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Intracoronary Administration of Epinephrine in the Refractory No-Reflow Phenomenon in Patients With Acute Myocardial Infarction

Aim	To evaluate the efficacy and safety of intracoronary epinephrine for the treatment of refractory no-reflow phenomenon in patients with ST-segment elevation myocardial infarction (STEMI) during percutaneous coronary intervention (PCI).
Material and methods	A single-site prospective controlled study «Intracoronary administration of epinephrine for refractory no-reflow phenomenon in patients with acute myocardial infarction» was conducted (registration on ClinicalTrials.gov: NCT04573751). The study included 40 patients with refractory no-reflow phenomenon, which was identified when it was not resolved with at least one of the following means: nitroglycerin, adenosine, papaverine, platelet receptor inhibitors IIB/IIIA, or thromboaspiration. Patients were divided into 2 groups: patients of group 1 (n=18) were injected with intracoronary epinephrine 100 μg, patients of group 2 (n=22) received standard therapy without epinephrine. The groups did not differ in the main baseline clinical and anamnestic characteristics, with the exception of the predominance of men in the control group: 86.4% vs. 55.6% (p=0.03).
Results	In the epinephrine group, TIMI 3 blood flow was more often achieved: 55.6% vs. 0% (p<0.01); reduction in ST elevation >50% within 1 hour after PCI: 72.2% vs. 31.8% (p=0.01). Concentrations of troponin I 12–24 h after PCI were significantly lower in the epinephrine group than in the control group: 15.2 (6;25) ng/ml vs. 25 (10;40) ng/ml (p=0.03). No life-threatening hemodynamic disorders or cardiac arrhythmias were recorded after the administration of epinephrine. No statistically significant differences were found in cardiac ultrasound data and MACE (Major Adverse Cardiovascular Events) during 30 days of follow-up.
Conclusions	Intracoronary epinephrine 100 μg in STEMI patients with refractory no-reflow phenomenon during PCI is a safe and effective method for improving the blood flow in the infarct-related coronary artery. The prevalence of refractory no-reflow phenomenon among STEMI patients in our study reached 4.6%.

Keywords	Myocardial infarction; percutaneous coronary intervention; no-reflow phenomenon
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Introduction

Percutaneous coronary intervention (PCI) represents the most effective and preferred method of restoring coronary blood flow in patients with acute ST-segment elevation myocardial infarction (STEMI) [1]. In some cases, PCI is complicated by the development of no-reflow phenomenon, which is defined as persistent impairment of myocardial perfusion in the area of blood supply of the infarct-related coronary artery (IRCA) after restoration of its potency. This phenomenon is characterized by a decrease in angiographic coronary blood flow of less than 3 points on the TIMI scale [2]. This phenomenon has been known for over three decades. During this period, research has been conducted into the pathogenesis of the disease, and diagnostic criteria and prognostic methods have been developed [3–5].

The no-reflow phenomenon has been linked to adverse left ventricular (LV) remodeling, progressive LV failure, an elevated risk of LV wall rupture, and an increased mortality rate [6, 7]. The no-reflow phenomenon has been identified as an independent predictor of one-year mortality, with an adjusted risk of death that is three times higher in patients with STEMI undergoing PCI [8]. Therefore, the no-reflow phenomenon negates the advantages of early restoration of IRCA potency.

At present, a number of pharmacological agents and therapeutic modalities are available for the prevention of no-reflow phenomenon [9]. Some medications and

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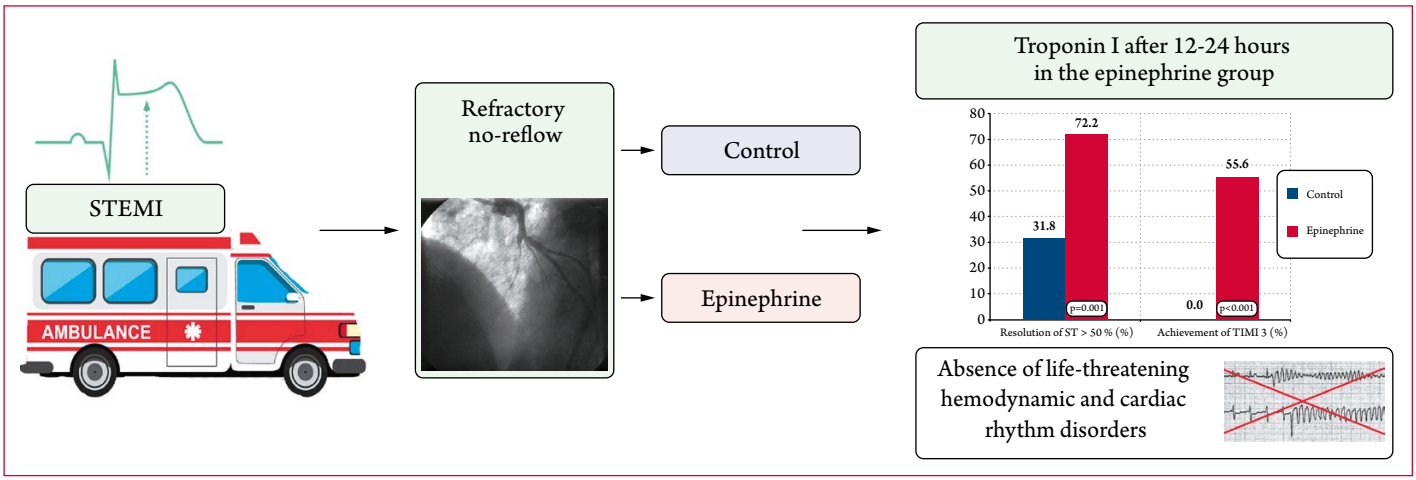
Central illustration. Intracoronary Administration of Epinephrine in the Refractory No-Reflow Phenomenon in Patients With Acute Myocardial Infarction



* – p <0,05; STEMI – ST-Elevation Myocardial Infarction; TIMI – Thrombolysis In Myocardial Infarction.

modalities, including calcium channel blockers, platelet IIb/IIIa receptor inhibitors, adenosine, and thrombus extraction, have demonstrated variable success in improving coronary blood flow [9, 10], though there is no evidence that they improve disease outcomes [11]. Nevertheless, in certain instances, the no-reflow phenomenon remains unresponsive to the administration of conventional treatments. Currently, there is a paucity of scientific research evaluating the efficacy of treatments for refractory no-reflow phenomenon. The available data is limited to clinical cases [12] and pilot studies [13]. Therefore, this issue of emergency cardiology remains a pertinent and pressing concern which must be addressed [14].

In light of the fact that one of the principal potentially reversible factors in the pathogenesis of the no-reflow phenomenon is microvascular arteriolar spasm, it can be reasonably assumed that drugs with a thrombolytic effect will have a beneficial impact. Epinephrine, also known as adrenaline, is an example of such a pharmacological agent. Although high-dose epinephrine administration exerts beneficial inotropic and chronotropic actions through the stimulation of beta-1 adrenoreceptors, lower doses have been observed to cause coronary dilation due to their agonistic effects on beta-2 adrenoreceptors. The results of several small pilot studies on testing intracoronary administration of epinephrine for no-reflow phenomenon have been published, yielding preliminary positive results [13, 15–17]. However, the power of these studies is insufficient to introduce such a technique into practice. Therefore, additional clinical studies in this direction are needed.

Objective

The objective of this study is to evaluate the efficacy and safety of intracoronary epinephrine administration in the treatment of refractory no-reflow phenomenon in STEMI patients undergoing PCI.

Material and Methods

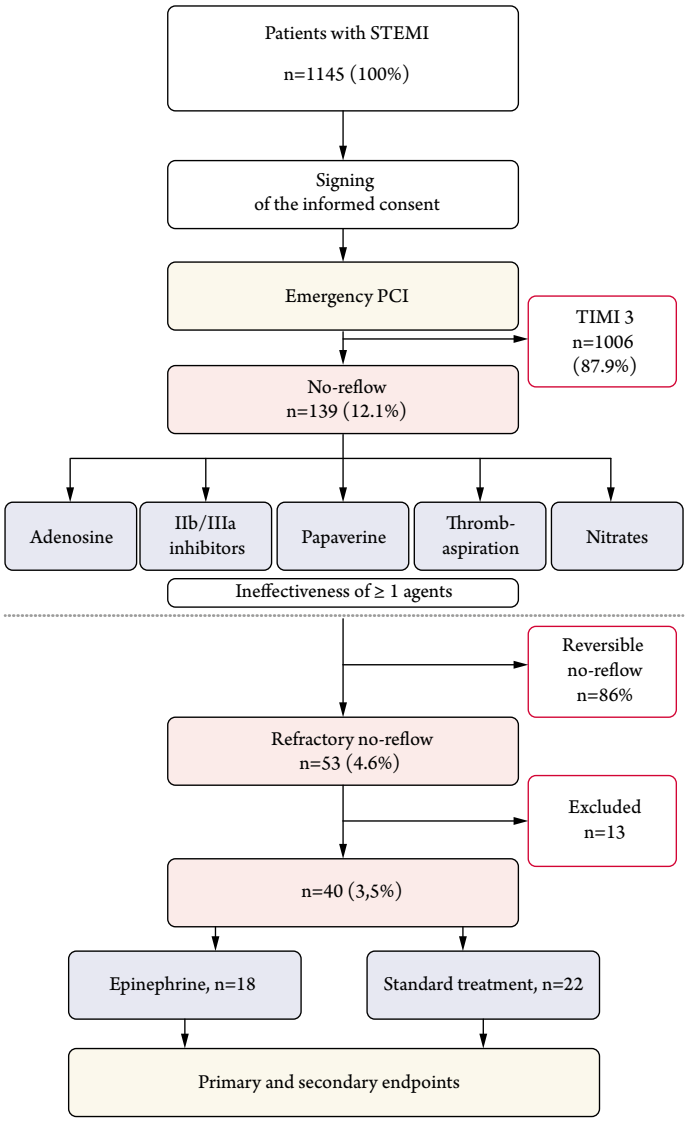
A single-center prospective controlled study, entitled «Intracoronary Administration of Epinephrine for Refractory No-Reflow Phenomenon in Patients with Acute Myocardial Infarction», was conducted at the Research Institute of Cardiology, a branch of the Tomsk National Research Medical Center. Prior to their inclusion in the study, all patients provided written informed consent for the intervention. The conduct of the study was approved by the local ethics committee (minutes no. 203 dated 14/10/2020). The protocol was registered on ClinicalTrials.gov under no. NCT04573751. The study was conducted in accordance with a protocol that was published in 2022 [18].

Inclusion criteria: 1. Acute ST-segment elevation myocardial infarction complicated by a refractory no-reflow phenomenon during PCI. 2. Signed informed consent form. *Exclusion criteria:* refractory cardiogenic shock requiring mechanical circulatory support.

The no-reflow phenomenon was defined as a reduction in anterograde angiographic blood flow in an infarct-related coronary artery (TIMI < 3), subsequent to stent deployment, in the absence of stent dissection and acute stent thrombosis. The no-reflow phenomenon was defined as refractory when it did not resolve with the administration of at least one of the following agents: nitroglycerin, adenosine, papaverine, glycoprotein IIB/IIIA inhibitors, and thrombaspiration.

In the event of the development of a refractory no-reflow phenomenon, the patients were divided into two groups. On even-numbered calendar days, the patients received standard therapy, which typically involved the administration of an additional drug from the aforementioned list, either

Figure 1. Study design



PCI, percutaneous coronary intervention.;
STEMI, ST-segment elevation myocardial infarction;
TIMI, Thrombolysis in Myocardial Infarction Score.

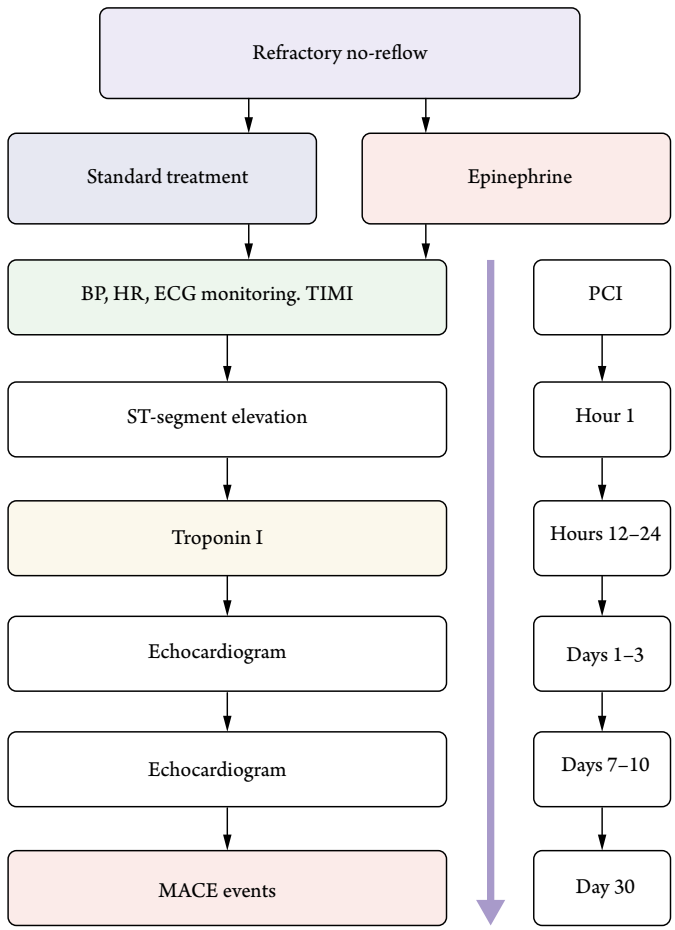
nitroglycerin or a platelet IIB/IIIA receptor inhibitor. Conversely, on odd-numbered calendar days, epinephrine 100 μg was administered once into the infarct-related coronary artery through a guiding catheter. One ampule of epinephrine 1 mL of 0.1% solution (1000 μg/mL) was diluted in 50 mL of physiologic solution (20 μg/mL). The prepared 5-mL syringe contained 100 μg of epinephrine. Figure 1 presents a flowchart outlining the temporal phases of standard therapeutic procedures.

Prior to PCI, patients were administered aspirin 250 mg, clopidogrel 600 mg, or ticagrelor 180 mg, a bolus of unfractionated heparin 70–100 IU/kg, followed by its infusion. The primary end point was the level of coronary blood flow in IRCA by TIMI scale following the administration of epinephrine. Secondary endpoints included: a) troponin I level 12–24 hours from admission; b) resolution of ST-segment elevation on ECG greater than 50% within 1 hour after PCI; c) left ventricular ejection fraction (LVEF), end-diastolic volume (LVEDV), end-systolic volume (LVESV), wall motion score index (WMSI) according to echocardiography at admission and after 7–10 days; d) changes in systolic and diastolic blood pressure (BP), heart rate (HR) after epinephrine administration; e) irregular heartbeats following epinephrine administration; f) MACE events within 30 days (Figure 2). MACE events were defined as cardiovascular deaths and hospitalizations for acute heart failure and acute myocardial infarction [19]. The clinical, laboratory, and investigational data pertaining to the patients were extracted from the case records. The 30 day clinical outcomes were obtained through telephone interviews.

Methods of statistical processing

The normality of the sample distribution of quantitative indicators was evaluated using the Shapiro–Wilk test. Normally distributed variables are represented by the mean and standard deviation, (m ± SD), and non-normally distributed variables are expressed by the median (Me) and

Figure 2. Research methods and endpoints



BP, blood pressure; PCI, percutaneous coronary intervention; HR, heart rate; ECG, electrocardiography; MACE, major adverse cardiovascular events;
TIMI, Thrombolysis in Myocardial Infarction Score.

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Table 1. Clinical and anamnestic characteristics of patients

Parameter	Epinephrine	Standard therapy	p
Patients, n (%)	18 (100)	22 (100)	
Age, years	62.0 (56.0; 70.0)	65.5 (61.0; 72.0)	0.20
Male, n (%)	10 (55.6)	19 (86.4)	0.03
Hypertensive heart disease, n (%)	18 (100)	21 (95.5)	0.27
Antihypertensive therapy, n (%)	8 (44.4)	8 (36.4)	0.60
Smoking status at admission / history of smoking, n (%)	10 (55.6)	15 (68.2)	0.41
Obesity, n (%)	7 (38.9)	11 (50)	0.78
Body mass index, kg/m^2	28.79 (25.5; 33.6)	29.35 (24.5; 33.6)	0.90
Diabetes mellitus, n (%)	9 (50)	12 (54.5)	0.77
History of angina pectoris, n (%)	4 (22.2)	6 (27.3)	0.71
PICS, n (%)	1 (5.6)	2 (9.1)	0.67
History of CVA, % (n)	3 (16.7)	2 (9.1)	0.47
Time from onset of ACS symptoms, patients admitted in the first 24 h, min	345.0 (190.0; 900.0)	320.0 (177.0; 600.0)	0.32
In the first 6 h, n (%)	9 (50)	11 (50)	0.77
6–24 h, n (%)	8 (44.4)	9 (40.9)	0.82
Later than 24 h, n (%)	1 (5.6)	2 (9.1)	0.88
Pre-hospital TLT, n (%)	5 (27.8)	5 (27.8)	0.97
AHF degree (Killip) at admission			
Killip I, n (%)	11 (61.1)	14 (63.6)	0.99
Killip II, n (%)	0 (0)	3 (13.6)	0.05
Killip III, n (%)	2 (11.1)	2 (9.1)	0.83
Killip IV, n (%)	5 (27.8)	3 (13.6)	0.27
Pre-hospital circulatory arrest, n (%)	1 (5.6)	3 (13.6)	0.38
Administration of P2Y12 platelet receptor inhibitors			
Clopidogrel, n (%)	8 (44.4)	14 (63.6)	0.22
Ticagrelor, n (%)	9 (50)	7 (31.8)	0.24
Prasugrel, n (%)	1 (5.6)	1 (4.6)	0.28
PCI parameters			
IRCA thrombosis, n (%)	10 (55.6)	12 (54.5)	0.92
Type of circulation			
Left, n (%)	2 (11.1)	3 (13.6)	0.81
Right, n (%)	12 (66.7)	8 (36.4)	0.06
Mixed, n (%)	4 (22.2)	11 (50)	0.07
IRCA:			
LAD, n (%)	8 (44.4)	11 (50)	0.73
LCX, n (%)	1 (5.6)	4 (18.2)	0.21
RCA, n (%)	7 (38.9)	5 (22.7)	0.27
PDA, n (%)	0 (0)	2 (9.1)	0.16
OM, n (%)	2 (11.1)	0 (0)	0.07
Anatomical location of MI			
Anterior, n (%)	8 (44.4)	11 (50)	0.73
Inferior, n (%)	10 (55.6)	11 (50)	0.73
NO-REFLOW management techniques			
Thrombaspiration, n (%)	7 (38.9)	7 (31.8)	0.72
IIb/IIIa inhibitor, n (%)	9 (50)	9 (40.9)	0.66
Papaverine, n (%)	2 (11.1)	0 (0)	0.07
Nitroglycerin, n (%)	15 (83.3)	17 (77.3)	0.85
Adenosine, n (%)	3 (16.7)	4 (18.2)	0.85
IABP, n (%)	0 (0)	1 (4.5)	0.27
IRCA blood flow (TIMI) following PCI prior to the administration of epinephrine			
TIMI 0, n (%)	2 (11.1)	4 (18.2)	0.53
TIMI 1, n (%)	4 (22.2)	3 (13.6)	0.48
TIMI 2, n (%)	12 (66.7)	15 (68.2)	0.92

Data are presented as median and interquartile range – Me (Q25; Q75), number of patients – n (%); AHF, acute heart failure; CVA, cerebrovascular accident; IABC, intra-aortic balloon counterpulsation; IRCA, infarct-related coronary artery; Killip, acute heart failure classification used in patients with confirmed acute coronary syndrome; LAD, left anterior descending artery; LCX, left circumflex branch; MI, myocardial infarction; OM, obtuse marginal branch; PCI, percutaneous coronary intervention; PDA, posterior descending artery; PICS, postinfarction cardiosclerosis; RCA, right coronary artery; TIMI, Thrombolysis in Myocardial Infarction Score; TLT, thrombolytic therapy.

interquartile range (Q25; Q75). Categorical indicators were expressed as absolute and relative (%) rates of incidence. The nonparametric Mann–Whitney test was employed to detect statistically significant differences in quantitative indices between independent patient groups receiving different treatment. Statistically significant changes in quantitative indicators were identified in dependent samples of normally distributed data using parametric repeated measures ANOVA (a comparison of changes in groups and paired Student's test for dynamic differences in each individual group). In dependent non-normally distributed samples, the non-parametric Wilcoxon test was employed. In independent groups, categorical indices were compared using either Pearson's chi squared test or Fisher's exact test. The threshold level of significance was set at p=0.05.

Results

From December 2020 to December 2022, a total of 1,145 patients with STEMI were referred for emergency PCI. Of the total number of patients, 139 (12.1%) exhibited the development of no-reflow phenomenon, which proved refractory to standard treatment in 53 (4.6%) cases. A total of 13 patients were identified as meeting the exclusion criteria. Accordingly, the 40 patients were distributed into two distinct groups. A total of 18 patients in Group 1 (the main group) received epinephrine, while 22 patients in Group 2 (the control group) received standard therapy without epinephrine (Figure 1).

The groups exhibited no significant differences in the main baseline clinical and anamnestic characteristics, with the exception of the control group, which included a greater percentage of males: 86.4% versus 55.6% (p = 0.03).

Table 2. Examination and treatment results

Parameter	Epinephrine, n=18	Standard therapy, n=22	p
Laboratory data			
Troponin I at admission, ng/mL	0.31 (0.08; 2.6)	1.49 (0.08; 2.4)	0.80
Troponin I after 12-24 hours, ng/mL	15.2 (6; 25)	25 (10; 40)	0.03
Clinical examinations			
Achievement of TIMI 3 at the end of PCI, n (%)	10 (55.6)	0 (0)	<0.001
ST-segment elevation resolution > 50 % within 1 hour, n (%)	13 (72.2)	7 (31.8)	0.01
Hemodynamic parameters and PCI complications			
SBP prior to agent administration, mm Hg	125.5 (±25.7)	133.1 (±17.7)	0.21
SBP after agent administration, mm Hg	141.7 (±15.9)	-	
DBP prior to agent administration, mm Hg	76.9 (±14.2)	83.6 (±12.9)	0.38
SBP after agent administration, mm Hg	84.1 (±9.3)	-	
HR prior to agent administration	77 (66; 92)	80.5 (69; 96)	0.55
HR after agent administration	110 (90; 124)	-	
VPB/SVPB after agent administration, n (%)	6 (33.3)	-	0.02
AF/AFL after agent administration, n (%)	3 (16.7)	-	0.55
VT after agent administration, n (%)	2 (11.1)	-	0.43
Echocardiographic measurements			
LVEDV, days 1–2, mL	95 (86; 109)	110 (98; 120)	0.19
LVESV, days 1–2, mL	50 (43; 61)	61 (48; 78)	0.21
LVEF, days 1–2, %	46 (43; 51)	45 (38;56)	0.73
WMSI, days 1–2	1.44 (1.31; 1.78)	1.69 (1.25; 2)	0.47
LVEDV, days 7–10, mL	101 (90; 115)	129 (110; 144)	0.08
LVESV, days 7–10, mL	44 (42; 59)	66.5 (42.5; 98)	0.15
LVEF, days 7–10, %	51 (48; 54)	48 (37.5; 55)	0.44
WMSI, days 7–10	1.44 (1.31; 1.75)	1.51 (1.24; 1.82)	0.71
Hospital mortality, n (%)	1 (5.6)	2 (9.1)	0.64
MACE events within 30 days, n (%)	2 (11.1)	5 (22.7)	0.37
30-day mortality, n (%)	1 (5.6)	3 (13.6)	0.41

Data are presented as median and interquartile range - Me (Q25; Q75), number of patients - n (%); AF, atrial fibrillation; AFL, atrial flutter; DBP, diastolic blood pressure; HR, heart rate; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-systolic volume; LVESV, left ventricular end-systolic volume; MACE, major adverse cardiovascular events; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; SVPB, supraventricular premature beat; TIMI, Thrombolysis in Myocardial Infarction Score; VPB, ventricular premature beat; VT, ventricular tachycardia; WMSI, wall motion score index.

The majority of patients in both groups presented with IRCA thrombosis: 54.5% and 55.6% in Groups 1 and 2, respectively (p=0.92). Furthermore, no differences were observed between the groups with regard to the treatment modalities and the degree of IRCA blood flow (TIMI) prior to the administration of epinephrine (Table 1).

The achievement of TIMI 3 blood flow was documented solely in the main group. Following the administration of epinephrine, a notable reduction in ST elevation of over 50% was observed within the first hour following PCI in the main group: 72.2% versus 31.8% (p=0.01) (Figure 3). Furthermore, troponin I levels 12 to 24 hours following PCI exhibited a notable decline in the main group in comparison to the control group: 15.2 (6;25) ng/mL versus 25 (10;40) ng/mL (p=0.03). In the main group, systolic BP increased from 125.5 ± 25.7 mm Hg to 141.7 ± 15.9 mm Hg (p=0.002), while diastolic BP increased from 76.9 ± 14.2 mm Hg to 84.1 (±9.3) mm Hg (p=0.005), and HR rose from 77 (66; 92) bpm to 110 (90; 124) bpm (p=0.002) following epinephrine administration. In the main group, supraventricular and ventricular extrasystoles were observed with greater frequency following epinephrine administration: 33.3% versus 0% (p=0.02). All episodes of elevated BP, HR, and extrasystoles were treated independently, and no further medication was required. The data obtained from cardiac ultrasound on days 7–10 of the disease indicated a reduction in left ventricular end-diastolic volume (LVEDV) and end-systolic volume (LVESV) and an increase in left ventricular ejection fraction in the main group when compared to the control group. However, this difference did not reach statistical significance (Table 2).

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ПОВЫШЕННОЕ СОДЕРЖАНИЕ ТРИГЛИЦЕРИДОВ В КРОВИ – НЕЗАВИСИМЫЙ ФАКТОР РИСКА СЕРДЕЧНО-СОСУДИСТОЙ И ОБЩЕЙ СМЕРТНОСТИ[1]

ДИАГНОСТИКА ДИСЛИПИДЕМИИ:

Всем лицам старше 40 лет рекомендуется скрининг, включающий анализ крови по оценке нарушений липидного обмена биохимический (липидный профиль) с целью стратификации сердечно-сосудистого риска по шкале SCORE-2

Определение ХС не-ЛВП рекомендовано всем пациентам для дополнительной оценки риска в системе SCORE-2

Пациентам любой категории риска рекомендован целевой уровень

ТГ 1,7 ммоль/л

Класс	Уровень
IIa	C

АЛГОРИТМ ТЕРАПИИ ГИПЕРТРИГЛИЦЕРИДЕМИИ

	Высокого и очень высокого риска, достигшим на терапии статинами уровня ТГ 1,7–2,3 ммоль/л	С уровнем ТГ > 2,3 ммоль/л на терапии статинами	С уровнем ТГ > 5,0 ммоль/л
Категория пациентов			
Рекомендация	+ Лекарственный препарат ПНЖК **ОМЕГА-3** доза: до 2 грамм 2 раза в день	**ФЕНОФИБРАТ** / **ФЕНОФИБРАТ + СТАТИН** предпочтительно в одной таблетке* **ИЛИ** + Лекарственный препарат ПНЖК **ОМЕГА-3** доза: до 2 г 2 раза в день	**ФЕНОФИБРАТ** **И** + Лекарственный препарат ПНЖК **ОМЕГА-3** доза: до 2 г 2 раза в день
Класс	IIa	IIa	IIa
Уровень	B	B	B

Достижение и удержание целевого уровня ХС ЛНП, ТГ является ключевым фактором, влияющим на прогноз и улучшающим сердечно-сосудистые исходы у пациентов как с ССЗ, так и СД

ВАЖНЫМИ ЦЕЛЯМИ ПРИ ЛЕЧЕНИИ ДИСЛИПИДЕМИИ ЯВЛЯЮТСЯ:

- максимальное снижение риска развития ССО и смертельных исходов;
- коррекция всех модифицируемых факторов риска (курение, избыточная масса тела, ожирение, гипергликемия, АГ).

1. Nordestgaard B. G. (2016). Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease: New Insights From Epidemiology, Genetics, and Biology. Circulation research, 118(4), 547–563. https://doi.org/10.1161/CIRCRESAHA.115.306249. * Зарегистрирован розувастатин+фенофибрат; ЦУ – целевой уровень; ТГ – триглицериды; ХС ЛНП – холестерин липопротеинов низкой плотности; ХС не-ЛНП – холестерин липопротеинов невысокой плотности; ПНЖК – полиненасыщенные жирные кислоты; СД – сахарный диабет; ССО - сердечно-сосудистые осложнения; АГ - артериальная гипертензия.
Клинические рекомендации «Нарушения липидного обмена» 2023, https://cr.minzdrav.gov.ru/recomend/752_1, Дата доступа: 16.06.2023.

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RUS2274693 (v1.2)

The mortality rate in the control group was three deaths during the hospital period, all of which were attributed to the development of cardiogenic shock. In the epinephrine cohort, one patient died due to hemorrhagic and cardiogenic shock. During the 30-day follow-up period, the incidence of MACE events was slightly lower in the epinephrine group: 11.1% versus 22.7% (p=0.37) (Table 2).

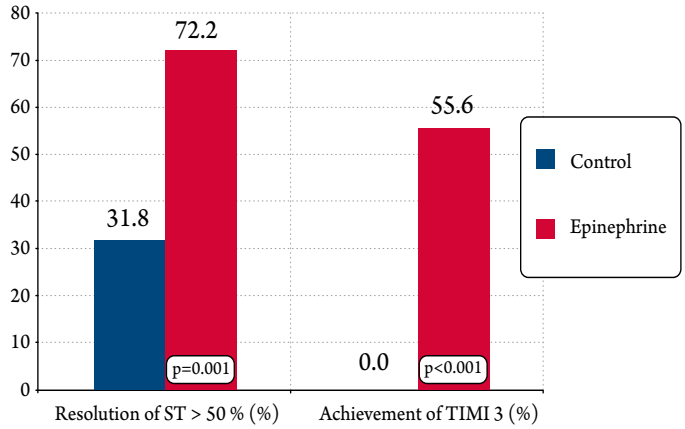
Discussion

It is established that the primary factor influencing the prognosis of STEMI is the duration of the IRCA occlusion. Nevertheless, the evidence from several studies indicates that reducing the door-to-balloon time does not result in a reduction in mortality in this disease [20]. One potential explanation for this is the no-reflow phenomenon, which has been demonstrated to reduce the efficacy of PCI. In the absence of a therapeutic alternative, epinephrine may be the optimal agent for the treatment of refractory no-reflow phenomenon. Refractory nature of the no-reflow phenomenon lacks a clear definition. In the RESTORE study, it was understood as the ineffectiveness of two treatment modalities [13], whereas in the study by Aksu et al., it was understood as the ineffectiveness of a single treatment modality [17]. The present study broadens the scope of indications for epinephrine by defining the concept as the ineffectiveness of a single treatment modality. In the RESTORE study, epinephrine was administered via a guiding catheter at the orifice of the occluded IRCA. We employed the same technique of administration. However, the available evidence indicates that the administration of epinephrine into the distal channel via the central lumen of the balloon catheter is more effective than at the orifice of the coronary artery [16]. However, the administration of epinephrine at the IRCA orifice is a more viable option, including for our own practice, and may be more widely adopted in clinical settings.

The findings of the study indicate that the administration of 100 μg of epinephrine via intracoronary route to patients presenting with refractory no-reflow phenomenon resulted in enhanced TIMI blood flow and a more rapid reduction of ST elevation (Figure 3). The relative safety of this treatment method was demonstrated by the absence of life-threatening complications in the main group following epinephrine administration (Table. 2).

Patients with IRCA thrombosis were found to be highly likely to have distal embolization as one of the primary factors in the pathogenesis of the no-reflow phenomenon. In contrast, in the others, persistent vasospasm, ischemic and reperfusion injury were identified as the predominant causes, although vasospasm was also identified as a significant contributor to distal embolization. This explains the beneficial effect of epinephrine. Lower levels of high-sensitivity troponin I in the main group (Table 2) are associated with a smaller volume of damaged myocardium, which can be considered a limitation of the volume of myocardial necrosis during epinephrine administration. All rhythm disturbances observed subsequent to epinephrine administration were noted in patients exhibiting improved blood flow in IRCA (Table 2). Therefore, these occurrences may be attributed to reperfusion syndrome, although the proarrhythmic effect of epinephrine cannot be discounted.

Figure 3. Impact of intracoronary epinephrine administration on angiographic blood flow and ST elevation changes



TIMI, Thrombolysis in Myocardial Infarction Score.

The observed downward trend in LVEDV and LVESV on days 7–10 of the disease (Table 2) may indicate a more favorable LV remodeling in the epinephrine group and, hence, a slight decrease in the incidence of MACE within 30 days. It can be reasonably anticipated that statistical significance for these indicators will be achieved with a larger patient cohort and a longer follow-up period. The collection of data in accordance with the established protocol is currently underway.

These findings are consistent with those of the RESTORE study, which included 30 patients with refractory no-reflow, and demonstrated the efficacy of epinephrine in improving angiographic coronary blood flow and better resolution of ST-segment elevation [13]. Additionally, these findings align with those of the COAR study, which showed the superiority of intracoronary administration of epinephrine over adenosine [21].

Limitations

The practice of allocating patients into groups based on the time of admission (even and odd days) does not constitute a complete randomization. A further limitation of the study is the relatively small number of patients included, which precluded the attainment of statistical significance in the observed trend towards improved echocardiographic parameters and clinical outcomes in the epinephrine group.

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Conclusions

The intracoronary administration of epinephrine at a dose of 100 mcg in patients with ST-segment elevation myocardial infarction and refractory no-reflow phenomenon during percutaneous coronary intervention is a safe and effective method to improve blood flow in the infarct-related coronary artery. The prevalence of refractory no-reflow phenomenon among patients presenting with ST-segment elevation myocardial infarction in the present study was 4.6%.

Ethics compliance

The study was conducted in accordance with the ethical standards set forth in the World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects, as amended in 2000, and the Rules of Clinical Practice in the Russian Federation, approved by Order No. 266 of the Ministry of Health of the Russian Federation dated June 19, 2003.

No conflict of interest is reported.

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