

# Impact of intracoronary contrast injection pressure on reperfusion during primary percutaneous coronary intervention in acute ST-segment elevation myocardial infarction: A prospective randomized pilot study

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## ARTICLE INFO

### Article history:

Received 6 July 2019

Received in revised form 27 July 2019

Accepted 12 August 2019

Available online 20 August 2019

### Keywords:

STEMI

Primary PCI

No-reflow phenomenon

Intracoronary pressure

Reperfusion

Myocardial blush grade

### Availability of data and materials:

The summarized data used to support the findings of this study have been deposited in the international registry [ClinicalTrials.gov](http://ClinicalTrials.gov) and can be found at appropriate web page ([clinicaltrials.gov](http://clinicaltrials.gov)) with the trial registration number. Also, the summarized data used to support the findings of this study are included within the article. The individual data used to support the findings of this study are restricted by the hospital's Ethics Committee (University Hospital Centre Sestre milosrdnice) in order to protect patients' privacy. Data are available from Ivan Zeljkovic, corresponding author, for researchers who meet the criteria for access to confidential data.

## ABSTRACT

**Background:** Distal embolization of plaque and thrombotic debris in the infarct-related artery (IRA) may lead to microvascular obstruction resulting in impaired myocardial reperfusion.

The aim of the study was to assess the impact of contrast injection pressure in IRA, during primary percutaneous coronary intervention (PCI), on myocardial reperfusion in patients with acute ST-segment elevation myocardial infarction (STEMI).

**Methods:** This prospective, randomized, open label, pilot trial evaluated acute STEMI patients who underwent primary PCI, with blinded evaluation of end points. Patients were assigned to higher injection pressure group A (550 pound/inch<sup>2</sup>) or lower injection pressure group B (200 pound/inch<sup>2</sup>). Primary endpoint was the postprocedural incidence of restored myocardial perfusion defined as myocardial blush grade (MBG) 3.

**Results:** Study included 100 consecutive acute STEMI patients, with median age of 63 (56–72) years (77% men) who were randomized to higher and lower injection pressure group. Baseline demographic, clinical and angiographic characteristics did not differ significantly between the groups. There were no significant differences between the study groups regarding difference in achieved MBG 3 (33 vs 36 patients,  $p = 0.247$ ) nor regarding the ST-segment deviation score neither immediately after (3 vs 4 mm,  $p > 0.3$ ) nor 24 h after primary PCI (2 vs 3 mm,  $p > 0.3$ ).

**Conclusion:** There was no impact of lower intracoronary contrast injection pressure in comparison to higher injection pressure, during primary PCI in patients with acute STEMI, on myocardial reperfusion as assessed by MBG or ST segment changes in the ECG.

The study was registered at registry [ClinicalTrials.gov](http://ClinicalTrials.gov) with the registration number: NCT03445364, on February 26th 2018.

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## 1. Background

Primary percutaneous coronary intervention (PCI) is the preferred treatment for patients with acute ST-segment elevation myocardial infarction (STEMI) and is effective in most instances, particularly when using coronary stents in infarct-related artery (IRA) [1,2]. Although completely revascularized patients yield better clinical results, assessing

complete patency of IRA does not necessarily lead to myocardial reperfusion [3]. Moreover, in up to 40% of patients, despite rapid and sustained patency of previously occluded coronary artery, microvascular obstruction with diminished myocardial reperfusion can still be observed [3,4]. This occurrence is known as no-reflow phenomenon and is contributing to increased infarct size, unfavorable left ventricle remodeling and poor clinical prognosis [4–6]. Embolization of plaque or thrombotic debris downstream in the IRA, which can occur either spontaneously or be induced by PCI, may lead to microvascular obstruction limiting the extent of myocardial reperfusion [4–6]. Myocardial perfusion can be assessed by angiographic

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myocardial blush grade (MBG) and by resolution of ST-segment changes on the 12-lead ECG, as well as by other methods the application of which during the acute STEMI is difficult and time consuming (Technetium-99 m Macroaggregated Albumin Scintigraphy and other types of scintigraphy, volumetric intravascular ultrasound, myocardial contrast echocardiography, thermodilution measurements of great cardiac vein flow) [5,7–9]. The high frequency of sub-optimal myocardial reperfusion after primary PCI resulted in an attempt to develop additional pharmacological interventions and mechanical devices to prevent and treat microvascular obstruction. Unfortunately, none of which showed clear and expressed efficacy, especially on clinical outcome [8,10–12].

The study hypothesis was: by using the controlled lower injection pressure of contrast during primary PCI in patients with acute STEMI, additional peripheral embolization of thrombi could be reduced (due to lower injection pressure with consequent lower dissipation of thrombus burden) and it would result in better final result of the procedure, assessed by MBG and resolution of ST-segment changes in ECG.

## 2. Methods

This was a single-center, randomized, prospective, open label, pilot study involving the blinded evaluation of the end points. In the period of 6 months, consecutive patients with acute STEMI were included in the study. The acute STEMI was confirmed according to the clinical, ECG and cardioselective enzymes criteria [13]. Patients eligible for inclusion: with type 1 myocardial infarction [13], underwent primary PCI within 12 h from the onset of symptoms, had typical chest pain lasting >30 min, had ST-segment elevation of  $\geq 1$  mm in  $\geq 2$  contiguous leads in ECG and ECGs recorded at admission, 60 min and 24 h after primary PCI. Exclusion criteria were: patients who had cardiogenic shock and/or underwent cardiopulmonary resuscitation before or during primary PCI, with symptoms lasting >12 h, with left bundle branch block in ECG at admission, with diameter stenosis <50% of the culprit lesion or normal coronary blood flow, with severe left main coronary artery or multivessel disease who required emergency cardiac-surgery revascularization, with permanent cardiac pacemaker or implantable cardioverter-defibrillator, with anemia (hemoglobin <100 g/L) at admission, who underwent cardiothoracic surgery or had a history of moderate or high degree valvular pathology, who had life-expectancy of <1 year and who did not sign informed consent (Fig. 1). Patients were admitted through the Emergency Department, where they were evaluated for onset and duration of pain, comorbidities and risk factors. Vital signs and complete physical status were recorded. All patients underwent 12-lead ECG and patients with acute STEMI were taken immediately to the catheterization laboratory for primary PCI. All patients who met the inclusion criteria were randomized into two groups by means of sealed envelopes. 100 envelopes (50 with letter A and 50 with B) were located in one box, and a cardiologist has drawn the envelope for each patient and assigned the treatment, and each time the envelope was returned to the box and mixed with the rest, thus generating the randomization sequence. There were no important changes to study protocol or methods used after trial commencement.

### 2.1. Coronary angiography

After randomization, primary PCI was performed according to the then existing international guidelines [2]. All coronary angiographies were performed using a transfemoral approach and 6 French catheters were used in all included patients. In most cases to probe the left coronary artery the 4-cm left Judkins type catheters, and for the right coronary artery the right 4-cm Judkins catheters (InfinityTM, Cordis Corporation, Miami, FL, U.S.) were chosen. The

injection pressure of the coronary contrast was provided and regulated by using the ACIST CVi Contrast Delivery System with AngioTouch hand controller (ACIST Medical System Inc. - ACIST Europe, Netherlands), calibrated to pound per square inch (psi) as unit of pressure. One psi is approximately 6894.75 Pascal (Pa) which is a standard SI unit ( $\text{Pa} = \text{N/m}^2$ ). In patients in group A (higher injection pressure) the injection of contrast in coronary artery was provided with pressure of 550 psi (3792 kPa), and in patients in group B (lower injection pressure) with pressure of 200 psi (1379 kPa). As a radiographic contrast medium we used Omnipaque 350 (GE Healthcare, General Electric Company, USA). The preselected values of contrast were: 4 ml of contrast with 5 ml/s of contrast flow per injection for left coronary artery/basin and 3 ml with 3 ml/s of contrast flow for the right coronary artery. The coronary angiographic images were acquired before and after the PCI. Basal thrombolysis in myocardial infarction (TIMI) flow was graded on the first angiogram and both TIMI flow and MBG were evaluated from the angiograms taken immediately after primary PCI. TIMI flow grades were assessed as previously described [14]. Myocardial blush grade was graded according to the dye density score described by van't Hof et al. [15]: grade 0 = absence of contrast opacification in the myocardial infarct zone or persistent stain without washout; blush grade 1 = minimal contrast opacification; blush grade 2 = reduced but clearly evident blush in the infarct zone compared to the ipsilateral or contralateral noninvolved epicardial vessel(s); and blush grade 3 = myocardial contrast filling equal to or greater than that seen in the noninvolved epicardial vessel(s). To facilitate the subjective grading of MBG and TIMI flow, images of coronary angiograms were stored on CDs and analyzed off-line by two experienced interventional cardiologists who were blinded to the patient's identity and all related data. In cases of inter-observer disagreement, the third (very well experienced) interventional cardiologist was consulted and gave the final judgement. After detecting the IRA, stent implantation in culprit lesion was performed using standard techniques [2]. The IRA was the only target during primary PCI and coronary stents were used without restrictions [2,16]. Patients were given intracoronary weight-adjusted dose of eptifibatid during the procedure [2,16]. Both the stent implantation and additional balloon pre- or post-dilatation, as well as intracoronary administration of nitroglycerine and aspiration of the thrombi were performed during primary PCI at the operator's discretion [2]. Following the procedure, all patients were admitted to the coronary care unit. They received routine therapy for patients with acute STEMI according to the international guidelines [2,16]. Additional medical therapy was left to the discretion of the attending physician depending on the patient's clinical status. Patients were discharged from hospital 4–7 days after the admission and continued to receive therapy according to the international guidelines [16].

### 2.2. 12-lead ECG

A 12-lead ECG was recorded at admission, 15–60 min and 24 h after the primary PCI. ST-segment changes on postprocedural ECGs were compared with those on the ECG at admission. All ECGs were analyzed by one experienced cardiologist, unaware of the patients' clinical and angiographic data. The sum of the ST-segment elevation (STe) and the sum of the ST-segment deviation score (STdev), defined as the sum of the ST-segment depression and ST-segment elevation, were measured manually 20 ms after the end of QRS complex using the TP segment as an isoelectric baseline [9,17]. Resolution of STe and STdev after primary PCI was quantified as a percentage of the value obtained from the admission ECG and was categorized as complete ( $\geq 70\%$ ), partial (30–70%) and none ( $\leq 30\%$ ) and additionally STdev was also categorized as <2 mm, 2–10 mm and > 10 mm [17].

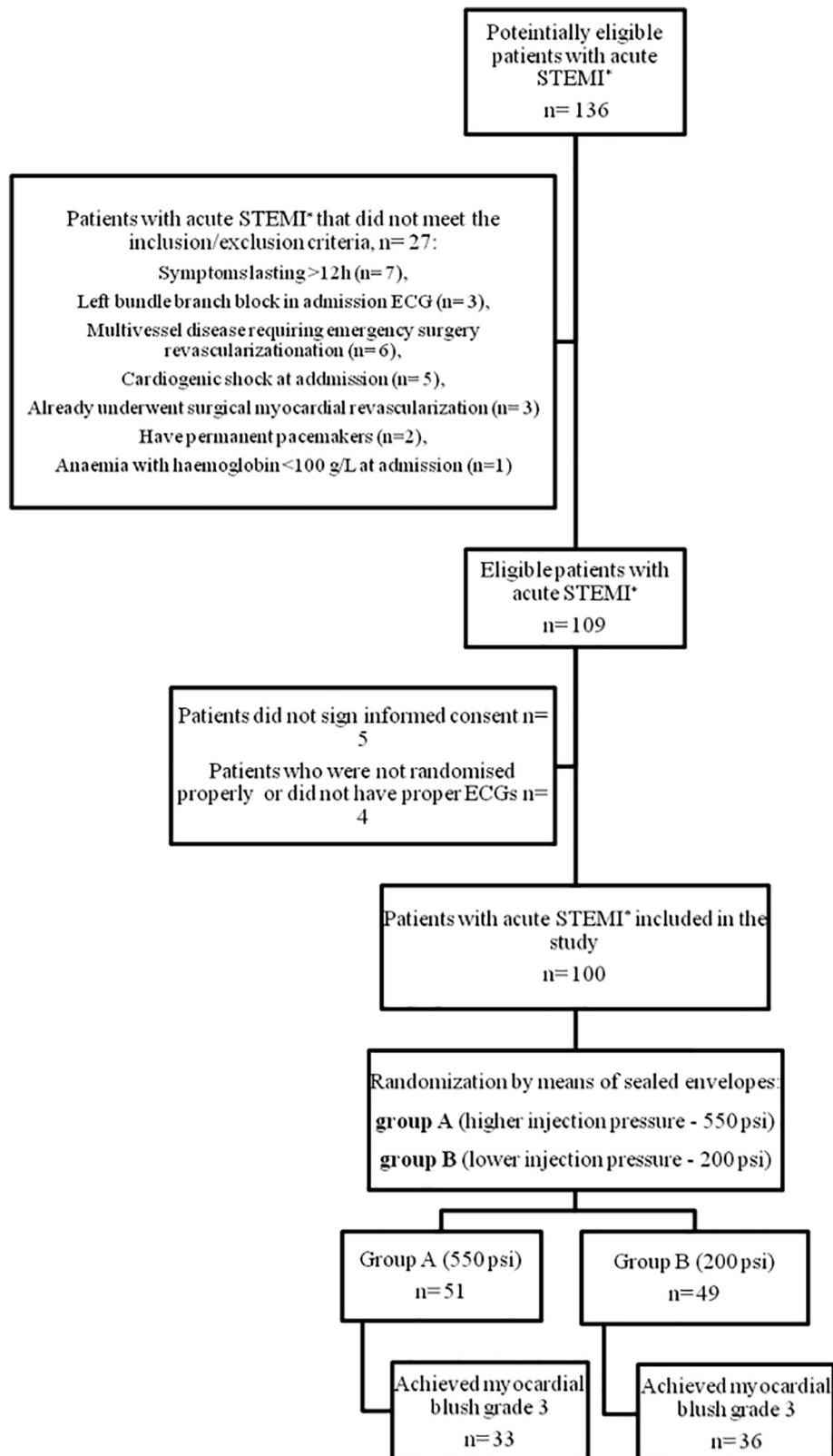


Fig. 1. Course of the study.

### 2.3. Blood sampling

Peripheral blood samples were collected into plastic tubes (EDTA 1.5 mg/ml) on admission, every 6 h for the first 24 h and every 8–12 h

in the next 24 h. Creatine-kinase (CK) serum levels were monitored until normalization, using spectrophotometry (Olympus 680, Beckman Coulter Inc., California, USA) and the laboratory sets the normal value between 0 and 153 U/L at 37 °C. The serum levels of

cardiac troponin T (cTnT) was determined by using conventional electrochemiluminescence assay (Cobas e 411, Roche Diagnostics GmbH, Mannheim, Germany) and positive cTnT was defined as any value above the upper range of 0.1 µg/L.

#### 2.4. End points

Primary end point was the postprocedural incidence of restored myocardial perfusion defined as MBG 3. Secondary end points were myocardial reperfusion evaluated with: STdev score resolution, STe resolution, postprocedural TIMI flow grade 3, as well as peak CK levels.

#### 2.5. Statistical analysis

Baseline characteristics of the study population were presented as median with interquartile range and mean  $\pm$  standard deviation. Independent continuous variables were compared using the Mann-Whitney test and categorical variables using the  $\chi^2$  test with Yates correction. Statistical analysis was done by received treatment. ST deviations score and ST elevation resolution, as well as CK values were compared between the groups with linear mixed model by using the heterogeneous covariance type. Multinomial logistic regression was used to analyze the association between MBG and other parameters. Binary logistic regression was used to analyze the association between injection pressure and MBG and to adjust for all confounding factors detected in multinomial regression analysis. *P* values <0.05 were considered significant. The statistical analysis was done using SPSS Version 20 (IBM SPSS Statistics, New York, USA).

### 3. Results

Out of a total of 136 consecutive acute STEMI patients admitted to our hospital during the study period, 109 patients met the inclusion/exclusion criteria (Fig. 1). Additionally, five patients refused to participate in the study, whereas two of them were not randomized properly and two did not have proper ECGs (1 in each group). Out of six patients who needed emergency surgery revascularization, 4 were randomized in group A and 2 in B. Consequently, the study population included 100 consecutive acute STEMI patients, with median age of 63 (56–72) years and 77% were men. These patients were randomly assigned to either higher injection pressure group A (*n* = 51) or lower injection pressure group B (*n* = 49). Baseline demographics, clinical and angiographic characteristics did not differ significantly between the two groups (Table 1). 73 patients had total occlusion of IRA with TIMI 0 flow (37 in group A vs 36 in group B, *p* = NS) and the rest had 95–99% stenosis with TIMI I or II flow (*p* = 0.083). In addition, there were no significant differences in average amount of contrast used (151 ml in group A vs 154 ml in group B, *p* > 0.3) as well as the difference in number of injections of contrast in IRA (13 vs 14, *p* > 0.3).

Concerning the subjective assessment of TIMI flow and MBG between the two study operators, total inter-observer agreement was 94% and the Cohen's kappa coefficient was 0.89. There were no significant differences in achieved MBG 3 (33 patients in group A vs 36 patients in group B, *p* > 0.3) after primary PCI between the study groups, or other MBG grades and composite of MBG 2 and 3 (47 in group A vs 43 in group B, *p* > 0.3). Patients in both groups had similar TIMI flow grade before (*p* = 0.083) and achieved TIMI flow grade 3 after primary PCI (45 vs 43 patients, *p* > 0.3) (Table 2). There was no significant difference between the study groups regarding CK peak values (2489 vs 2544 U/L at 37 °C, *p* > 0.3) (Table 2). The risk ratio was 0.75 (95%CI 0.41–1.36), the relative risk reduction was 25% (95%CI –36%–59%), the absolute risk reduction was 8.8% (95%CI –9.3%–26.8%) and the number needed to treat was 12 (95%CI 11 needed to harm – 4 needed to treat). No patient died during hospitalization, and after primary PCI two patients from group A and three from group B developed heart failure (*p* > 0.3). Regarding the

incidence of arrhythmia or other complications after the primary PCI, there were no significant differences between the study groups (Table 2). There were no significant differences between the study groups regarding the sum of STdev immediately after (3 vs 4 mm, *p* > 0.3) or 24 h after primary PCI (2 vs 3 mm, *p* > 0.3). A similar result was obtained even when STdev score resolution was categorized as complete ( $\geq 70\%$ ), partial (30–70%) or none ( $\leq 30\%$ ), and <2 mm, 2–10 mm or >10 mm (Table 2). There were no significant differences between the study groups regarding the STe resolution immediately after (3 vs 2 mm, *p* > 0.3) or 24 h after the primary PCI (2 vs 2 mm, *p* > 0.3). There were no differences in the STe resolution (mm and percentage) or when it was classified as complete ( $\geq 70\%$ ), partial (30–70%) and none ( $\leq 30\%$ ) (Table 2).

However, patients who achieved MBG 3 were younger and had lower diastolic blood pressure; they also had lower prevalence of diabetes mellitus as well as arterial hypertension. Multinomial logistic regression analysis confirmed the associations between MBG and age, diastolic blood pressure, diabetes mellitus, incidence of heart failure and atrial fibrillation (Table 3). However, even after adjustment for all mentioned confounding factors, we found no association between coronary injection pressure during primary PCI and MBG.

### 4. Discussion

This was a single-center, hypothesis generating pilot trial which included usage of different intracoronary contrast injection pressure as an attempt to provide a better final result of the primary PCI. Our research has shown no association between intracoronary injection pressure during primary PCI and achieved MBG 3 or composite of MBG 2 and 3. Similar results were obtained with TIMI flow grade and peak CK values. Also, when we observed ST segment changes in ECG, there were no significant differences between the study groups, neither regarding the sum of STdev nor the STe resolution. The use of lower intracoronary contrast injection pressures in patients with acute STEMI did not show efficiency, as we hypothesized. Still, the pathogenesis underlying the no-reflow phenomenon is multifactorial and very complex, including multiple combinations of mechanisms such as increased vasoactivity, intravascular platelet aggregation, microvascular inflammation, distal atherothrombotic embolization, ischemic and reperfusion injury as well as emphasized susceptibility of coronary microcirculation to injury [18–20]. Despite progress achieved in understanding the pathogenesis and diagnosis of no-reflow phenomenon, its treatment remains a weakness in treating acute STEMI patients [3,4,18–20]. Our study was an attempt to provide a relatively simple and inexpensive mechanical method to achieve a better final myocardial reperfusion during primary PCI in acute STEMI patients, which is very important especially for poor and developing countries. Moreover, to the authors' best knowledge, this study was first to examine this specific method as a mechanical attempt to achieve better myocardial reperfusion. Nowadays, the prevention and treatment of no-reflow phenomenon is being carried out by using different therapeutic strategies, however due to the complex interaction of factors, it is unlikely that a single method could be effective in all patients [18–21]. Regarding the mechanical methods, repetitive balloon inflations during primary PCI seem to be cardioprotective, whereas on the basis of large meta-analysis of 20,822 patients it seems that additional thrombus aspiration during primary PCI may be linked to improved myocardial reperfusion but with no benefits in relation to the clinical outcome [22,23]. Use of distal protection devices and intracoronary drugs make no significant improvements in relation to a lower risk of major adverse cardiac events [21,24,25]. Moreover, the simple use antiaggregation therapy (ASA and prasugrel or ticagrelor), statin therapy and strict blood glucose control in acute phase of STEMI, confirmed to be the only beneficial therapy with improved clinical outcome [16,18,20]. Furthermore, the study showed

**Table 1**

Baseline characteristics of the study population divided based on injection intracoronary pressure used during primary percutaneous coronary intervention (PCI).

	Group A (higher injection pressure – 550 psi <sup>a</sup> ) n = 51	Group B (lower injection pressure – 200 psi <sup>a</sup> ) n = 49	p Value
	Median (25%–75%)	Median (25%–75%)	
Age (years)	64 (57–72)	60 (55–70)	0.196
BMI (kg/m <sup>2</sup> ) <sup>b</sup>	27.5 (24.6–30.7)	26.8 (24.9–30.2)	>0.3
Creatin-kinase (U/L 37 °C)	270 (130–672)	204 (110–665)	>0.3
Troponin T (µg/L)	0.087 (0.034–0.802)	0.100 (0.041–1.310)	>0.3
Hemoglobin (g/L)	134 (127–144)	137 (126–141.5)	>0.3
Platelets (x10 <sup>9</sup> /L)	215 (177–244)	224 (187–246)	>0.3
Prothrombin time (%)	97 (86–106)	100 (92–106)	>0.3
Fibrinogen (g/L)	4.7 (3.9–5.2)	4.2 (3.5–5.4)	>0.3
Blood glycaemia	6.6 (4.9–11.7)	6.8 (4.4–12.4)	>0.3
C-reactive protein (mg/L)	3.1 (2.4–4.3)	4.7 (2.1–11.0)	>0.3
Systolic BP <sup>c</sup> (mmHg)	130 (110–150)	130 (110–150)	>0.3
Diastolic BP <sup>c</sup> (mmHg)	75 (70–90)	70 (70–85)	>0.3
Heart rate (beats/min)	72 (60–85)	76 (68–80)	>0.3
	% (n)	% (n)	p Value
Male	74.5 (38)	79.6 (39)	>0.3
Hypertension	70.6 (36)	75.5 (37)	>0.3
Diabetes mellitus	27.5 (14)	22.4 (11)	>0.3
Smoking	54.9 (28)	55.1 (27)	>0.3
Family history of CAD <sup>d</sup>	54.9 (28)	65.3 (32)	>0.3
Hyperlipidaemia	52.9 (27)	44.9 (22)	>0.3
Killip class 1	70.6 (36)	77.6 (38)	>0.3
Killip class 2	27.5 (14)	18.4 (9)	>0.3
Killip class 4	2.0 (1)	4.1 (2)	>0.3
Myocardial infarction localisation			>0.3
Anteroseptal	19.6 (10)	18.4 (9)	>0.3
Anterolateral	17.6 (9)	10.2 (5)	>0.3
Inferior	7.8 (4)	18.4 (9)	>0.3
Inferoposterior	37.3 (19)	34.7 (17)	>0.3
Inferoposterior and right ventricle	17.6 (9)	18.4 (9)	>0.3
STdev before pPCI (mm)	11 (8–17)	14 (9–20)	0.112
STe before pPCI (mm)	9 (6–14)	9 (6–16)	0.243
	Group A (higher injection pressure – 550 psi <sup>a</sup> ) n = 51	Group B (lower injection pressure – 200 psi <sup>a</sup> ) n = 49	
Angiography	Median (25%–75%)	Median (25%–75%)	p Value
Heparin dose per body mass (I.U./kg)	71.4 (66.67–77.77)	70.6 (65.8–75.2)	>0.3
Coronary stent length (mm)	23 (16–36)	23 (18–28)	>0.3
Coronary stent diameter (mm)	3 (3–4)	4 (3–4)	>0.3
	% (n)	% (n)	p Value
Eptifibatide intracoronary during PCI	94.1 (48)	100 (49)	0.243
Thrombus aspiration	15.7 (8)	20.4 (10)	>0.3
Baloon predilatation	74.5 (38)	69.4 (34)	>0.3
Eptifibatide intravenous after PCI	15.7 (8)	20.4 (10)	>0.3
Nitroglycerine intracoronary	39.2 (20)	42.8 (21)	>0.3
Culprit lesion			>0.3
LAD <sup>f</sup>	39.2 (20)	28.6 (14)	
ACx <sup>g</sup>	17.6 (9)	14.3 (7)	
RCA <sup>h</sup>	43.1 (22)	57.1 (28)	
TIMI <sup>i</sup> flow prior pPCI <sup>e</sup>			0.083
0	72.5 (37)	73.5 (36)	
1	7.8 (4)	18.4 (9)	
2	19.6 (10)	6.1 (3)	
3	0.0 (0)	2.0 (1)	

<sup>a</sup> Psi – pound per square inch.<sup>b</sup> BMI – body mass index.<sup>c</sup> BP – blood pressure.<sup>d</sup> CAD – coronary artery disease.<sup>e</sup> pPCI – primary percutaneous coronary intervention.<sup>f</sup> LAD – left anterior descending artery.<sup>g</sup> ACx – left circumflex artery.<sup>h</sup> RCA – right coronary artery.<sup>i</sup> TIMI – thrombolysis in myocardial infarction.

that patients with MBG 3 were younger, had lower diastolic blood pressure, had a lower prevalence of diabetes mellitus as well as the incidence of heart failure and atrial fibrillation, which was confirmed by

multinomial logistic regression analysis. This corresponds to previous studies [18,19,23,26], and indicate that achieving high MBG is multifactorial and does not depend exclusively on the primary PCI.

**Table 2**  
Coronary angiography and laboratory treatment outcome in patients divided based on injection intracoronary pressure used during primary percutaneous coronary intervention (PCI).

	Group A (higher injection pressure – 550 psi <sup>b</sup> ) n = 51	Group B (lower injection pressure – 200 psi <sup>b</sup> ) n = 49	p Value
	% (n)	% (n)	
Myocardial blush grade (MBG) after pPCI <sup>a</sup>			0.247
0	3.9 (2)	2.0 (1)	
1	3.9 (2)	10.2 (5)	
2	27.5 (14)	14.3 (7)	
3	64.7 (33)	73.5 (36)	
TIMI <sup>f</sup> flow after pPCI			>0.3
1	2.0 (1)	2.0 (1)	
2	9.8 (5)	10.2 (5)	
3	88.2 (45)	87.8 (43)	
CK <sup>d</sup> peak values within 12 h after PCI	92.2 (47)	85.7 (42)	>0.3
Ventricular tachycardia	7.8 (4)	10.2 (5)	>0.3
Ventricular fibrillation	3.9 (2)	8.2 (4)	>0.3
Atrial fibrillation	13.7 (7)	4.1 (2)	0.16
Atrioventricular block II or III degree	2.0 (1)	0.0 (0)	>0.3
Heart failure	3.9 (2)	6.1 (3)	>0.3
Re-intervention	2.0 (1)	6.1 (3)	>0.3
CK peak values	Median (25%–75%) 2489 (1102–4295)	Median (25%–75%) 2544 (1350–4860)	p Value >0.3
<sup>e</sup> STdev <1 h after pPCI (mm)	3 (1–4)	4 (2–7)	>0.3
STdev 24 h after pPCI (mm)	2 (1–4)	3 (1–4)	>0.3
<sup>f</sup> STe <1 h after pPCI (mm)	3 (1–4)	2 (1–5.5)	>0.3
STe 24 h after pPCI (mm)	2 (0–4)	2 (1–3.5)	>0.3
STdev resolution <1 h after pPCI (%)	72.2 (53.8–87)	73.9 (55.6–85.7)	>0.3
STdev resolution 24 h after pPCI (%)	80 (62.5–92.9)	82.6 (71.4–90)	>0.3
STe resolution <1 h after pPCI (%)	73.4 (54.1–86.7)	75.1 (50.4–88.3)	>0.3
STe resolution 24 h after pPCI (%)	82.9 (60.3–100)	80.4 (59.9–82.9)	>0.3
	Group A (higher injection pressure – 550 psi <sup>b</sup> ) n = 51	Group B (lower injection pressure – 200 psi <sup>b</sup> ) n = 49	p Value
	% (n)	% (n)	
STdev after PCI			0.294
<2 mm	41.2 (21)	36.7 (18)	
2–10 mm	51.0 (26)	44.9 (22)	
>10 mm	7.8 (4)	18.4 (9)	
STdev 24 h after PCI			0.199
<2 mm	52.9 (27)	49.0 (24)	
2–10 mm	47.1 (24)	44.9 (22)	
>10 mm	0 (0)	6.1 (3)	
STdev resolution <1 h after pPCI			>0.3
>70%	54.9 (28)	57.1 (28)	
30–70%	41.2 (21)	34.7 (17)	
<30%	3.9 (2)	8.2 (4)	
STdev resolution 24 h after pPCI			>0.3
>70%	68.6 (35)	75.5 (37)	
30–70%	29.4 (15)	22.4 (11)	
<30%	2.0 (1)	2.0 (1)	
STe resolution <1 h after pPCI			>0.3
>70%	56.9 (29)	61.2 (30)	>0.3
30–70%	35.3 (18)	34.7 (17)	>0.3
<30%	7.8 (4)	4.1 (2)	>0.3
STe resolution 24 h after pPCI			>0.3
>70%	64.7 (33)	67.3 (33)	>0.3
30–70%	33.3 (17)	28.6 (14)	>0.3
<30%	2 (1)	4.1 (2)	>0.3

<sup>a</sup> pPCI – primary percutaneous coronary intervention.

<sup>b</sup> Psi – pound per square inch.

<sup>c</sup> TIMI – thrombolysis in myocardial infarction.

<sup>d</sup> CK – creatinine-kinase.

<sup>e</sup> STdev – ST segment deviation score.

<sup>f</sup> STe – ST segment elevation score.

#### 4.1. Limitations

The results of this study should be considered in light of several limitations. This was a pilot-study which represents a single-center experience on a small study sample. As calculated in a post-hoc analysis (according to a Simon two-stage optimal design for phase II clinical

trials [27]) larger trial with at least 600 patients may have shown differences. The intraobserver and interobserver variability associated with subjective angiographic assessment of MBGs represents a limitation, however only two experienced interventional cardiologist assessed MBGs in the attempt to standardize the clinical information provided by this variable. Time delays to primary PCI were not taken into account

**Table 3**

Multinomial logistic regression showing the association of several parameters in grade 1 and grade 2 MBG status compared with grade 3 status.

	MBG 1		MBG 2	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age	1.05 (0.97–1.12)	0.212	1.047 (1.001–1.094)	0.044
Arterial hypertension	1.33 (0.04–2.94)	0.322	1.33 (1.09–2.55)	0.103
Diabetes mellitus 2	1.14 (1.03–1.73)	0.019	1.31 (1.1–1.92)	0.035
Diastolic blood pressure	1.95 (1.92–1.99)	0.014	1.97 (1.96–2.02)	0.375
Heart failure	1.09 (1.01–10.6)	0.100	1.09 (1.01–1.9)	0.040
Atrial fibrillation	1.11 (1.02–1.85)	0.034	1.19 (1.04–1.95)	0.043

MBG – myocardial blush grade, OR – odds ratio, CI – confidence interval.

in our study due to lack of this information in majority of study patients, but are also associated with sustained no reflow phenomenon. In addition, routinely GP IIb/IIIa inhibitors (eptifibatide) usage, instead in particular cases as “bail-out” strategy, most probably influenced the postprocedural TIMI flow and MBG. However, GP IIb/IIIa inhibitor (eptifibatide) usage was not different between the study groups ( $p = NS$ ). Finally, our study evaluated short-term clinical and angiographic data only, and thrombus burden was not taken into account.

## 5. Conclusion

There was no impact of different contrast injection pressures in coronary arteries, during primary PCI in patients with acute STEMI, on achieving better myocardial reperfusion as assessed by MBG and ST segment resolution changes in the ECG.

## Ethics approval and consent to participate

Before coronary angiography was done, signed informed consent for participation in the study was obtained from all enrolled patients. The study protocol complied with the Good Clinical Practice as well as the Declaration of Helsinki and the hospital's Ethics Committee gave its approval of the study. The study was registered in Clinical Trials registry ([clinicaltrials.gov](http://clinicaltrials.gov)) as a prospective clinical trial with trial number NCT03445364.

## Consent for publication

As part of informed consent, patients agreed for their data to be published. However, any data that could reveal their identity was censored.

## Funding

The study was undertaken without any grant support.

## Authors' contribution

KS conceived the study, managed the technical and organizational aspects, performed data acquisition, data interpretation, and drafted the manuscript. TK conceived the study, performed data acquisition, interpreted the data and participated in manuscript design and drafting. IZ performed data acquisition, interpreted the data and participated in manuscript design and drafting.

All authors have critically read and reviewed this paper. All authors approved the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Declaration of competing interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

## Acknowledgments

N/A.

## References

- [1] E.C. Keeley, J.A. Boura, C.L. Grines, Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials, *Lancet* 361 (2003) 13–20.
- [2] S. Windecker, P. Kolh, F. Alfonso, J.P. Collet, J. Cremer, V. Falk, et al., 2014 ESC/EACTS guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI), *Eur. Heart J.* 35 (37) (2014) 2541–2619.
- [3] A.M. Lincoff, E.J. Topol, Illusion of reperfusion. Does anyone achieve optimal reperfusion during acute myocardial infarction? *Circulation* 88 (1993) 1361–1374.
- [4] H. Ito, A. Maruyama, K. Iwakura, S. Takiuchi, T. Masuyama, M. Hori, et al., Clinical implication of the “no reflow” phenomenon: a predictor of complication and left ventricular remodelling in reperfused anterior wall myocardial infarction, *Circulation* 93 (1996) 223–228.
- [5] G.W. Stone, M.A. Peterson, A.J. Lansky, G. Dangas, R. Mehran, M.B. Leon, Impact of normalized myocardial perfusion after successful angioplasty in acute myocardial infarction, *J. Am. Coll. Cardiol.* 39 (2002) 591–597.
- [6] J.P. Henriques, F. Zijlstra, J.P. Ottervanger, M.J. de Boer, A.W. van 't Hof, J.C. Hoorntje, H. Suryapranata, Incidence and clinical significance of distal embolization during primary angioplasty for acute myocardial infarction, *Eur. Heart J.* 23 (2002) 1112–1117.
- [7] J.P. Henriques, F. Zijlstra, A.W. van 't Hof, M.J. de Boer, J.H. Dambrink, M. Gosselink, J.C. Hoorntje, H. Suryapranata, Angiographic assessment of reperfusion in acute myocardial infarction by myocardial blush grade, *Circulation* 107 (2003) 2115–2119.
- [8] J. Kotani, G.S. Mintz, J. Pregowski, L. Kalinczuk, A.D. Pichard, L.F. Satler, W.O. Suddath, R. Waksman, N.J. Weissman, Volumetric intravascular ultrasound evidence that distal embolization during acute infarct intervention contributes to inadequate myocardial perfusion grade, *Am. J. Cardiol.* 92 (2003) 728–732.
- [9] A. Poli, R. Fèveau, P. Vandoni, G. del Rosso, M. D'Urbano, G. Seveso, et al., Integrated analysis of myocardial blush and ST-segment elevation recovery after successful primary angioplasty: real-time grading of microvascular reperfusion and prediction of early and late recovery of left ventricular function, *Circulation* 106 (2002) 313–318.
- [10] G. De Luca, E.P. Navarese, H. Suryapranata, A meta-analytic overview of thrombectomy during primary angioplasty, *Int. J. Cardiol.* 166 (2013) 606–612.
- [11] Y.J. Shimada, N.C. Nakra, J.T. Fox, Y. Kanei, Meta-analysis of prospective randomized controlled trials comparing intracoronary versus intravenous abciximab in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention, *Am. J. Cardiol.* 109 (2012) 624–628.
- [12] F. Burzotta, L. Testa, F. Giannico, G.G. Biondi-Zoccai, C. Trani, E. Romagnoli, et al., Adjunctive devices in primary or rescue PCI: a meta-analysis of randomized trials, *Int. J. Cardiol.* 123 (2008) 313–321.
- [13] K. Thygesen, J.S. Alpert, A.S. Jaffe, M.L. Simoons, B.R. Chaitman, H.D. White, et al., Writing group on the joint ESC/ACCF/AHA/WHF task force for the universal definition of myocardial infarction; ESC Committee for practice guidelines (CPG). Third universal definition of myocardial infarction, *Eur. Heart J.* 33 (20) (2012) 2551–2567.
- [14] The TIMI Study Group, The thrombolysis in myocardial infarction (TIMI) trial: phase I findings, *N. Engl. J. Med.* 312 (1985) 932–936.
- [15] A.W. Van't Hof, A. Liem, H. Suryapranata, J.C. Hoorntje, M.J. de Boer, F. Zijlstra, Angiographic assessment of myocardial reperfusion in patients treated with primary angioplasty for acute myocardial infarction: myocardial blush grade, *Circulation* 97 (1998) 2302–2306.
- [16] P.G. Steg, S.K. James, D. Atar, L.P. Badano, C. Blömstrom-Lundqvist, M.A. Borger, et al., Task force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology. ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation, *Eur. Heart J.* 33 (20) (2012) 2569–2619.
- [17] P.J. Vlaar, T. Svilaas, I.C. van der Horst, G.F. Diercks, M.L. Fokkema, B.J. de Smet, et al., Cardiac death and reinfarction after 1 year in the thrombus aspiration during percutaneous coronary intervention in acute myocardial infarction study (TAPAS): a 1-year follow-up study, *Lancet* 371 (2008) 1915–1920.

- [18] D.T. Wong, R. Puri, J.D. Richardson, M.I. Worthley, S.G. Worthley, Myocardial 'no-reflow'-diagnosis, pathophysiology and treatment, *Int. J. Cardiol.* 167 (2013) 1798–1806.
- [19] G. Galasso, S. Schiekofe, C. D'Anna, G.D. Gioia, R. Piccolo, T. Niglio, et al., No-reflow phenomenon: pathophysiology, diagnosis, prevention, and treatment. A review of the current literature and future perspectives, *Angiology* 65 (2014) 180–189.
- [20] A. Feher, S.Y. Chen, Z. Bagi, V. Arora, Prevention and treatment of no-reflow phenomenon by targeting the coronary microcirculation, *Rev. Cardiovasc. Med.* 15 (2014) 38–51 (Review).
- [21] G. Niccoli, R.K. Kharbanda, F. Crea, A.P. Banning, No-reflow: again prevention is better than treatment, *Eur. Heart J.* 31 (2010) 2449–2455.
- [22] G. Wang, S. Zhang, S.J. Joggerst, J. McPherson, D.X. Zhao, Effects of the number and interval of balloon inflations during primary PCI on the extent of myocardial injury in patients with STEMI: does postconditioning exist in real-world practice? *J. Invasive Cardiol.* 21 (2009) 451–455.
- [23] A. Briasoulis, M. Palla, L. Afonso, Clinical outcomes of manual aspiration thrombectomy in patients with acute myocardial infarction: an updated meta-analysis, *Cardiology* 132 (2015) 124–130.
- [24] B. Jin, X.H. Dong, C. Zhang, Y. Li, H.M. Shi, Distal protection devices in primary percutaneous coronary intervention of native coronary artery lesions: a meta-analysis of randomized controlled trials, *Curr. Med. Res. Opin.* 28 (2012) 871–876.
- [25] KK. Aung Naing, LL. Li, QQ. Su, TT. Wu, Adenosine and verapamil for no-reflow during primary percutaneous coronary intervention in people with acute myocardial infarction, *Cochrane Database Syst. Rev.* 6 (2013), CD009503.
- [26] H. Zhou, X.Y. He, S.W. Zhuang, J. Wang, Y. Lai, W.G. Qi, et al., Clinical and procedural predictors of no-reflow in patients with acute myocardial infarction after primary percutaneous coronary intervention, *World J Emerg Med* 5 (2014) 96–102.
- [27] R. Simon, Optimal two-stage designs for phase II clinical trials, *Control. Clin. Trials* 10 (1989) 1–10.