Původní sdělení | Original research article

Predictors and Outcomes of No-reflow among Acute ST-Segment Elevation Myocardial Infarction Patients

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SOUHRN

Kontext: No-reflow fenomén (no-reflow phenomenon, NRP) se může vyskytovat až u 40 % pacientů po primární perkutánní koronární intervenci (PPCI) pro akutní infarkt myokardu s elevacemi úseku ST (acute ST-segment elevation myocardial infarction, STEMI). NRP významně zmenšuje přínos reperfuzní terapie; výsledkem je větší rozsah infarktu a horší výsledný stav pacienta. I když přesná patofyziologie poškození tkání po období bez perfuze není zcela známa, mohou k němu přispívat různé faktory různými mechanismy.
Cíl: V této studii bylo cílem zkoumat klinické a intervenční prediktory NRP a jejich dopady na nemocniční výsledky v kohortě pacientů po akutním STEMI převezených na pracoviště terciární péče v Egyptě.
Metody: Do nemocnice Kasr Al Ainy v egyptské Káhiře bylo přijato celkem 1 015 pacientu s vysoce rizikovým akutním koronárním syndromem, z tohoto počtu 502 se STEMI a 513 s NSTEMI. Do naší prospektivní studie bylo zařazeno 337 pacientů s bolestí na hrudi trvající 20 minut během posledních 48 hodin před příjmem, splňovali kritéria akutního STEMI a byla u nich provedena PPCI. Tito pacienti byli podle angiografického nálezu rozděleni do dvou skupin: skupina „no-reflow" (n = 72) a skupina „reflow" (n = 265).
Výsledky: Obě skupiny si byly podobné z hlediska věku a poměru muži : ženy. Průměrný věk ve skupině „no-reflow" byl 56 ± 10 let a ve skupině „reflow" 55 ± 10 let. Více bylo mužů a ve skupině „reflow" byl častěji přítomen diabetes mellitus (p = 0,034). Většina pacientů v obou skupinách prodělala infarkt myokardu (IM) přední stěny (61 % v „no-reflow" vs. 56 % v „reflow"; p = 0,1). Ve skupině „no-reflow" byla zjištěna delší prodleva před převozem do nemocnice (medián 6,5 hodiny) ve srovnání se skupinou „reflow" (medián 5,0 hodiny); 61 % pacientů ve skupině „no-reflow" bylo do nemocnice přivezeno pozdě (bolest na hrudi > 6 hodin) versus 45,7 % ve skupině „reflow" (p < 0,024). Většině pacientů byly aplikovány nasycovací dávky duální antiagregační terapie (DAPT), převážně clopidogrel (82 % vs. 18 % ticagrelor), bez statisticky významných rozdílů mezi skupinami. Medián doby od převezení pacienta ke vstupu do nemocnice do zavedení vodiče (door-to-wire crossing time) byl delší ve skupině „no-reflow" (110 vs. 90 minut; p = 0,007). Pouze prodleva do převozu do nemocnice (> 6 hodin) (p = 0,024) a doba „door-to-wire crossing" (p = 0,007) byly spojeny s „no-reflow", přičemž doba „door-to-wire crossing" byla nezávislým prediktorem (p = 0,009). Ve skupině „no-reflow" došlo k více komplikacím během pobytu v nemocnici a v uvedené skupině se závažné nežádoucí kardiovaskulární příhody vyskytly častěji než ve skupině „reflow" (24 % vs. 12,4 %; p = 0,024). Ve skupině „no-reflow" byly rovněž naměřeny nižší hodnoty ejekční frakce po katetrizaci (medián 42 % vs. 50 %; p < 0,0001).
Závěr: Přes veškerý pokrok v léčbě infarktu myokardu s elevacemi úseku ST zůstává incidence „no-reflow" fenoménu po primární PCI statisticky významná a souvisí s vyšší mortalitou s nepříznivou prognózou. Tato studie prokázala, že větší prodleva při přepravě pacienta do nemocnice (více než 6 hodin) a delší doba „door-to-wire crossing" představují nezávislé prediktory vzniku no-reflow fenoménu. Je třeba soustředit veškeré úsilí na zkrácení prodlevy při přepravě pacienta do nemocnice a optimalizaci organizace příjmu pacienta a zkrátit tak dobu „door-to-wire crossing" na minimum.

Keywords:
No-reflow phenomenon
Primary PCI
STEMI

ABSTRACT

Background: The no-reflow phenomenon (NRP) can occur in up to 40% of patients after primary percutaneous coronary intervention (PPCI) for acute ST-segment elevation myocardial infarction (STEMI). NRP significantly diminishes the benefits of reperfusion therapy, leading to increased infarct size and poorer outcomes. Although the exact pathophysiology of non-reperfusion injury (NRP) is not fully understood, various factors may contribute to it through different mechanisms.

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Aim: In this study, we aim to investigate clinical and interventional predictors of no-reflow and their impact on in-hospital outcomes among a cohort of acute STEMI patients presenting to a tertiary care center in Egypt.

Methods: A total of 1,015 patients were admitted to Kasralainy Hospital with high-risk acute coronary syndrome, including 502 with STEMI and 513 with NSTEMI. This prospective study included 337 patients who had chest pain for over 20 minutes in the 48 hours before admission, met the criteria for acute STEMI, and underwent PPCI. These patients were divided into two groups based on the angiography findings: the no-reflow group (n = 72) and the reflow group (n = 265).

Results: Both groups were similar in age and gender, with average ages of 56 ± 10 years in the no-reflow group and 55 ± 10 years in the reflow group. Males were predominant, and the reflow group had a higher rate of diabetes mellitus (p = 0.034). Most patients in both groups had anterior myocardial infarction (MI) (61% in no-reflow vs. 56% in reflow, p = 0.1). The no-reflow group had a longer median pre-hospital delay (6.5 hours) compared to the reflow group (5.0 hours), with 61% of no-reflow patients presenting late (chest pain > 6 hours) versus 45.7% in the reflow group (p <0.024). Most patients received loading doses of dual antiplatelet therapy (DAPT), predominantly clopidogrel (82% vs. 18% for ticagrelor), with no significant differences between groups. The median door-to-wire crossing time was longer in the no-reflow group (110 vs. 90 minutes; p = 0.007). Only pre-hospital delay (> 6 hours) (p = 0.024) and door-to-wire crossing time (p = 0.007) were associated with no-reflow, with the latter being an independent predictor (p = 0.009). The no-reflow group experienced more in-hospital complications, with major adverse cardiovascular events occurring more frequently compared to the reflow group (24% vs. 12.4%, p = 0.024). Furthermore, they had lower post-catheterization ejection fractions (median 42% vs. 50%; p <0.0001).

Conclusion: Despite advances in managing ST-segment elevation myocardial infarction, the no-reflow incidence after primary PCI remains significant, linked to higher mortality and poor prognosis. This study found that prolonged pre-hospital delay (over 6 hours) and longer door-to-wire crossing times are independent predictors of no-reflow. Efforts should focus on reducing pre-hospital delays and optimizing in-hospital pathways to minimize door-to-wire times.

Background

The "no-reflow" phenomenon (NRP) is defined as failure of restoration of myocardial perfusion despite opening the occluded epicardial coronary artery with a balloon or stent in the absence of flow-limiting residual stenosis (<50%), or mechanical obstruction.[1] The incidence of NRP after PPCI for acute ST-segment elevation myocardial infarction (STEMI) is high, reaching up to 40% in some studies.[2]

When it occurs, NRP can be reversible after prompt intervention during the PCI procedure; however, if it becomes persistent, it significantly attenuates the beneficial impact of reperfusion therapy, resulting in postprocedural myocardial infarction or a larger infarct size with poor short- and long-term outcomes.[3] Patients who develop NR show lower left ventricular ejection fraction, adverse left ventricular remodeling in the remote stage of myocardial infarction, and increased incidences of heart failure, cardiac rupture, and death, compared with patients without NR.[4]

The pathophysiology of non-reperfusion injury (NRP) is not yet fully understood, but several factors can contribute to it through various mechanisms. These include leukocyte infiltration, vasoconstriction, activation of inflammatory pathways, vascular damage, and increased endothelial permeability. Due to its harmful effects, it is crucial to prevent and treat NRP promptly to avoid permanent myocardial damage and improve prognosis.

In this study, we aim to investigate clinical and interventional predictors of no-reflow and their impact on in-hospital outcomes among a cohort of acute STEMI patients presenting to a tertiary care center in Egypt.

Methods

Throughout the study period (from December 2021 to August 2023), 1015 patients were admitted to Kasralainy Hospital with high-risk acute coronary syndrome, including STEMI (n = 502 patients) and NSTEMI (n = 513 patients). The inclusion criteria were patients aged >18 years with chest pain or equivalent symptoms of more than 20 minutes within the last 48 hours before admission to the hospital, who fulfilled the diagnosis of acute STEMI according to the ESC guidelines for the management of STEMI[5] and underwent PPCI treatment. The exclusion criteria were patients who refused treatment and whose clinical data of admission and hospital course were deficient.

After all the criteria were met, this study included 337 patients who were divided according to the presence/absence of the no-reflow phenomenon during the angiography procedure into no-reflow (n = 72) and reflow (n = 265) groups. **Figure 1** contains the flow chart of study population.

The study protocol was approved by the Ethics Committee of Faculty of Medicine, Cairo University. A written informed consent was obtained from all participants at the time of enrollment.

Data collection

Upon patients' presentation to the Emergency Department (ED), a detailed history including age, sex, and conventional risk factors for atherosclerotic cardiovascular disease (ASCVD) such as smoking, hypertension, diabetes mellitus, dyslipidemia, and family history of premature CAD were obtained, in addition to any history of previous cardiac and non-cardiac diseases. Physical exami-

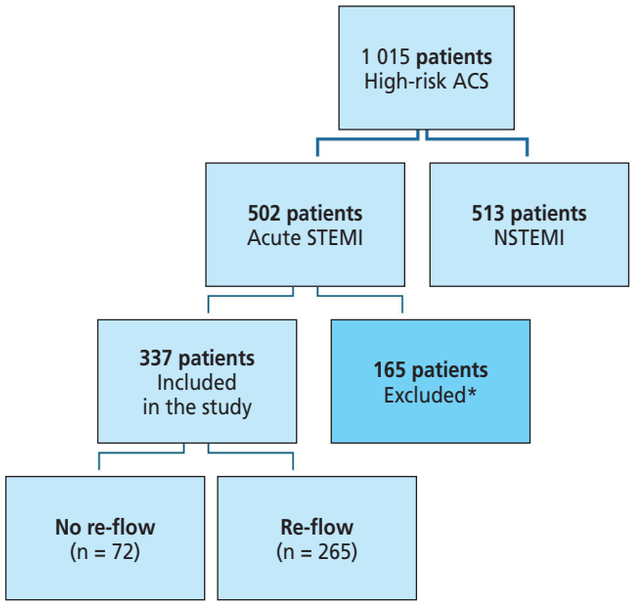

Fig. 1 – Study population. ACS – acute coronary syndrome; NSTEMI – non-ST-segment elevation myocardial infarction; STEMI – ST-segment elevation myocardial infarction. * Patients with missed STEMI, those treated without stenting, or with inadequate clinical or investigational data.

nation during admission focused on vital signs, defining Killip class, and mechanical complications.

Definitions and outcomes

No-reflow was defined as post-PCI angiographic documentation of a TIMI flow grade ≤2, or a TIMI flow grade 3 with a TIMI myocardial perfusion grade (TMPG) of 0 or 1, in the absence of post-procedural residual stenosis ≥50%, or mechanical obstruction (e.g. dissection, or perforation).[6] TIMI myocardial perfusion grade (TMPG): was defined according to the following scale: (grade: 0, no myocardial blush; grade 1: minimal myocardial blush or contrast density; grade 2: moderate myocardial blush or contrast density, but less than that obtained during angiography of a contralateral non-infarct-related coronary artery; and grade 3: normal myocardial blush or contrast density, similar to that obtained during angiography of a contralateral non-infarct-related coronary artery).[7] Transient was defined as no-reflow occurred during the procedure, which improved with treatment.

The primary outcome was a composite major adverse cardiovascular event (MACE): defined as mortality, or heart failure, while the secondary outcomes were individual complications: mortality, heart failure, cardiogenic shock, ejection fraction, and hospital stay length.

Statistical analysis

Results were expressed as mean ± standard deviation (SD), median, minimum, and maximum in quantitative data and using frequency and percentage for categorical data. Comparisons between quantitative variables were made using analysis of variance (ANOVA) in normally distributed quantitative variables while the non-parametric Kruskal–Wallis's test and Mann–Whitney test were used for non-normally distributed quantitative variables. Correlations between quantitative variables were done using Spearman correlation coefficient. *P*-values less than 0.05 were considered statistically significant. The Statistical Package for Social Sciences (SPSS, Inc, Chicago, IL, USA, version 25) was used for statistical analysis.

Results

Baseline characteristics

This prospective study included 337 STEMI patients presented to Kasraliny Hospital, Cairo University. The pati-

Table 1 – Baseline demographic, risk factors, and laboratory data of both study groups

Patient characteristics	No-reflow number (%) (N = 72)	Reflow number (%) (N = 265)	*p-value*
Age mean ± SD	56 ± 10 years	55 ± 10 years	0.652
Male gender, n (%)	64 (89%)	211 (80%)	0.65
Cardiovascular risk factors			
Diabetes mellitus, n (%)	16 (22%)	96 (36%)	0.034*
Hypertension, n (%)	20 (28%)	99 (37%)	0.164
Current cigarette smokers, n (%)	48 (67%)	175 (66%)	0.83
Dyslipidemia, n (%)	16 (57%)	118 (76%)	0.063
Drug/Cannabis addiction, n (%)	1 (1.4%)	7 (2.7%)	1
FH, n (%)	1 (1.4%)	11 (4.2%)	0.47
Coronary artery disease, n (%)	11 (15%)	36 (14%)	0.7
Cerebrovascular stroke/TIA, n (%)	2 (2.8%)	14 (5.3%)	0.54
Chronic kidney disease (GFR< 60 ml/min/1,73 m^2), n (%)	2 (2.8%)	7 (2.7%)	1

FH – family history of premature cardiovascular disease; GFR – glomerular filtration rate; SD – standard deviation; TIA – transient ischemic attacks. * *p*-value <0.05 was considered significant.

ents were divided into 2 groups according to TIMI flow grades after PPCI: the no-reflow group (n =72) and the reflow group (n = 265). **Tables 1** and **2** demonstrate the baseline demographic, risk factors, laboratory, echocardiographic, and interventional data of patients in the no-reflow group compared to those in the reflow group.

Both groups were homogeneous in terms of age and gender. The mean age of both groups was 56 ± 10 years for the no-reflow group and 55 ± 10 years for the reflow group, respectively. The male gender was predominant in both groups. The rate of diabetes mellitus was higher in the reflow group (p = 0.034).

The other risk factors, such as hypertension, dyslipidemia, current smoking, family history of coronary artery disease, and previous coronary artery disease (CAD), were not significantly different between the reflow group and the no-reflow group (p >0.05).

Most of the patients of both groups had anterior MI (61% in NR vs 56% in reflow, p = 0.1). Patients in the NR group had a longer pre-hospital delay, with the median

Table 2 – Baseline clinical and laboratory data of both study groups

Patient characteristics		No-reflow median (IR) (N = 72)	Reflow median (IR) (N = 265)	*p*-value
Pre-hospital delay (hours)		6.5 (4–12)	5.0 (3–10)	0.099
Chest pain >6 hrs, n (%)		44 (61%)	118 (45.7%)	0.024*
Pre-infarction angina, n (%)		31 (43%)	128 (49%)	0.426
Anterior MI, n (%)		48 (66%)	148 (56%)	0.107
Q wave, n (%)		33 (45%)	107 (41%)	0.503
DAPT before presentation, n (%)		4 (6%)	30 (12%)	0.135
$P2Y_{12}$ inhibitor, n (%)	Clopidogrel	55 (76.4%)	222 (84.2%)	0.161
	Ticagrelor	17 (23.6%)	42 (15.8%)	
Killip class, n (%)	I	57 (79.2%)	240 (91.3%)	0.71
	II	9 (12.5%)	12 (4.6%)	
	III	3 (4.2%)	6 (2.3%)	
	IV	2 (2.8%)	3 (1.1%)	
BP systole, median (IR)		120 (10–150)	130 (110–150)	0.425
BP diastole, median (IR)		80 (70–90)	80 (70–90)	0.331
HR, median (IR)		90 (70–100)	80 (70–95)	0.122
HB (gm/dl), median (IR)		14 (13.1–15.2)	14 (12.6–15.4)	0.642
TLC (10^9/L), median (IR)		10.2 (8.3–13.7)	10 (8–14.8)	0.488
PLTS (10^9/L), median (IR)		272 (228–247)	276 (226–336)	0.600
RBS (mg/dl), median (IR)		161.50 (118–232)	160.5 (121–245)	0.450
Door-to-balloon (min), median (IR)		110 (73–122)	90 (60–120)	0.007*

BP – blood pressure; HR – heart rate; HB – hemoglobin; IR – interquartile range; PLTs – platelets; RBS – random blood sugar; TLC – total leucocytic count. * p-value <0.05 was considered significant.

Table 3 – Complications at presentation

Complications	No-reflow median (IR) (N = 72)	Reflow median (IR) (N = 265)	*p*-value
Arrest, n (%)	1 (1.4%)	2 (0.8%)	NS
VT, n (%)	1 (1.4%)	7 (2.6%)	NS
Shock, n (%)	3 (4.2%)	2 (0.8%)	NS
Heart block, n (%)	1 (1.4%)	7 (3.0%)	NS
Hypotension, n (%)	2 (2.8%)	7 (3.0%)	NS
DKA, n (%)	1 (1.4%)	5 (1.9%)	NS
CVS, n (%)	1 (1.4%)	2 (0.8%)	NS

CVS – cerebrovascular stroke; DKA – diabetic ketoacidosis; NS – non-significant; VT – ventricular tachycardia.

pre-hospital delay of 6.5 hours compared to 5.0 hours in the reflow group. About 61% of patients in the NR group were late presenters (chest pain > 6 hours), compared to 45.7% in the reflow group (p <0.024). Both groups had similar rates of pre-infarction angina during the last few days before presentation. The presence of Q waves in the initial ECG showed no difference between both groups, and it couldn't be used as a predictor for the occurrence of no-reflow. There was no statistically significant difference in both groups regarding the vital signs and basic laboratory findings upon presentation.

Most patients received loading doses of dual antiplatelet therapy (DAPT) before PCI. Clopidogrel as a $P2Y_{12}$ inhibitor was the most frequently used compared to ticagrelor (82% vs 18%), with no statistically significant difference between the two groups. More patients in the reflow group were preloaded with DAPT before hospital presentation; however, this didn't result in a significant impact on the occurrence of NR. The minority of patients in both groups presented with either cardiac or non-cardiac complications, such as illustrated in **Table 3**.

The median door-to-wire crossing time was longer in the NR group compared to the reflow group (110 vs 90 minutes) with a statistically significant difference (p = 0.007).

Angiographic findings and PCI characteristics

Femoral access was utilized in most of the study population. The left anterior descending artery was the most common culprit vessel in both groups. The initial TIMI flow and thrombus grade (after passing a wire) show no statistically significant difference between the groups (**Table 4**).

The mean reference vessel diameter and target lesion length were comparable in both groups. Regarding lesion preparation, balloon pre-dilatation was done in most of the patients in both groups, compared to direct stenting. The number of stents deployed, and their length and diameter, didn't show a statistically significant difference between the two groups. The failure of >50% resolution of ST-segment was more frequent in NR compared to the reflow group (45% and 23%, respectively, p <0.0001).

Predictors of no-reflow

Among different variables, only pre-hospital delay (>6 hours) (p = 0.024) and door-to-wire crossing time (p = 0.007) were associated with the occurrence of no-reflow. Using the multivariate regression analysis, only the door--to-wire crossing time was an independent predictor factor for no-reflow (p = 0.009).

Table 4 – Angiographic and PCI findings

Variables		No-reflow number (%) (N = 72)	Reflow number (%) (N = 265)	*p-value*
Radial access, n (%)		29 (40%)	78 (29%)	0.088
Culprit vessel, n (%)	LAD	50 (69%)	153 (57.7%)	0.092
	LCx	6 (8.3%)	38 (14.3%)	
	RCA	14 (19.4%)	70 (26.4%)	
	SVG	2 (2.7)	2 (0.8)	
	LIMA	–	2 (0.8)	
TIMI flow, n (%)	0	57 (79.2%)	180 (67.9%)	0.099
	I	3 (4.2%)	10 (3.8%)	
	II	10 (13.9%)	42 (15.8%)	
	III	2 (2.8%)	33 (12.5%)	
Thrombus grade, n (%)	High (4/4)	46 (63.9%)	139 (52.5%)	0.232
	Low (1–3/4)	26 (36.1%)	126 (47.5%)	
Lesion length >20 mm, n (%)		50 (69.4%)	162 (61.1%)	0.217
Coronary ectasia, n (%)		4 (8.2%)	14 (7.8%)	1.0
Method of reperfusion, n (%)	Pre-dilatation	66 (91.7%)	222 (83.8%)	0.130
	Direct stent	6 (6.3%)	43 (16.2%)	
Post dilatation, n (%)		36 (50%)	144 (54.3%)	0.594
More than 1 stent, n (%)		15 (20.8%)	54 (20.3%)	0.566
Stent diameter, median (IR)		3.2 ± 0.6mm	3.2 ± 0.5 mm	0.427
Stent length, median (IR)		35 ± 14 mm	36 ± 13 mm	0.615
Post-cath absence of ST-segment resolution >50%, n (%)		33 (45%)	58 (23%)	<0.0001*

LAD – left anterior descending coronary artery; LCx – left circumflex artery; LIMA – left internal mammary artery; RCA – right coronary artery; SVG – saphenous venous graft. * p-value <0.05 was considered significant.

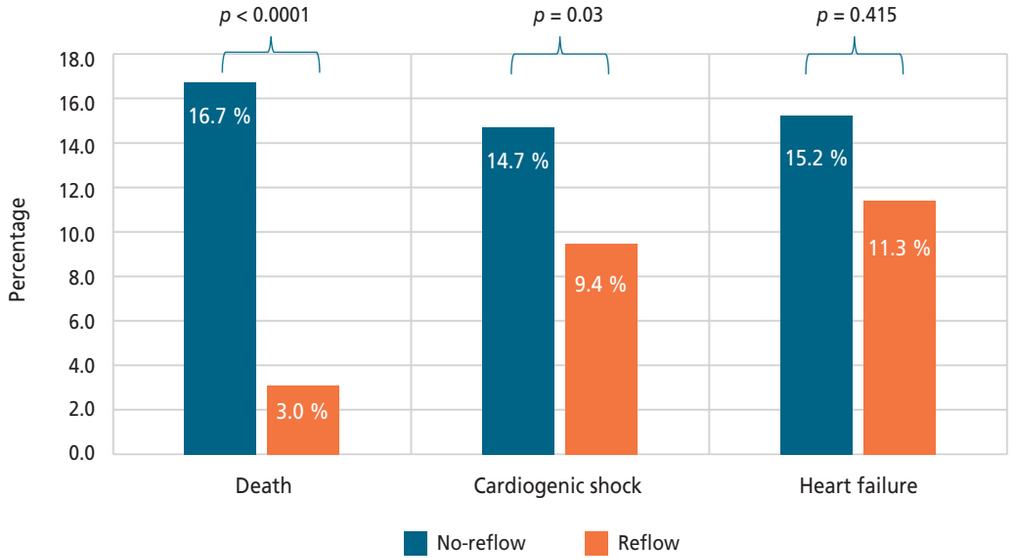

Fig. 2 – Adverse cardiovascular outcomes.

Table 5 – Incidence of adverse clinical outcomes in both groups

Variables	No-reflow number (%) (N = 72)	Reflow number (%) (N = 265)	*p*-value
MACE, n (%)	17 (24%)	33 (12.4%)	0.024*
Death, n (%)	12 (16.7%)	8 (3%)	<0.0001*
HF, n (%)	11 (15.2%)	30 (11.3%)	0.415
Cardiogenic shock, n (%)	5 (14.7%)	13 (9.4%)	0.03*
EF % median (IR)	42 (35–52)	50 (40–55)	<0.0001*
EF <35%, n (%)	16 (27.1%)	28 (12.6%)	0.009*
Atrial fibrillation, n (%)	2 (5.9)	13 (4.9)	0.684
Hospital duration (day), median (IR)	3 (2.5–5)	3 (2–5)	0.278

EF – ejection fraction; HF – heart failure; IR – interquartile range; MACE – major adverse cardiac events. * *p*-value <0.05 was considered significant.

Outcomes of no-reflow

Compared to the reflow group, patients who had NR were more likely to develop in-hospital complications. Major adverse cardiovascular events, defined as death or heart failure, were more frequent in NR vs reflow group (24% vs 12.4%, respectively, $p = 0.024$). Individual complications such as death and cardiogenic shock were also more common in NR group (*p*-value <0.0001 and 0.03, respectively). Patients in the NR group had lower post-catheter EF compared to the reflow group (median 42% vs 50%, respectively, $p < 0.0001$) (**Table 5 and Fig. 2**).

Discussion

The present study assessed the predictors and outcomes of the no-reflow phenomenon among 337 patients with acute ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention.

Among the study cohort, the incidence of no-reflow after primary percutaneous coronary intervention (PCI) was 21.3%. The incidence of no-reflow in different studies varies (11% to 41%), depending mainly on the clinical setting and the methods used for diagnosis.[8]

Outcomes of no-reflow

In this study, patients who developed no-reflow had worse clinical outcomes compared to patients who achieved successful reperfusion. A nearly five-fold increase in mortality in NR group compared to the reflow group (16.7% vs. 3%, $p < 0.0001$). Similarly, major adverse cardiovascular events occurred in 24% of NR patients, compared to 12.4% in the reflow group ($p = 0.024$). Also, patients with no-reflow had significantly lower post-procedure ejection fractions (42% vs. 50%,

p <0.0001) and a higher incidence of severe left ventricular dysfunction (EF <35%).

Our results agreed with prior research demonstrating the detrimental impact of no-reflow on clinical outcomes in STEMI patients. A study by Choo et al. similarly found that patients with no-reflow had higher in-hospital mortality and an increased incidence of heart failure compared to those with successful reperfusion.[9] Additionally, Ndrepepa et al. reinforced the association between no-reflow and adverse left ventricular remodeling, demonstrating that no-reflow patients exhibited lower ejection fractions and larger infarct sizes in both the acute and chronic phases of myocardial infarction.[10]

At present, there are no specific therapies recommended for the routine management of no-reflow. However, the main pathological targets for pharmacological treatment are platelet activation pathway and vasoconstriction. In our study, the management of no-reflow was guided by the operator's judgment, and we did not evaluate the impact of different therapies on the outcomes. Some clinical trials have demonstrated the role of GPIIB/IIIA inhibitors in reducing NR.[11] However, its benefits may be less evident in the current era of potent $P2Y_{12}$ inhibitors. The use of intracoronary adenosine was associated with improved TIMI flow and reduced infarct size;[12] however, some studies reported no benefit in mortality.[13] Also, the other vasoactive substances showed variable efficacy include epinephrine,[14] sodium nitroprusside,[15] verapamil,[16] and nicorandil.[17] On the other hand, there are some drugs with less supportive evidence, including immunosuppressive agents such as cyclosporine,[18] and the tissue-specific modulator of vascular permeability, angiopoietin-like 4.[19] Recently, some experimental studies showed a potential benefit of imatinib, a tyrosine-kinase inhibitor, in the reduction of NR and infarct size.[20]

Predictors of no-reflow

Several clinical, procedural, and angiographic factors were identified as significant predictors of no-reflow, highlighting the importance of early risk stratification and intervention.

Patients in the no-reflow group were more likely to present with prolonged pre-hospital delay (>6 hours) and longer door-to-wire crossing time, which is a well-established contributor to microvascular dysfunction and myocardial injury. Consistent with our findings, previous studies have highlighted prolonged ischemic time and thrombus burden as key predictors of no-reflow, further supporting their role in microvascular injury and endothelial dysfunction.[21,22] This also underscores the clinical importance of early identification and management of patients at high risk for no-reflow. Therefore, efforts should be made to reduce pre-hospital and door-to-balloon delays.

NR patients demonstrated a higher incidence of post-procedure failure of resolution of ST-segment elevation, which correlates with impaired myocardial perfusion. This can be used to identify patients with a high likelihood of no-reflow who should be closely monitored post-procedure for early signs of heart failure and left ventricular dysfunction, allowing the timely initiation of cardioprotective therapies.[23]

While most previous studies corroborate our results, some studies have reported different predictors and outcomes of no-reflow. For instance, a study by Iwakura et al. suggested that pre-procedural TIMI flow and collateral circulation play a more significant role in predicting no-reflow than ischemic duration alone.[24] In contrast, our study did not find a statistically significant association between pre-procedural TIMI flow and no-reflow, potentially due to differences in patient populations and procedural techniques.

Additionally, some reports have suggested that preloading with $P2Y_{12}$ inhibitors such as ticagrelor may significantly reduce the risk of no-reflow.[25] However, in our study, although a greater proportion of reflow patients received dual antiplatelet therapy (DAPT) prior to PCI, this difference did not reach statistical significance. This discrepancy may be attributed to variations in timing of DAPT administration, and using clopidogrel in majority of patients compared to ticagrelor. Therefore, further investigation using larger prospective trials is warranted.

In the current cohort, there were no differences concerning artery diameter, mean lesion length, the length and diameter of the deployed stent between NR and reflow groups.

In contrast to Hideki Kitahara et al, who showed that an IRA diameter above 3.5 mm increased the occurrence of no-reflow,[26] our study demonstrates that large luminal size and stent size didn't show a significant impact on the occurrence of no-reflow.

The no-reflow phenomenon remains a significant challenge in STEMI management, with considerable implications for short- and long-term outcomes. Our study confirms that prolonged ischemic time, high thrombus burden, and procedural delays are key predictors of no-reflow and that affected patients experience significantly worse clinical outcomes.

While our findings align with existing literature, variations in predictors and interventions suggest the need for further research to refine risk stratification and optimize treatment strategies. Future studies should focus on novel therapeutic approaches aimed at preserving microvascular function and improving myocardial recovery in patients at high risk of no-reflow.

Conclusion

Despite new advances in the management of ST-segment elevation myocardial infarction, the incidence of no-reflow after primary PCI is still high, and it is associated with increased mortality and poor prognosis. In this study, the prolonged pre-hospital delay (greater than 6 hours) and the door-to-wire crossing time were identified as independent predictors of no-reflow. Therefore, all efforts should be made to modify factors associated with pre-hospital delay and establishing in-hospital fast pathways to shorten door-to-wire crossing time.

Conflict of interest

The authors declare that they have no competing interest.

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Ethical statement
The present study was conducted in accordance with the Declaration of Helsinki. Ethical approval was formally granted by the Cairo University Ethics Committee (ref. n. MD-406-2021).

Informed consent
Prior to inclusion, written informed consent was obtained from all individual participants.

References

1. Ndrepepa G, Tiroch K, Fusaro M, et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. J Am Coll Cardiol 2010;55:2383–2389.
2. Fajar JK, Heriansyah T, Rohman MS. The Predictors of No Reflow Phenomenon after Percutaneous Coronary Intervention in Patients with ST Elevation Myocardial Infarction: A Meta-Analysis. Indian Heart J 2018;70:S406–S418.
3. Kim MC, Cho JY, Jeong HC, et al. Long-Term Clinical Outcomes of Transient and Persistent No Reflow Phenomena Following Percutaneous Coronary Intervention in Patients with Acute Myocardial Infarction. Korean Circ J 2016;46:490–498.
4. Berg R, Buhari C. Treating and Preventing No Reflow in the Cardiac Catheterization Laboratory. Curr Cardiol Rev 2012;8:209–214.
5. Byrne RA, Rossello X, Coughlan JJ, et al. 2023 ESC guidelines for the management of acute coronary syndromes. Eur Heart J 2023;44:3720–3826. Erratum in: Eur Heart J 2024;45:1145.
6. Ndrepepa G, Tiroch K, Fusaro M, et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. J Am Coll Cardiol 2010;55:2383–2389.
7. van't Hof AW, Liem A, Suryapranata H, et al. Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction: myocardial blush grade. Circulation 1998;97:2302–2306.
8. Allencherril J, Jneid H, Atar D, et al. Pathophysiology, diagnosis, and management of the no-reflow phenomenon. Cardiovasc Drugs Ther 2019;33:589–597.
9. Choo EH, Kim PJ, Chang K, et al. The impact of no-reflow phenomena after primary percutaneous coronary intervention: a time-dependent analysis of mortality. Coron Artery Dis 2014;25:392–398.
10. Ndrepepa G, Tiroch K, Fusaro M, et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. J Am Coll Cardiol 2010;55:2383–2389.
11. Khattak S, Townend JN, Thomas MR. Impact of antiplatelet therapy on microvascular thrombosis during ST-elevation myocardial infarction. Front Mol Biosci 2024;11:1287553.
12. Ross AM, Gibbons RJ, Stone GW, et al. A randomized, double-blinded, placebo-controlled multicenter trial of adenosine as an adjunct to reperfusion in the treatment of acute myocardial infarction (AMISTAD-II). J Am Coll Cardiol 2005;45:1775–1780.
13. Navarese EP, Buffon A, Andreotti F, et al. Adenosine improves post-procedural coronary flow but not clinical outcomes in patients with acute coronary syndrome: a meta-analysis of randomized trials. Atherosclerosis 2012;222:1–7.
14. Jafari Afshar E, Samimisedeh P, Tayebi A, et al. Efficacy and safety of intracoronary epinephrine for the management of the no-reflow phenomenon following percutaneous coronary interventions: a systematic review study. Ther Adv Cardiovasc Dis 2023;17:17539447231154654.
15. Su Q, Li L, Naing KA, et al. Safety and effectiveness of nitroprusside in preventing no-reflow during percutaneous coronary intervention: a systematic review. Cell Biochem Biophys 2014;68:201–206.
16. Wang L, Cheng Z, Gu Y, et al. Short-term effects of verapamil and diltiazem in the treatment of no-reflow phenomenon: a meta-analysis of randomized controlled trials. Biomed Res Int 2015:2015:382086.
17. Fischell TA, Maheshwari A. Current applications for nicardipine in invasive and interventional cardiology. J Invasive Cardiol 2004;16:428–432.
18. Piot C, Croisille P, Staat P, et al. Effect of cyclosporine on reperfusion injury in acute myocardial infarction. N Engl J Med 2008;359:473–481.
19. Galaup A, Gomez E, Souktani, et al. Protection against myocardial infarction and no-reflow through preservation of vascular integrity by angiopoietin-like 4. Circulation 2012;125:140–149.
20. Konijnenberg LS, Luiken TT, Veltien A, et al. Imatinib attenuates reperfusion injury in a rat model of acute myocardial infarction. Basic Res Cardiol 2023;118:2.
21. Khalfallah M, Allaithy A, Maria DA. Impact of the total ischemia time on no-reflow phenomenon in patients with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention. Anatol J Cardiol 2022;26:382–387.
22. Liang T, Liu M, Wu C, et al. Risk factors for no-reflow phenomenon after percutaneous coronary intervention in patients with acute coronary syndrome. Rev Invest Clin 2017;69:139–145.
23. Brodie BR, Stuckey TD, Hansen C, et al. Relation between electrocardiographic ST-segment resolution and early and late outcomes after primary percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2005;95:343–348.
24. Iwakura K. Modulation of individual susceptibility to the no-reflow phenomenon after acute myocardial infarction. Curr Pharm Des 2013;19:4519–4528.
25. Dai W, Ye Z, Li L, Su Q. Effect of preoperative loading dose ticagrelor and clopidogrel on no-reflow phenomenon during intervention in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a systematic review and meta-analysis. Drug Des Devel Ther 2018:12:2039–2049.
26. Kitahara H, Okada K, Kimura T, et al. Impact of stent size selection on acute and long-term outcomes after drug-eluting stent implantation in de novo coronary lesions. Circ Cardiovasc Interv 2017;10:e004795.