	30 (81.1%)	0.002*
TIMI I	3 (3.6%)	7 (18.9%)	
TIMI II	12 (14.5%)	0 (0.0%)	
TIMI III	3 (3.6%)	0 (0.0%)	
Thrombus grade			
Nil (Grade 0)	11 (13.3%)	0 (0%)	<0.001*
Low (Grade 1 – 2)	41 (49.4%)	3 (8.1%)	
Moderate (Grade 3)	22 (26.5%)	7 (18.9%)	
High (Grade 4 – 5)	9 (10.8%)	27 (73%)	
Myocardial blush			
> 2	82 (98.8%)	1 (2.7%)	<0.001*
≤ 2	1 (1.2%)	36 (97.3%)	
Culprit vessels			
LAD	59 (71.1%)	24 (64.9%)	0.632
RCA	10 (12%)	4 (10.8%)	
LCX	14 (16.9%)	9 (24.3%)	
Number of affected vessels			
Single vessel	46 (55.4%)	16 (43.2%)	0.021*
Two vessels	29 (34.9%)	10 (27%)	
Multiple vessels	8 (9.6%)	11 (29.7%)	

Data presented as frequency (%). * Significant P value <0.05. PCI: Percutaneous coronary intervention, TIMI: Thrombolysis In Myocardial Infarction, LAD: Left Anterior Descending artery, RCA: Right Coronary Artery, LCX: Left Circumflex artery.

Table 5 - Comparison between normal reflow and no reflow according to outcomes.

	Normal reflow (n=83)	With no reflow (n=37)	P
Outcomes			
Heart failure	10 (12.0%)	21 (56.8%)	<0.001*
AF	8 (9.6%)	12 (32.4%)	0.002*
Shock	8 (9.6%)	4 (10.8%)	1.000
Cardiac arrest	6 (7.2%)	7 (18.9%)	0.107
In hospital mortality	3 (3.6%)	3 (8.1%)	0.371

Data presented as frequency (%). * Significant P value <0.05, AF: atrial fibrillation.

Univariate logistic regression analysis identified multiple variables as significant predictors of the no-reflow phenomenon. Among the clinical predictors, advanced age ($P < 0.001$, OR 1.182; 95% CI: 1.081–1.293), hypertension ($P = 0.026$, OR 2.566; 95% CI: 1.122–5.873), and dyslipidemia ($P = 0.033$, OR 2.549; 95% CI: 1.079–6.021) were strongly linked to a higher risk. Several laboratory parameters were also significant: elevated platelet count ($P < 0.001$, OR 1.036; 95% CI: 1.020–1.052), higher triglyceride levels ($P < 0.001$, OR 1.144; 95% CI: 1.078–1.214), increased serum urea ($P < 0.001$, OR 1.922; 95% CI: 1.498–2.467), and elevated uric acid ($P = 0.032$, OR 126.008; 95% CI: 1.525–10409.51). Conversely, lower HDL ($P < 0.001$, OR 0.613; 95% CI: 0.516–0.727) and reduced GFR ($P < 0.001$, OR 0.554; 95% CI: 0.409–0.749) were associated with higher no-reflow risk. A regression model involving multiple variables demonstrated that low systolic blood pressure ($P = 0.036$, OR 0.461; 95% CI: 0.224–0.950) and elevated platelet count ($P = 0.047$, OR 1.151; 95% CI: 1.002–1.323) were independent predictors of no-reflow. These

findings emphasize the role of hemodynamic instability and platelet activation in the no-reflow pathophysiology and the value of early risk stratification to improve post-PPCI outcomes. **Table 6.**

Discussion

In our investigation, the no-reflow manifestation was identified in a notable proportion of patients (30.83%) presenting with STEMI who received PPCI. This high incidence may be attributed to the study's exclusive focus on diabetic patients.

Several clinical and laboratory factors were known as significant predictors of no-reflow, including advanced age, hypertension, low HDL, elevated TGs, renal impairment, increased serum uric acid, decreased GFR, and high thrombus burden.

Patients with no-reflow experienced significantly worse in-hospital outcomes, particularly an elevated occurrence of HF and AF. However, the rates of cardiogenic shock, cardiac arrest, and in-

Table 6 - Univariate and multivariate logistic regression analysis of risk factors affecting no reflow.

	Univariate			Multivariate		
	P	OR	95% CI	P	OR	95% CI
Age (years)	<0.001*	1.182	1.081 – 1.292	0.053	1.486	0.994 – 2.221
Sex (Female)	0.800	1.114	0.484 – 2.561	-	-	-
HTN	0.026*	2.566	1.122 – 5.873	0.058	286480.764	0.649 – 1.264
History of dyslipidemia	0.033*	2.549	1.079 – 6.021	0.058	0.0	0.0 – 2.182
History of CAD	0.740	1.144	0.518 – 2.527	-	-	-
SBP (mmHg)	<0.001*	0.773	0.701 – 0.853	0.036*	0.461	0.224 – 0.950
DBP (mmHg)	0.014*	0.890	0.812 – 0.977	0.712	0.931	0.635 – 1.364
Hemoglobin (gm/dl)	0.497	0.831	0.486 – 1.419	-	-	-
Platelets (x103/fl)	<0.001*	1.036	1.020 – 1.052	0.047*	1.151	1.002 – 1.323
HDL (mg/dl)	<0.001*	0.613	0.516 – 0.727	-	-	-
TGs (mg/dl)	<0.001*	1.144	1.078 – 1.214	-	-	-
RBG (mg/dl)	0.294	0.982	0.949 – 1.016	-	-	-
HbA1C (%)	0.880	0.902	0.237 – 3.433	-	-	-
Serum Creatinine (mg/dl)	0.992	4.1582E81	0.0 – 0.0	-	-	-
Serum Urea (mg/dl)	<0.001*	1.922	1.498 – 2.467	-	-	-
Uric Acid (mg/dl)	0.032*	126.008	1.525- 10409.51	-	-	-
Serum Na (Meq/L)	0.409	1.079	0.901 – 1.293	-	-	-
GFR (ml/hr/1.73 m ²)	<0.001*	0.554	0.409 – 0.749	-	-	-
ECG (STEMI Type)				-	-	-
Anterior STEMI®		1.000			1.000	
Lateral STEMI	0.386	0.614	0.204 – 1.849	1.000	0.0	0.0 –
Inferior STEMI	0.863	1.122	0.303 – 4.16	1.000	0.0	0.0 –
Posterior STEMI	0.999	0.0	0.0 – 0.0	0.999	0.0	0.0 –
Culprit Vessel						
LAD®		1.000			1.000	
RCA	0.979	0.983	0.281 – 3.442	0.999	0.0	0.0
LCX	0.351	1.580	0.604 – 4.138	1.000	0.001	0.0
Affected vessel number (>2)	0.219	1.632	0.747 – 3.564	1.000	0.751	0.0

*: significant as P value ≤ 0.05 , OR: Odds ratio, C.I.: Confidence interval, LL: Lower limit, UL: Upper Limit, HTN: hypertension, SBP: systolic blood pressure, DBP: diastolic blood pressure, ECG: Electrocardiograph, STEMI: ST elevation myocardial infarction, LDL: low density lipoprotein, HDL: high density lipoprotein, GFR: Glomerular filtration rate, TIMI: Thrombolysis In Myocardial Infarction, LAD: Left Anterior Descending artery, RCA: Right Coronary Artery, LCX: Left Circumflex artery.

hospital mortality were comparable between patients with no-reflow and those with normal reflow.

The no-reflow rate of 30.8% in this cohort aligns with earlier research, including studies conducted by Hassan et al. [6], who recorded a 31% incidence of no-reflow in 293 STEMI patients undergoing PPCI.

Conversely, Hesham Refaat et al. [7] found a higher no-reflow incidence (43%) among 400 STEMI patients. The increased rate in their study may be attributed to the older patient population (mean age 65.21 ± 11.8 years vs. 54.78 ± 8.4 years in our study) or higher thrombus burden (81.4% vs. 73% in our study). Alternatively, Amr Elkammash et al. [8] reported a lower incidence (17.5%) in 120 STEMI patients. Differences in patient characteristics may explain the discrepancy, as our study exclusively included diabetic patients, whereas their study had only 40.8% diabetic participants.

Our investigation confirmed that advanced age is a significant risk factor for no-reflow, consistent with findings from Tasar et al. [9] who reported that no-reflow patients were older (63.6 ± 12.3 years vs.

58.1 ± 11.7 years, $P < 0.001$). Age-related factors such as vascular stiffness, endothelial dysfunction, and increased thrombus burden may contribute to this phenomenon.

Hypertension was identified as a significant predictor of no-reflow. HTN contributes to endothelial dysfunction, microvascular disease, and increased thrombus formation, all of which impair coronary microcirculation [10]. This finding aligns with previous studies demonstrating higher no-reflow rates in hypertensive patients. The findings of Mirbolouk et al. [11], who found that individuals with hypertension had a significantly elevated incidence of no-reflow, show an odds ratio (OR) of 2.91 for hypertension as a predictor (95% CI: 1.35-6.27, $p < 0.001$). Also, Harrison et al. [12] found that hypertension was observed as a significant marker of no-reflow (hypertension present in 32% of patients who experienced no-reflow, in comparison to 23% in the normal reflow group ($p = 0.02$)).

Our study identified low HDL levels and high TG levels as significant predictors of no-reflow. However, total cholesterol and LDL cholesterol were not found to be significant markers. These

findings align with those of an investigation conducted by Ma et al. [13], which revealed a meaningful relationship between high TG levels and no-reflow ($P < 0.001$), while cholesterol ($P = 0.725$) and LDL ($P = 0.628$) showed no significant correlation. Conversely, a separate study by Kim et al. [14] recorded that LDL cholesterol ($P = 0.000$) was determined to be an independent contributor to the risk of no-reflow. This discrepancy may be attributed to the fact that a large proportion (38.33%) of our patients were adherent to target-dose statin therapy, which could have mitigated the effect of LDL on no-reflow incidence.

Notably, the Triglyceride-Glucose (TyG) index, although not directly calculated in this study, has gained recognition as a reliable surrogate marker for insulin resistance, and it strongly correlates with both triglycerides and fasting glucose levels [15]. Recent literature has emphasized the TyG index as an emerging predictor of no-reflow in STEMI patients. For instance, studies by Ma et al. [16] and Wang et al. [17] demonstrated that a high TyG index was associated with an increased risk of no-reflow after PCI in AMI patients with T2DM. The index reflects chronic metabolic stress and endothelial dysfunction, which synergize to impair microvascular perfusion even after successful epicardial revascularization [15].

While metabolic parameters like TyG represent chronic metabolic derangements, other markers, such as admission hyperglycemia and C-reactive protein (CRP), provide insight into acute pathophysiological states. Khalfallah et al. [18] demonstrated that higher blood glucose levels on admission were associated with reduced TIMI flow in patients with STEMI after PPCI. The hyperglycemic state promotes oxidative stress, platelet aggregation, and neutrophil activation, all contributing to microvascular injury. In addition, Mansour et al. [19] reported that there was a highly significant correlation between CRP level and no reflow in STEMI patients after primary PCI. CRP is an indicator of acute-phase inflammation and a mediator of atherosclerosis, stimulating the expression of adhesion molecules and inflammatory cells. It enhances the uptake of oxidized low-density lipoprotein into macrophages through the expression of tissue factor, leading to plaque formation and thrombosis. CRP is also thought to contribute to vasoconstriction at the microvascular level and endothelial damage, in which no-reflow is involved [20].

Renal function also played a significant role in predicting no-reflow in our study. Increased serum concentrations of creatinine, urea, and uric acid showed a strong association with no-reflow, possibly attributable to their involvement in endothelial impairment, heightened oxidative stress, and inflammatory pathways. The observed outcomes are consistent with the study conducted by Namazi et al. [21] observed a significant difference in mean serum creatinine levels ($P = 0.022$) between no-reflow and normal reflow groups in a cohort of 306 STEMI patients undergoing PPCI.

Regarding the correlation between WBC count and no-reflow, our study did not identify WBC count as an independent predictor, aligning with Tasar et al. [9]. However, Namazi et al. [21] reported significantly higher WBC levels in the no-reflow group ($10.8 \pm 2.3 \times 10^3/\mu\text{L}$ vs. $8.9 \pm 2.0 \times 10^3/\mu\text{L}$, $P < 0.05$). Potential explanations for this discrepancy include the smaller sample size in our study (120 patients vs. 346 in their study) and differences in the timing of blood

sample collection, as our samples were obtained the day after PPCI. Similarly, Asoglu et al. [22] found significantly higher WBC counts in no-reflow patients ($12.08 \pm 3.1 \times 10^3/\mu\text{L}$ vs. $10.5 \pm 2.6 \times 10^3/\mu\text{L}$, $P < 0.01$).

Platelet count emerged as a significant marker of no-reflow in our study ($P < 0.001$, OR 1.036, 95% CI 1.020–1.052). Platelet activation and aggregation contribute significantly to the pathogenesis of thrombus formation and microvascular obstruction, which are key mechanisms underlying the no-reflow phenomenon. Increased platelet aggregation can impair myocardial perfusion even after successful PCI. A study by Kulickowski et al. [23] in Poland also found that poor response to antiplatelet therapy, often due to higher platelet activity, was significantly correlated with an elevated occurrence of the no-reflow phenomenon in diabetic patients undergoing PCI.

The adverse impact of the no-reflow phenomenon on clinical outcomes was demonstrated in the current investigation. The occurrence of HF was significantly elevated among individuals in the no-reflow group compared to those with normal reflow (56.76% vs. 12.05%, $P < 0.001$). Similarly, the occurrence of AF was markedly elevated in the no-reflow group (32.43% vs. 9.64%, $P = 0.002$). Although in-hospital mortality was elevated in individuals with no-reflow (8.11% vs. 3.61%), the observed difference failed to achieve statistical significance ($P = 0.371$).

These results are consistent with the findings reported by Refaat et al. [24] who observed significantly higher rates of heart failure ($P < 0.001$) and arrhythmias ($P < 0.01$) in the no-reflow group. However, their study also found significantly higher in-hospital mortality, which may be attributed to their larger sample size (400 patients vs. 120 in our study) and a higher reported incidence of no-reflow (43% vs. 30.83%).

This study has several limitations that should be acknowledged. First, the use of TIMI flow grade as the sole method for diagnosing the no-reflow phenomenon represents a potential limitation as it primarily reflects epicardial blood flow and may not fully capture microvascular tissue-level reperfusion. More sensitive techniques, such as Myocardial Blush Grade (MBG) or Cardiovascular Magnetic Resonance (CMR) imaging, provide more accurate assessments of myocardial perfusion and microvascular obstruction. Second, important confounding factors, such as the duration of symptoms before reperfusion and the specific type of stent platform used, were not captured or analyzed, which may influence outcomes related to no-reflow and myocardial recovery. Additionally, the single-center design, small sample size, potential patient selection bias excluding more severe cases, and reliance on retrospective medical records may reduce statistical power, generalizability, and data accuracy.

To enhance clinical outcomes and minimize the occurrence of no-reflow, we recommend optimal control of cardiovascular risk factors, particularly HTN, dyslipidemia, and renal dysfunction. Early identification and management of high-risk patients using predictive markers such as platelet count, HDL, TGs, and renal function. Personalized antiplatelet therapy to prevent thrombus formation and microvascular obstruction. Aggressive lipid-lowering strategies to mitigate microvascular dysfunction.

Conclusion

The no-reflow phenomenon is a common complication in diabetic patients presenting with STEMI undergoing PPCI. It is influenced by a combination of clinical and laboratory factors, including advanced age, smoking, hypertension, dyslipidemia, renal impairment, elevated serum uric acid levels, and reduced GFR. Patients who develop no-reflow are at a markedly increased risk of adverse in-hospital outcomes, particularly HF and AF. Identifying these high-risk factors is essential to optimizing outcomes and improving prognosis during and after PCI.

Ethics Compliance

We confirm that the study was conducted in compliance with ethical guidelines and that all necessary approvals and consents were obtained.

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Competing interests

The authors have no financial or proprietary interests in any material discussed in this article.

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List of Abbreviations

- AMI:** Acute myocardial infarction
PPCI: Primary percutaneous coronary intervention
SBP: Systolic blood pressure
DBP: Diastolic blood pressure
HDL: High-density lipoprotein
TGs: Triglycerides
GFR: Glomerular filtration rate
STEMI: ST-elevation myocardial infarction
CHD: Coronary heart disease
DM: Diabetes mellitus
PCI: Percutaneous coronary intervention
CABG: Coronary artery bypass grafting
IRA: Infarct-related artery
ACT: Activated clotting time
MBG: Myocardial blush grade
DES: Drug-eluting stents
MACE: Major adverse cardiac events
TIMI: Thrombolysis In Myocardial Infarction

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