Clinical, Laboratory, and Procedural Predictors of No-Reflow in Patients Undergoing Primary Percutaneous Coronary Intervention

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Abstract

Background: No-reflow is a major challenging issue in the management of patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PPCI). This study aimed to investigate the clinical, laboratory, and procedural predictors of no-reflow.

Methods: This study was conducted on 378 patients with STEMI admitted to Dr. Heshmat Educational and Remedial Center (a referral heart hospital in Rasht, Iran) between 2015 and 2017. The study population was divided based on the thrombolysis in myocardial infarction (TIMI) flow grade and the myocardial blush grade into no-reflow and reflow groups. The clinical, laboratory, and procedural characteristics at admission were compared between the 2 groups using the multivariate logistic regression analysis.

Results: The mean age of the participants was 58.57±11.49 years, and men comprised 74.1% of the study population. The no-reflow phenomenon was found in 77 patients. The no-reflow group was significantly older and more likely to be female; additionally, it had higher frequencies of hypertension, diabetes mellitus, hyperlipidemia, and a history of cardiovascular diseases. The multivariate logistic regression analysis showed that age >60 years (OR=1.05, 95% CI:1.00–1.09), hypertension (OR=2.91, 95% CI:1.35–6.27), diabetes (OR=4.18, 95% CI:1.89–9.22), a low systolic blood pressure (OR=3.53, 95% CI:1.02–12.2), a history of cardiovascular diseases (OR=4.29, 95% CI:1.88–9.77), chronic heart failure (OR=4.96, 95% CI:1.23–20), a low initial TIMI flow grade (OR=7.58, 95% CI:1.46–39.2), anemia (OR=3.42, 95% CI:1.33–8.77), and stenting vs. balloon angioplasty (OR=0.42, 95% CI:0.19–0.91) were the significant independent predictors of no-reflow.

Conclusion: This study revealed some clinical, laboratory, and procedural predictors of no-reflow for the prediction of high-risk patients and their appropriate management to reduce the risk of no-reflow.

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Keywords: ST elevation myocardial infarction; Percutaneous coronary intervention; No-reflow phenomenon

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Introduction

Primary percutaneous coronary intervention (PPCI) is a nonsurgical treatment for the myocardial reperfusion of patients with ST-segment elevation myocardial infarction (STEMI). However, in a significant proportion of patients, myocardial perfusion is not successful, leading to the no-reflow phenomenon, which itself is an independent predictor of major adverse cardiovascular events.¹,² No-reflow, defined as the inability of the reperfusion of an ischemic region in a recanalized infarcted coronary artery,³ is a major challenging issue in the management of patients undergoing PPCI and is associated with a worse outcome and a higher incidence of complications and mortality.⁴,⁵ The reason behind no-reflow is not fully distinguished, and a combination of clinical and inflammatory mechanisms have been proposed.⁶,⁷ The present study aimed to identify the clinical, procedural, and laboratory predictors of no-reflow in patients with STEMI undergoing PPCI.

Methods

This study was performed on 378 consecutive patients diagnosed with STEMI who underwent PPCI within a 12-hour period from the onset of symptoms at Dr. Heshmat Educational and Remedial Center (a referral heart hospital in Rasht, Iran) between 2015 and 2017. Acute STEMI was diagnosed upon the presence of persistent anginal chest pains lasting for ≥20 minutes accompanied by >1 mm (0.1 mV) ST-segment elevation in 2 or more contiguous precordial leads or the presence of new left bundle branch block. The primary sample size was calculated based on a prior estimate of 25% for no-reflow. Assuming 5% precision and 10 extra cases for every 15 predictors, we estimated a total of 380 cases. Patients with cardiogenic shock at admission, active infection, a history of systemic inflammatory diseases, hemorrhagic disorders, liver disease, known malignancy, and kidney failure were excluded from the study. The study protocol was approved by the Review Board of Guilan University of Medical Sciences.

All the patients received 325 mg of aspirin orally and 600 mg of clopidogrel before PPCI. The PPCI procedures were performed via the standard femoral approach with Judkins catheters. The use of balloon angioplasty and thrombectomy was left to the operator’s discretion. Immediately after the decision to perform coronary intervention, 50–70 unit/kg of an intravenous bolus of unfractionated heparin was administered to the patients who were not treated with enoxaparin before coronary angiography. For the patients having received an initial enoxaparin dose of 1 mg/kg before angiography, no additional booster dose of enoxaparin was administered within 8 hours of the first dose. An additional booster of 0.3 mg/kg of enoxaparin was given intravenously between 8 and 12 hours after the first dose. The application of the thrombus aspiration catheter in the patients with high thrombus burden and the administration of eptifibatide (a glycoprotein IIb/IIIa inhibitor with a 180 mcg/kg IV bolus dose over 1–2 minutes, followed by a continuous infusion of 2 mcg/kg/min with another 180 mcg/kg IV bolus dose 10 minutes after the first one for at least 12 hours) were at the discretion of the interventional cardiologist.

The clinical and demographic information of the patients was obtained from their medical records. A history of cardiovascular diseases was defined as having a previous stroke and coronary and peripheral artery diseases. For all the patients, venous blood samples were drawn from the antecubital vein during emergency admission. Complete blood count parameters were measured using a Sysmex AutoAnalyzer within 5 minutes of sampling. Anemia was defined as a serum hemoglobin level <12 g/dL. The postprocedural thrombolysis in myocardial infarction (TIMI) flow grades were evaluated by 2 cardiologists blinded to the grouping of the study population. The myocardial blush grade (MBG) was assessed during angiography according to the Van't Hof and Gibson method.⁸ The no-reflow group was defined as a TIMI flow grade of 0–2 with an MBG ≤1, and the reflow group was defined as a TIMI flow grade of 3 with an MBG ≥2.

The data were described as the mean and the standard deviation for the continuous variables and frequencies and percentages for the categorical variables. Normal distribution was assessed using the Kolmogorov–Smirnov test. The 2 groups were compared using the t-test or the Mann–Whitney test for the continuous variables and the χ² test for the categorical variables. To identify the independent predictors of no-reflow and estimate adjusted odds ratios with 95% confidence intervals, we employed multivariate logistic regression. Stepwise multivariate logistic regression was created using variables with P values <0.05. All the statistical analyses were performed in Stata, version 13 (StataCorp LP, College Station, Texas).

Results

Seventy-seven (20.3%) patients were in the no-reflow group and 301 (79.6%) in the normal reflow group. Table 1 illustrates the baseline characteristics of the patients. The no-reflow group was older and more likely to be women. The prevalence of smoking in the no-reflow group (25.0%) was significantly lower than that of the reflow group (39.0%). In contrast, the prevalence rates of hyperlipidemia, hypertension, diabetes mellitus, and a history of congestive heart failure and cardiovascular diseases in the no-reflow group were significantly higher than those in the reflow group (Table 1). There were no significant differences in the use of thrombus aspiration, antiplatelet medical treatment,
The results of the multivariate logistic regression are shown in Table 2. The model had good discrimination capability (area under the ROC curve=0.89) and goodness of fit (Hosmer–Lemeshow test=326; P=0.112). According to the multivariate adjusted logistic regression results, age, hypertension, diabetes mellitus, a history of cardiovascular diseases, chronic heart failure, systolic blood pressure (SBP), anemia, type of reperfusion, and the initial TIMI flow grade were the significant independent predictors of no-reflow. Advanced age was associated with 5% increases in the odds of no-reflow. The hypertensive patients were over twice as likely as the non-hypertensive patients to have no-reflow. A current SBP <100 mmHg increased the odds of no-reflow by 253.0%. The odds of no-reflow in the diabetic patients were 4.18 higher than those in the nondiabetic patients. A history of cardiovascular diseases and chronic heart failure were also associated with increased odds of no-reflow (OR=4.96 and 4.29, respectively). The odds of developing no-reflow in the patients with hemoglobin levels < 12 g/dL, defined as anemic patients, were 242.0% higher than those of the patients with normal levels of hemoglobin. Low initial TIMI flow grades were associated with increased odds of no-reflow.

| Table 1. Clinical, angiographic, and laboratory characteristics of the study groups at admission |
|-----------------------------------------------|
| **Reflow Group** | **No-Reflow Group** | **P** |
| **(n=301)**       | **(n=77)**          |       |
| Age (y)           | 57.07±11.16         |       |
| Male gender       | 231 (76.7)          | 49 (63.6) | 0.011 |
| Smoking           | 118 (39.2)          | 19 (24.7) | 0.018 |
| Hyperlipidemia    | 68 (22.6)           | 37 (48.1) | 0.001 |
| Hypertension      | 104 (34.5)          | 57 (74.0) | 0.001 |
| Diabetes          | 60 (19.9)           | 38 (49.3) | 0.001 |
| History of CHF    | 4 (1.3)             | 21 (27.3) | 0.001 |
| History of CVA    | 4 (1.3)             | 6 (7.8) | 0.002 |
| Systolic blood pressure (mmHg) | 136.57±23.77 | 124.44±29.72 | 0.001 |
| Diastolic blood pressure (mmHg) | 80.72±12.90 | 75.10±15.98 | 0.001 |
| LVEF (%)           | 38.22±7.82          | 33.18±8.92 | 0.001 |
| Creatinine (mg/dL) | 1.02±0.19          | 1.19±0.62 | 0.001 |
| Hemoglobin (g/dL) | 13.97±3.72          | 12.96±1.83 | 0.021 |
| Anemia             | 33 (11.9)           | 26 (38.2) | 0.001 |
| GFR                | 79.08±15.23         | 66.87±17.21 | 0.001 |
| Initial TIMI flow grade | 0.009           |       |
| 0-1                | 262 (87.1)          | 75 (97.4) | 0.009 |
| 2-3                | 39 (12.9)           | 2 (2.6) | 0.001 |
| PCI type           |                     |       |
| Balloon angioplasty | 64 (21.3)         | 33 (42.9) |       |
| Stenting           | 237 (78.7)          | 44 (57.1) |       |
| Stent length (mm)  | 26.88±7.49          | 27.48±7.13 | 0.615 |
| Lesion length (mm) | 17.65±7.72          | 17.26±7.20 | 0.690 |
| Antiplatelet use   | 197 (65.4)          | 53 (68.8) | 0.576 |
| Thrombus aspiration use | 102 (33.9)     | 25 (32.5) | 0.814 |
| Symptom onset to PPCI (min) | 163.80±133.38 | 178.38±115.20 | 0.380 |
| White blood cell count (>10⁹/L) | 11.95±3.83 | 12.26±3.64 | 0.541 |
| Platelet count (>10⁹/L) | 240.85±70.39 | 250.39±84.16 | 0.336 |
| Monocyte count (>10⁹/L) | 0.22±0.14        | 0.21±0.12 | 0.840 |
| Lymphocyte count (>10⁹/L) | 2.67±1.18        | 2.35±0.79 | 0.050 |
| Neutrophil count (>10⁹/L) | 8.91±3.90        | 9.48±3.78 | 0.297 |

Data are presented as mean±SD, n (%).
CHF, Chronic heart failure; LVEF, Left ventricular ejection fraction; GFR, Glomerular filtration rate; PPCI, Primary percutaneous coronary intervention; TIMI, Thrombolysis in myocardial infarction
Table 2. Multivariate adjusted predictors of the no-reflow phenomenon using the logistic regression analysis

| Predictor                          | Adjusted OR | 95% CI       | P     |
|-----------------------------------|-------------|--------------|-------|
| Age (y)                           | 1.05        | 1.00-1.09    | 0.026 |
| Sex (female)                      | 0.90        | 0.37-2.18    | 0.817 |
| Smoking                           | 0.72        | 0.29-1.76    | 0.482 |
| Hypertension                      | 2.91        | 1.35-6.27    | 0.007 |
| Diabetes mellitus                 | 4.18        | 1.89-9.22    | 0.001 |
| Hyperlipidemia                    | 1.05        | 0.48-2.31    | 0.901 |
| History of CHF                    | 4.96        | 1.23-20.01   | 0.024 |
| History of CVD                    | 4.29        | 1.88-9.77    | 0.001 |
| SBP <100 mmHg                     | 3.53        | 1.02-12.17   | 0.046 |
| DBP <50 mmHg                      | 0.40        | 0.15-1.10    | 0.076 |
| GFR                               | 0.99        | 0.96-1.03    | 0.652 |
| Creatinine mg/dL                  | 0.91        | 0.18-4.56    | 0.910 |
| Anemia                            | 3.42        | 1.33-8.77    | 0.010 |
| LVEF                              | 0.98        | 0.94-1.03    | 0.513 |
| PCI type (stenting vs. balloon angioplasty) | 0.42       | 0.19-0.91    | 0.029 |
| Initial TIMI flow grade (0-1)     | 7.58        | 1.46-39.25   | 0.016 |

CVD, Cardiovascular diseases; CHF, Chronic heart failure; DBP, Diastolic blood pressure; LVEF, Left ventricular ejection fraction PCI, Percutaneous coronary intervention; TIMI, Thrombolysis in myocardial infarction (OR=7.58). Direct stenting as the method of reperfusion decreased the odds of no-reflow by 58.0%.

**Discussion**

The findings of the current study revealed some clinical, procedural, and laboratory predictors of the no-reflow phenomenon. No-reflow, a major limitation of infarcted artery recanalization, is prevalent among patients with STEMI undergoing PPCI. In the current study, no-reflow was found in 20.0% of the patients, which is consistent with previous reports of no-reflow rates and much higher than the 4.1% rate estimated by Ashraf et al. We used recent comprehensive criteria to define no-reflow according to the TIMI flow grade and the MBG, which are the preferred methods to evaluate myocardial blood flow rather than the epicardial flow, which is estimated by the TIMI flow grade. The reason behind the development of no-reflow is multifactorial.

Similar to previous studies, we found that advanced age is an important predictor of no-reflow. In addition to the existence of several comorbidities, some conditions such as severe vascular calcification and disrupted microvascularization are more common in older patients. These conditions predispose them to the development of no-reflow more frequently than younger patients.

In the present study, hypertension was a strong predictor of no-reflow and showed a 2.91-fold higher rate of no-reflow than that in the non-hypertensive patients. This finding is in agreement with previous reports. The coronary flow reserve has been shown to be reduced in hypertensive patients through some mechanisms including endothelial dysfunction, abnormalities of left ventricular diastolic relaxation, functional changes of the intramyocardial coronary arteries, and increased afterload. However, in the current study, a current SBP <100 mmHg was independently associated with a 4-fold increase in the odds of no-reflow. Likewise, some previous studies have demonstrated that a lower SBP is associated with the increased risk of no-reflow because of a decreased coronary and collateral blood flow. Therefore, it can be inferred that both the long-term consequences of hypertension on the function and structure of the coronary arteries and a current low SBP through lowering the coronary blood flow can be considered mechanisms contributing to the development of no-reflow. Moreover, our subgroup analysis showed that a low SBP was significantly associated with the increased odds of no-reflow only among the hypertensive group. This finding emphasizes the importance of the hypotension risk for developing no-reflow in patients suffering from chronic hypertension. Still, this issue remains questionable and needs to be verified in further research.

We found anemia to be the independent predictor of no-reflow in that it increased the odds of no-reflow by 3.42-fold. Based on our latest literature review, no previous studies have found anemia as a determinant of no-reflow in multivariate adjusted models. However, the effect of anemia on reducing oxygen-carrying capacity and viscosity of the blood has been well introduced. Anemia is also associated with decreased coronary reserve. The effect of anemia and its mechanism on no-reflow need to be established in further prospective studies.
research.

In accordance with previous reports, our study showed that diabetic patients were more likely to develop the no-reflow phenomenon independent of other clinical and laboratory characteristics. Because of the emergency situation of the STEMI patients, in the current study, it was not possible to measure fasting blood glucose. Nonetheless, some previous studies have shown that hyperglycemia is the strongest predictive factor of no-reflow. In line with this finding, Malmberg et al. demonstrated that optimal blood sugar control before the PCI procedure improved long-term prognosis in diabetic patients with acute myocardial infarction. It has also been demonstrated that pretreatment with metformin can reduce the incidence of no-reflow in diabetic patients. Low initial TIMI flow grades have been consistently reported as a major risk factor for no-reflow. Similarly, we found higher odds of developing no-reflow in our patients with lower TIMI flow grades at admission. Higher initial TIMI grades suggest smaller infarct size and higher thrombus burden.

Although some studies have found an association between delayed reperfusion and the no-reflow phenomenon, there is still controversy regarding the harmful and beneficial effects of prompt vs. deferred stenting on no-reflow and other major adverse outcomes following PCI. In the current study, chinning in with some previous studies, there was no significant association between the time of symptom onset to PCI and the no-reflow phenomenon. In the present study, all the patients underwent PCI in a range of 10 to 700 minutes following the onset of symptoms.

Direct stenting as the method of reperfusion without pre-dilatation has been shown to reduce the risk of no-reflow compared with ballooning. Our study confirms this finding in that it showed a 58% decrease in the risk of no-reflow in stenting relative to balloon angioplasty. The complete and direct scaffolding of the mural thrombus and the diminished likelihood of thrombus dislodgment and further distal embolization have been explained as the possible mechanisms of the reduced risk in direct stenting in comparison with balloon angiography.

In a previous investigation, blood indices such as the white blood count were found to be the strong predictors of no-reflow. In contrast, we did not find inflammatory markers and renal dysfunction to be the independent predictors of no-reflow. Additionally, similar to a previous investigation in Iran, we did not find an independent association between smoking status and the no-reflow phenomenon.

This study suffered from some limitations. Firstly, we could not measure some other confounding variables including high-sensitivity C-reactive protein (as a specific inflammatory marker), the syntax score (for the severity of atherosclerosis), troponin and CK-MB levels (to detect infarct size as a potential confounding variable), and some other laboratory markers such as albumin that have been previously found to be the important predictors of no-reflow. Secondly, our study was performed in a single center on a relatively small sample size. Thirdly, due to the emergency and acute condition of STEMI patients, the blood sample could not be taken from a small group of the patients before PPCI.

**Conclusion**

This study found some clinical, laboratory, and procedural predictors of the no-reflow phenomenon. The results of this study can be used for the identification of high-risk patients and their appropriate management to reduce the no-reflow phenomenon in STEMI patients undergoing PPCI.

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**References**

1. van Kranenburg M, Magro M, Thiele H, de Waha S, Eitel I, Cochet A, Cottin Y, Atar D, Buser P, Wu E, Lee D, Bodi V, Klug G, Metzler B, Delevi R, Bernhardt P, Rotbauer W, Boersma E, Zijlstra F, van Guens RJ. Prognostic value of microvascular obstruction and infarct size, as measured by CMR in STEMI patients. JACC Cardiovasc Imaging 2014;7:930-939.

2. Gupta S, Gupta M. No reflow phenomenon in percutaneous coronary interventions in ST-segment elevation myocardial infarction. Indian Heart Journal 2016;68:539-551.

3. Durante A, Camici PG. Novel insights into an “old” phenomenon: the no reflow. Int J Cardiol 2015;187:273-280.

4. Kurtul A, Yarloglues M, Murat SN, Ergun G, Duran M, Kasapkarca HA, Demirelci MB, Cetin M, Ocek AH. Usefulness of the platelet-to-lymphocyte ratio in predicting angiographic reflow after primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction. Am J Cardiol 2014;114:342-347.

5. Stone GW, Peterson MA, Lansky AJ, Dangas G, Mehran R, Leon MB. Impact of normalized myocardial perfusion after successful angioplasty in acute myocardial infarction. J Am Coll Cardiol 2002;39:591-597.

6. Harrison RW, Aggarwal A, Ou FS, Klein LW, Rumsfeld JS, Roe MT, Wang TY. Incidence and outcomes of no-reflow phenomenon during percutaneous coronary intervention among patients with acute myocardial infarction. Am J Cardiol 2013;111:178-184.

7. Rezkalla SH, Kloner R. No-reflow phenomenon. Circulation 2002;105:656-662.

8. Rezkalla SH, Kloner RA. Coronary no-reflow phenomenon: from the experimental laboratory to the cardiac catheterization laboratory. Catheter Cardiovasc Interv 2008;72:950-957.

9. Henriques JP, Zijlstra F, van ’t Hof AW, de Boer MJ, Dambrik JH, Gosselink M, Hoormjje JC, Suryapranata H. Angiographic assessment of reperfusion in acute myocardial infarction by myocardial blush grade. Circulation 2003;107:2115-2119.
10. Niccoli G, Buzzotta F, Galiuto L, Crea F. Myocardial no-reflow in humans. J Am Coll Cardiol 2009;54:281-292.
11. Gibson CM, Cannon CP, Murphy SA, Ryan KA, Mesley R, Marble SJ, McCabe CH, Van Der Werf F, Braunwald E. Relationship of TIMI myocardial perfusion grade to mortality after administration of thrombolytic drugs. Circulation 2006;101:125-130.
12. Ito H, Okamura A, Iwakura K, Masuyama T, Hori M, Takiuchi S, Negoro S, Nakatsuki Y, Taniyama Y, Higashino Y, Fujii K, Minamino T. Myocardial perfusion patterns related to thrombolysis in myocardial infarction perfusion grades after coronary angioplasty in patients with acute anterior wall myocardial infarction. Circulation 1996;93:1993-1999.
13. Krima C, Izgi A, Dundar C, Tanalp AC, Oduncu V, Aung SM, Sonmez K, Mutlu B, Ozdemir N, Erentug V. Clinical and procedural predictors of no-reflow phenomenon after primary percutaneous coronary interventions: experience at a single center. Circ J 2008;72:716-721.
14. Reffellmann T, Kloner RA. The "no-reflow" phenomenon: basic science and clinical correlates. Heart 2002;87:162-168.
15. Ashraf T, Khan MN, Afqae SM, AamirKF, Kumar M, Sagarhi T, Rasool SI, Rizvi SNH, Sial JA, Nadeem A, Khan AA, Karim M. Clinical and procedural predictors and short-term survival of the patients with no-reflow phenomenon after primary percutaneous coronary intervention. Int J Cardiol 2019;294:27-31.
16. Choesebro JH, Knatterud G, Roberts R, Borer J, Cohen LS, Dalen J, Dodge H, Francis CK, Hillis D, Ludbrook J, P. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. Circulation 1987;76:142-154.
17. Alidosti M, Lotfi R, Lotfii-Tokaldany M, Nematipour E, Salarifar M, Poorhosseini H, Jalali A. Correlates of the "no-reflow" or "slow-flow" phenomenon in patients undergoing primary percutaneous coronary intervention. J Teh Univ Heart Ctr 2018;13:108-114.
18. 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 Suppl 3:S406-S418.
19. Mazhar J, Mashicharan M, Farshid A. Predictors and outcome of no-reflow post primary percutaneous coronary interventional for ST elevation myocardial infarction. Int J Cardiol Heart Vasc 2015;8:8-12.
20. Zhou H, He XY, Zhuang SW, Wang J, Lai Y, Qi WG, Yao YA, Liu XB. Clinical and procedural predictors of no-reflow in patients with acute myocardial infarction after primary percutaneous coronary intervention. World J Emerg Med 2014;5:96-102.
21. Ipek G, Onuk T, Karatas MB, Gungor B, Keskin M, Ozepke O, Hurlitz S, Nicol P, Waldenström H. Evaluation of the clinical and procedural predictive factors of delayed and no-reflow as recognized with thrombolysis in myocardial infarction [TIMI] flow grade following primary angioplasty. Angiology 2015;66:278-285.
22. Minamino T. Myocardial perfusion patterns related to thrombolysis in myocardial infarction normal coronary angiograms. J Am Coll Cardiol 1985;6:1254-1259.
23. Hashemi-Jazi M, Hosseini SM, Gholanrezaei A. Factors associated with the no-reflow phenomenon following percutaneous intervention of saphenous vein coronary bypass grafts. ARYA Atheroscler 2017;13:221-229.
24. Galderisi M, de Simone G, Cicala S, Parisi M, D’Errico A, Innelli P, de Divitiis M, Mondillo S, de Divitiis O. Coronary flow reserve in hypertensive patients with hypercholesterolemia and without coronary heart disease. Am J Hypertens 2007;20:177-183.
25. Kozakóvá M, Palombo C, Prezat L, Pintella G, Galetti L’Abbate A. Mechanisms of coronary flow reserve impairment in human hypertension. An integrated approach by transthoracic and transesophageal echocardiography. Hypertension 1997;29:551-559.
26. Kozakóvá M, Ferrannini E, Palombo C. Relation between left ventricular midwall function and coronary vasodilator capacity in arterial hypertension. Hypertension 2003;42:528-533.
27. Chen Y, Wang C, Yang X, Wang L, Sun Z, Liu H, Chen L. Independent no-reflow predictors in female patients with ST-elevation acute myocardial infarction treated with primary percutaneous coronary intervention. Heart Vessels 2012;27:243-249.
28. Ishikura F, Miki A, Iwata A, Toshida T, Shakudo M, Asanuma T, Kitakaze M, Shinozaki Y, Mori H, Beppu S. Effect of systemic blood pressure on microcollateral circulation evaluated by real-time contrast echocardiography. J Am Soc Echocardiogr 2008;21:765-769.
29. Varat MA, Adolph RJ, Fowler NO. Cardiovascular effects of anemia. Am Heart J 1972;83:415-426.
30. Marcus ML, White CW. Coronary flow reserve in patients with normal coronary angiograms. J Am Coll Cardiol 1985;6:1254-1256.
31. Dogan NB, Ozpelti E, Akdeniz S, Bilgin M, Baris N. Simple clinical risk score for no-reflow prediction in patients undergoing primary percutaneous coronary intervention with acute STEMI. Pak J Med Sci 2013;31:576-581.
32. Iwakura K, Ito H, Ikuishima M, Kawano S, Okamura A, Asano K, Kuroda T, Tanaka K, Masuyama T, Hori M, Fuji K. Association between hyperglycemia and the no-reflow phenomenon in patients with acute myocardial infarction. J Am Coll Cardiol 2003;41:1-7.
33. Zhao J, Yang YJ, Pei WD, Sun YH, Chen JL. The effect of statins on the no-reflow phenomenon: an observational study in patients with hyperglycemia before primary angioplasty. Am J Cardiovasc Drugs 2009;9:81-89.
34. Mahlbring K, Ryden L, Efendic S, Herlitz J, Nicol P, Waldenström A, Wedel H, Welin L. Randomized trial of insulin-glucose infusion followed by subsequent insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. J Am Coll Cardiol 1995;26:57-65.
35. Zhao JL, Fan CM, Yang YJ, You SJ, Gao X, Zhou Q, Pei WD. Chronic pretreatment of metformin is associated with the reduction of the no-reflow phenomenon in patients with diabetes mellitus after primary angioplasty for acute myocardial infarction. Cardiovasc Ther 2013;31:60-64.
36. Bahrehmand M, Sadeghi E, Shafee A, Nozari Y. Predictors of delayed and no-reflow as recognized with thrombolysis in myocardial infarction (TIMI) flow grade following primary percutaneous coronary angioplasty. J Med Life 2015;8(Spec Iss 3):59-65.
37. De Maria GL, Alkhalil M, Oikonomou EK, Wolfurm M, Choudhry RP, Banning AP. Role of deferred stenting in patients with ST elevation myocardial infarction treated with primary percutaneous coronary intervention: a systematic review and meta-analysis. J Interv Cardiol 2017;30:264-273.
38. Mahmoud AH, Taha NM, Baraka K, Ashraf M, Shahata S. Clinical and procedural predictors of suboptimal myocardial reperfusion in primary percutaneous coronary intervention. Int J Cardiol Heart Vasc 2019;23:100357.
39. Kurtul A, Ocek AH, Murat SN, Yarlioglues M, Demircelik MB, Duran M, Ergun G, Cay S. Serum albumin levels on admission are associated with angiographic no-reflow after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. Angiology 2015;66:278-285.
40. Abdi S, Rafizadeh O, Peighambari M, Basiri H, Bakhsheidhe H. Evaluation of the clinical and procedural predictive factors of no-reflow phenomenon following primary percutaneous coronary intervention. Res Cardiovasc Med 2015;4:e25414.
41. Sensoy B, Uzunget SB, Arıkgoz S, Sensoy N, Sen F, Acar B, Canpolat U, Özeke O, Cay S, Maden O. Renal dysfunction on admission predicts no-reflow phenomenon in patients undergoing...
42. Kurtul A, Murat SN, Yarlioglu M, Duran M, Celik IE, Kilic A. Mild to moderate renal impairment is associated with no-reflow phenomenon after primary percutaneous coronary intervention in acute myocardial infarction. Angiology 2015;66:644-651.

43. Shemirani H, Tafti FD, Amirpour A. Comparison of no-reflow phenomenon after percutaneous coronary intervention for acute myocardial infarction between smokers and nonsmokers. J Res Med Sci 2014;19:1068-1073.

44. Magro M, Nauta ST, Simsek C, Boersma E, van der Heide E, Regar E, van Domburg RT, Zijlstra F, Serruys PW, van Geuns RJ. Usefulness of the SYNTAX score to predict "no reflow" in patients treated with primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Am J Cardiol 2012;109:601-606.

45. Şahin DY, Gür M, Elbasan Z, Kuloğlu O, Şeker T, Kivrak A, Tanboğa İH, Gözübüyük G, Kirim S, Çaylı M. SYNTAX score is a predictor of angiographic no-reflow in patients with ST-elevation myocardial infarction treated with a primary percutaneous coronary intervention. Coron Artery Dis 2013;24:148-153.