The Value of Pre-Infarction Angina and Plasma D-Dimer in Predicting No-Reflow After Primary Percutaneous Coronary Intervention in ST-Segment Elevation Acute Myocardial Infarction Patients

Hongyu Zhang*
Baohua Qiu*
Yan Zhang
Yanjun Cao
Xia Zhang
Zhiguo Wu
Shujing Wang
Lianlian Mei

* These authors contributed equally to this study
Corresponding Author: Yanjun Cao, e-mail: lili_ch2@163.com
Source of support: Departmental sources

Background: Primary percutaneous coronary intervention (PCI) has improved outcomes greatly in patients with ST-elevation myocardial acute infarction (STEMI). However, the no-reflow phenomenon significantly reduces its efficacy.

Material/Methods: In this study, we investigated the value of combining plasma D-dimer level on admission and pre-infarction angina (PIA) in predicting no-reflow phenomenon in STEMI patients after primary PCI. A total of 926 STEMI patients who underwent primary PCI were included.

Results: The average age was 52.6 years, 617 (66.6%) of them had experienced a PIA, and 435 (47.9%) showed no-reflow phenomenon after primary PCI. Both PIA and plasma D-dimer on admission were independent predictors of no-reflow, with a risk of 0.516 (95% CI: 0.380 to 0.701) and 2.563 (95% CI: 1.910 to 3.439), respectively. Plasma D-dimer level had an area under curve (AUC) of 0.604 (95% CI: 0.568~0.641) in predicting no-reflow phenomenon, and PIA had an AUC of 0.574 (95% CI: 0.537 to 0.611). Importantly, the new signature combining D-dimer level on admission and PIA showed an increased AUC (0.637, 95%CI: 0.601 to 0.673) in predicting the no-reflow phenomenon. Moreover, the patients with high D-dimer level on admission but without PIA had significantly increased ratio of no-reflow phenomenon and in-hospital mortality compared to the other patients (P<0.001 and P=0.041, respectively).

Conclusions: Based on these solid results, we conclude that combining plasma D-dimer level on admission and PIA might create a good signature for use in predicting the no-reflow phenomenon after primary PCI in STEMI patients.

MeSH Keywords: Angina, Stable • Coronary Thrombosis • Myocardial Infarction • No-Reflow Phenomenon • Percutaneous Coronary Intervention

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/909360
Background

Primary percutaneous coronary intervention (PCI) has substantially enhanced outcomes in patients with ST-elevation myocardial infarction (STEMI) and has become the favored reperfusion strategy in patients with STEMI [1–3]. However, the no-reflow phenomenon significantly reduces the efficacy of PCI treatment for STEMI [4,5]. “No-reflow phenomenon” is the term used to describe inadequate myocardial reperfusion of a given coronary segment after an obstruction or conduit vessel spasm in an epicardial vessel has been removed [4,5]. No-reflow phenomenon is clinically important because of its independent association with higher incidences of inhospital mortality, malignant arrhythmias, and cardiac failure [6,7]. In addition, the no-reflow phenomenon is associated with poor long-term prognosis due to post-procedural myocardial infarction [8]. Although some potential predictors of no-reflow phenomenon have been reported, such as the platelet/lymphocyte ratio and monocyte count [9, 10], more predictors are still urgently needed.

Pre-infarction angina (PIA) occurring shortly before the onset of acute myocardial infarction (AMI) has a cardioprotective effect [11]. PIA has been shown to preserve microvascular function after reperfusion in STEMI patients [11]. Mechanistically, the protective roles are through the ischemic preconditioning mechanism, i.e., the phenomenon by which brief episodes of ischemia induce the tolerance of the myocardial cells to a subsequent major ischemic attack [12]. Clinically, PIA predicts thrombus burden in patients admitted for STEMI [13]. However, the association between PIA and no-reflow phenomenon has received little research attention.

During thrombus formation, fibrinogen is converted to fibrin monomers. Cross-linking of the fibrin monomers then takes place in the region termed the “D-domain.” Adjacent D-domains are covalently linked and form a fibrin-specific feature of a thrombus. Fibrin polymers can be degraded by plasmin during the fibrinolytic process. One of the terminal products of the fibrinolytic process is the covalently linked D-Domain called the D-dimer. Adjacent D-domains are covalently linked and form a fibrin-specific feature of a thrombus. Fibrin polymers can be degraded by plasmin during the fibrinolytic process. One of the terminal products of the fibrinolytic process is the covalently linked D-Domain called the D-dimer. Thus, the D-dimer level emerged as a useful marker of procoagulant activity and ongoing fibrinolysis [14]. D-dimer tests are widely used as a non-invasive triage biomarker in patients with acute thoracic pain [15]. In STEMI patients, high D-dimer level is associated with increased in-hospital cardiovascular mortality and 6-month all-cause mortality in patients after primary PCI [16]. Another study showed a correlation between D-dimer level and no-reflow phenomenon [17]. However, the predictive value of a single biomarker is usually limited. In the present study, we combined the PIA and D-dimer level as a predictive signature, aiming to enhance the accuracy of no-reflow prediction.

Material and Methods

Patient’s selection

This study had a prospective design. Patient admission started in March 2008 and ended in September 2015. A balanced number of reflow (531 cases) and no-reflow (530 cases) STEMI patients were randomly selected from the reflow patient population and the no-reflow patient population, respectively. We further selected patients based on the following exclusion criteria: 1) primary PCI was performed after 12 h of admission to hospital or no stent was implanted during the PCI; 2) age >75 years; 3) major surgeries or severe injuries in the past 6 months; 4) high risk of bleeding (patients who underwent anticoagulant therapy within 12 months before admission, had history of bleeding disorder, vascular abnormality, a count of platelet <100 000/mm³, or severe chronic liver disease); 5) bypass grafting or stenting treatment due to previous myocardial infarction; 6) thrombolysis failure and rescue PCI; 7) class IV heart failure; 8) severe respiratory, renal, or hepatic dysfunction or failure; 9) history of thromboembolic disease, treated cancer, inflammatory process, and pregnancy. All patients signed the inform consent. This study was approved by the local ethics committee of Tianjin Baodi Hospital.

PCI procedure and angiographic analysis

We performed the PCI procedure by a femoral approach with a 6F guiding catheter. A bolus of heparin (5000 IU) was administered before the procedure. After routine wire crossing, we performed balloon pre-dilatation, followed by stenting implantation whenever possible. After vessel recanalization, intracoronary nitrates were administered. Before and after vessel recanalization, we collected the following angiographic data: 1) coronary TIMI flow grading; 2) corrected TIMI frame count (CTFC); 3) TIMI score. To prevent bias, 2 independent angiographers who were blind to the aim of this study did the assessment; their final consistency was 92%. Any disagreements were resolved by consensus. The no-reflow phenomenon was defined as a coronary TIMI flow grade less than 3 after vessel reopening by PCI. Presence of PIA was determined by asking the patient to recall symptoms of angina that presented within 72 h before admission. The symptoms include chest pain (may be described as pressure or discomfort), pain in shoulders (or in back, arms, or neck), dizziness, weakness, nausea, fatigue, and shortness of breath.

Key laboratory assays

We collected venous blood from a branchial vein using EDTA tubes and non-anticoagulant tubes before the PCI procedure on the day of patient admission to the hospital. Blood samples were then centrifuged for 10 min at 10 000 rpm. The aliquots
of plasma and serum were stored at –80°C until assayed. We measured the D-dimer using the human D-dimer ELISA kit (EHDDIMER, Thermo Fisher Scientific, Waltham, MA, USA) with a sensitivity of 0.08 pg/mL. Serum creatine kinase (CK) and CK-MB fraction were evaluated at admission, every 4 h during the first day, and every 24 h in the following 5 days, using routine methods. Left ventricular ejection fraction (LVEF) at admission and within 2 h after PCI was measured by a 2D echocardiography (Simpson method). Other clinical information and laboratory tests were obtained through routine clinical tests.

Statistical analysis

All the statistical analysis and data visualization were performed using SPSS software 14.0 (SPSS Inc., Chicago, IL, USA) and Prism GraphPad software (San Diego, CA, USA). Data are presented as means with standard deviation (SD) or frequencies (n) and percentages. Comparisons between 2 groups were conducted using the t test. Relationships between nominal or ordinal variables were analyzed by chi-squared test. Univarient and multivariant logistic regression were performed to analyze the value of variables in predicting the no-reflow phenomenon. Receiver operating characteristic (ROC) curves were made to analyze the sensitivity and specificity of predicting the no-reflow phenomenon by using PIA and plasma D-dimer level. To evaluate the significance of combining PIA and plasma D-dimer level in predicting no-reflow phenomenon, patients were graded based on the 2 potential risk factors (no-PIA and high plasma D-dimer at admission): 0 for double-negative patients (with PIA and low D-dimer), 1 for single-positive patients (no-PIA or high D-dimer), and 2 for double-positive patients (no-PIA and high D-dimer. High D-dimer was defined as more than the mean value of all the patients (383.1 ng/ml). A two-tail P value less than 0.05 was defined as statistical significance.

Result

Characteristics of included patients

To explore the value of PIA and D-dimer level on admission in predicting no-reflow phenomenon after primary PCI, we included a total of 926 STEMI patients (Figure 1). The basic clinical characteristics of these patients are summarized in Table 1. Briefly, the average age of these patients was 52.6 years with

Table 1. Basic clinical features of the STEMI patients.

| Baseline feature                  | Data            |
|----------------------------------|-----------------|
| Age (year)                       | 52.6±7.81       |
| Male, n (%)                      | 429 (46.3)      |
| BMI (kg/m²)                      | 25.9±5.1        |
| Smoker, n (%)                    | 356 (38.4)      |
| Hypertension, n (%)              | 415 (55.2)      |
| History of ischemic heart disease, n (%) | 231 (24.9) |
| Diabetes, n (%)                  | 366 (39.5)      |
| Hyperlipemia, n (%)              | 415 (55.2)      |
| Angina, n (%)                    | 617 (66.6)      |
| D-dimer (ng/ml)                  | 383.1±264.2     |
| No-reflow, n (%)                 | 435 (47.0)      |
a standard deviation of 7.81 years. There were 429 (46.3%) males and 497 (53.7%) females and 617 (66.6%) of them had experienced angina before they were admitted to the hospital due to STEMI. No-reflow phenomenon after primary PCI was found in 435 (47.9%) and 491 (53.0%) showed a normal reflow after PCI.

Relationship between the no-reflow phenomenon and other clinical features of STEMI patients

To explore the potential factors related to the no-reflow phenomenon of STEMI patients after primary PCI, we analyzed the relationship between no-reflow and many important clinical features. As shown in Table 2, we found that there was a significantly higher ratio of hypertension, smoking, history of ischemic heart disease, diabetes, hyperlipemia, low TIMI grade (<3) at admission, and longer delay before primary PCI, higher CTFC before recanalization, TIMI score, and CK-MB levels among the patients with the no-reflow phenomenon (P: <0.001, 0.023, 0.012, <0.001, 0.008, <0.001, 0.001, <0.001, 0.001, and 0.004, respectively). Importantly, the patients with no-reflow phenomenon had significantly lower ratio of PIA than the patients with normal reflow (n=111 [25.5%] vs. n=198 [40.3%], P<0.001). No-reflow patients had significantly higher plasma D-dimer level than patients with normal reflow after primary PCI (P<0.001).

Table 2. Potential predictors of the no-reflow after PCI.

| Features                                      | Normal reflow (n=491) | No-reflow (n=435) | P value |
|-----------------------------------------------|-----------------------|-------------------|---------|
| Age (>53 year)                                | 269 (54.8)            | 238 (54.7)        | 0.982   |
| Male, n (%)                                   | 225 (45.8)            | 204 (46.9)        | 0.744   |
| BMI (kg/m²)                                   | 25.6±5.0              | 26.2±5.0          | 0.105   |
| Hypertension, n (%)                           | 240 (48.9)            | 271 (62.3)        | <0.001  |
| Smoke, n (%)                                  | 172 (35.0)            | 184 (42.3)        | 0.023   |
| History of ischemic heart disease, n (%)      | 106 (21.6)            | 125 (28.7)        | 0.012   |
| Diabetes, n (%)                               | 152 (31.0)            | 214 (49.2)        | <0.001  |
| Hyperlipemia, n (%)                           | 200 (40.7)            | 215 (49.4)        | 0.008   |
| TIMI grade at admission <3, n (%)             | 296 (60.3)            | 332 (76.3)        | <0.001  |
| CTFC before recanalization                    | 35.3±6.7              | 38.6±8.1          | <0.001  |
| TIMI score                                    | 3.8±0.44              | 4.3±0.67          | <0.001  |
| Total serum bilirubin (µmol/L)                | 11.5±6.3              | 12.3±7.4          | 0.076   |
| Pre-infarction angina, n (%)                  | 198 (40.3)            | 111 (25.5)        | <0.001  |
| Angina time                                   | 15.1±22.5             | 11.5±21.6         | 0.013   |
| Time before PCI (hour)*                       | 5.8±2.6               | 6.3±2.3           | 0.001   |
| CK-MB on admission (mmol/L)                   | 212.2±168.9           | 247.1±202.4       | 0.004   |
| LVEF, n (%)**                                 | 205 (41.8)            | 223 (51.3)        | 0.004   |
| D-dimer (ng/ml)                               | 272.0±218.9           | 508.5±254.7       | <0.001  |

* Time before PCI was defined as the interval between occurrence of infarction symptoms and execution of PCI procedures. ** n (%) indicated the number and percentage of patients with LVEF less than 45%.

PIA and plasma D-dimer level on admission are independent predictors of no-reflow phenomenon

Because our results indicated multiple potential clinical factors associated with the no-reflow phenomenon of STEMI patients, we performed logistic regression analysis to find the independent predictors of no-reflow. As shown in Table 3, in the univariate analysis, hypertension, smoking, history of ischemic heart disease, diabetes, hyperlipidemia, TIMI grade on admission, PIA, time before primary PCI, CK-MB level, LVEF, and D-dimer level on admission were potential predictors of no-reflow phenomenon. In the multivariate analysis, most of these potential predictors maintained their significance in predicting no-reflow phenomenon. Importantly, PIA was an independent protective predictor of no-reflow, with a risk of 0.516 (95% CI:
Plasma D-dimer level on admission was an adverse predictor of the no-reflow phenomenon, with a risk of 2.563 (95% CI: 1.910–3.439).

Combining PIA and plasma D-dimer on admission showed better prediction of the no-reflow phenomenon.

We plotted ROC curves to evaluate the accuracy of predicting the no-reflow phenomenon of PIA and plasma D-dimer level on admission. A high D-dimer level was defined as a D-dimer level more than the mean value of all patients included in this study (>383.1 ng/ml). As shown in Figure 2A, PIA had an area under the curve (AUC) of 0.574 (95% CI: 0.537–0.611), a sensitivity of 0.745, and a specificity of 0.403 in predicting no-reflow phenomenon, while the plasma D-dimer level on admission had an AUC of 0.604 (95% CI: 0.568–0.641, Figure 2B), with a sensitivity of 0.526 and a specificity of 0.682. Then, we combined the plasma D-dimer level on admission and the PIA to form a new signature. Using this new signature to predict no-reflow, the AUC was increased to 0.637 (95% CI: 0.601–0.673) with the best sensitivity of 0.871 and the best specificity of 0.819 (Figure 2C). These data suggest that combining PIA and plasma D-dimer on admission would be a sound signature for use in predicting the no-reflow phenomenon for STEMI patients.

Table 3. Logistic regression analysis of predictors of no-reflow in T2DM patients after PCI.

| Features                                      | Univariate analysis | Multi-variant analysis |
|-----------------------------------------------|---------------------|------------------------|
|                                              | P value | Risk  | 95% CI       | P value | Risk  | 95% CI       |
| Age (>53 vs. ≤53 years)                      | 0.982   | 1.003 | 0.774–1.300  | 0.818   | 0.967 | 0.724–1.290  |
| Male (yes vs. no)                            | 0.744   | 0.958 | 0.739–1.241  | 0.991   | 1.002 | 0.735–1.366  |
| BMI (kg/m²)                                  | 0.105   | 1.022 | 0.996–1.048  | 0.117   | 0.977 | 0.950–1.006  |
| Hypertension (yes vs. no)                    | <0.001  | 1.727 | 1.330–2.247  | <0.001  | 1.783 | 1.332–2.388  |
| Smoke (yes vs. no)                           | 0.023   | 1.359 | 1.043–1.773  | 0.078   | 1.330 | 0.969–1.825  |
| History of ischemic heart disease (yes vs. no) | 0.012   | 1.464 | 1.086–1.976  | 0.011   | 1.545 | 1.107–2.156  |
| Diabetes (yes vs. no)                        | <0.001  | 2.160 | 1.653–2.825  | <0.001  | 2.233 | 1.643–3.035  |
| Hyperlipemia (yes vs. no)                    | 0.008   | 1.422 | 1.096–1.845  | 0.438   | 1.126 | 0.834–1.521  |
| TIMI grade at admission (<3 vs. =3)          | <0.001  | 2.123 | 1.595–2.825  | <0.001  | 2.182 | 1.598–2.980  |
| Pre-infarction angina (yes vs. no)            | <0.001  | 0.507 | 0.383–0.671  | <0.001  | 0.516 | 0.380–0.701  |
| Time before PCI (hour)                       | 0.001   | 1.088 | 1.033–1.146  | 0.003   | 1.093 | 1.031–1.159  |
| CK-MB peak (mmol/L)                          | 0.005   | 1.001 | 1.002–1.00    | 0.015   | 1.001 | 1.000–1.002  |
| LVEF (%)                                      | 0.004   | 1.468 | 1.131–1.905  | 0.007   | 1.486 | 1.114–1.984  |
| D-dimer (ng/ml)                              | <0.001  | 2.387 | 1.828–3.115  | <0.001  | 2.563 | 1.910–3.439  |

0.516–0.380). Plasma D-dimer level on admission was an adverse predictor of the no-reflow phenomenon, with a risk of 2.563 (95% CI: 1.910–3.439).

**Combining PIA and plasma D-dimer on admission showed better prediction of the no-reflow phenomenon**

We plotted ROC curves to evaluate the accuracy of predicting the no-reflow phenomenon of PIA and plasma D-dimer level on admission. A high D-dimer level was defined as a D-dimer level more than the mean value of all patients included in this study (>383.1 ng/ml). As shown in Figure 2A, PIA had an area under the curve (AUC) of 0.574 (95% CI: 0.537–0.611), a sensitivity of 0.745, and a specificity of 0.403 in predicting no-reflow phenomenon, while the plasma D-dimer level on admission had an AUC of 0.604 (95% CI: 0.568–0.641, Figure 2B), with a sensitivity of 0.526 and a specificity of 0.682. Then, we combined the plasma D-dimer level on admission and the PIA to form a new signature. Using this new signature to predict no-reflow, the AUC was increased to 0.637 (95% CI: 0.601–0.673) with the best sensitivity of 0.871 and the best specificity of 0.819 (Figure 2C). These data suggest that combining PIA and plasma D-dimer on admission would be a sound signature for use in predicting the no-reflow phenomenon for STEMI patients.

**Plasma D-dimer level on admission and PIA are associated with mortality of STEMI patients**

All the patients were divided into 3 groups according to their plasma D-dimer level on admission and PIA: patients with high-D-dimer and without PIA, patients with either high D-dimer or no-PIA group, and patients with low D-dimer and PIA. The ratio of the no-reflow phenomenon and in-hospital all-cause mortality of these patients were compared. As shown in Figure 3A, the percentage of the no-reflow phenomenon among the patients with high D-dimer and without PIA was the highest among these 3 groups (P value <0.001). In addition, these patients had the highest all-cause in-hospital mortality (P value=0.041, Figure 3B).

**Discussion**

The no-reflow phenomenon has been investigated extensively in clinical settings and basic science laboratories. No-reflow phenomenon, which develops mostly within the first 2 h after reperfusion, is mainly the consequence of ischemic endothelial cell injury obstructing the capillary lumen [18,19]. The incidence of no-reflow phenomenon is around 20% in all AMI
patients after primary PCI and is the major cause of primary PCI failure [20]. However, it is still a challenge to predict no-reflow in STEMI patients in clinical practice.

PIA is the angina episode preceding the onset of definite AMI. Previous studies have shown that patients with PIA tend to have reduced infarct size and increased ejection fraction compared with patients without PIA [21,22]. Therefore, PIA was identified as a favorable prognosticator in patients with STEMI [23]. Mechanisms underlying this association are likely related to activation of ischemic preconditioning (IP) by PIA [24]. In animal models, IP can reduce infarct size by half [25]. In addition to infarct size reduction, the microcirculation may also be protected by IP after reperfusion, as previously shown in animal models [26]. This effect may be related to endothelial function improvement and prevention of neutrophil activation caused by ischemic reperfusion. The severe cell injury caused by ischemia is one of the major causes of no-reflow phenomenon[27]. Considering the mechanistic connections between the IP by PIA and no-reflow phenomenon, we expected that the absence of PIA could serve as a predictor of the no-reflow phenomenon. To this end, we designed a prospective study to evaluate the association between PIA and no-reflow in STEMI patients.

In the no-reflow cohort, the proportion of patients with PIA was significantly lower than in the normal reflow cohort. The multivariate analysis indicated that the presence of PIA could significantly reduce the odds of having no-reflow phenomenon (OR=0.516, 95%CI=0.380, 0.701). This observation is in line with a previous study reporting that absence of PIA is associated with higher risk of no-reflow in STEMI patients [28].
D-dimer is the final product of fibrin degradation by plasmin, the plasma concentrations of which are increased in ongoing or recent thrombosis. Earlier studies have already shown that plasma D-dimer levels were higher in patients with AMI than in patients with stable angina or in healthy individuals, meaning that the D-dimer level reflects the ongoing thrombotic disease [29]. Plasma D-dimer levels on admission were shown to be significantly associated with thrombus burden in AMI patients [30]. These facts highly suggest that the plasma D-dimer level on admission is a potential biomarker of no-reflow, which is positively influenced by the thrombus burden. In our study, plasma D-dimer level on admission was significantly higher in patients with no-reflow phenomenon than in those patients without no-reflow phenomenon. In the multivariate analysis, the plasma D-dimer level on admission was an independent predictor of no-reflow. This observation is in agreement with a previous publication by Ayhan et al. [17].

Our study also revealed several other independent predictors of no-reflow phenomenon after the primary PCI, such as hypertension, history of ischemic heart disease, and CK-MB peak level. These results suggest that no-reflow phenomenon is a multiple-factor-driven outcome. Some other potential risk factors of the no-reflow phenomenon of STEMI patients after PCI have also been reported by previous studies, such as the number of infarct-related Q-waves in the ECG precordial leads before the primary PCI, primary platelet/lymphocyte ratio, C-reactive protein level, and monocyte count on admission [9,10,31]. Many of these reported potential risk factors of the no-reflow phenomenon are related to the inflammation nature for use in predicting the no-reflow phenomenon after primary PCI in STEMI patients. It is important to include more parameters as extensively as possible to minimize the influence of the differences in baseline characteristics, unmeasured factors, such as cardiac troponin, could influence the time course of ongoing myocardial necrosis. Third, in the present study, we only combined PIA and plasma D-dimer level to predict the no-reflow phenomenon. To further improve the predictive value, it is important to include more parameters to form a comprehensive model. Overall, our findings indicate the needs for concomitant assessment of the clinical value of PIA, plasma D-dimer level, and more clinical parameters in well-defined or controlled patient populations.

Conclusions

Based on these solid results, we conclude that combining plasma D-dimer level on admission and PIA might be a useful signature for use in predicting the no-reflow phenomenon after primary PCI in STEMI patients. It may help to screen STEMI patients with relatively high risk of no-reflow on admission and help the physicians select the best treatment.

Conflict of interest

None.

Acknowledgement

We are grateful for grant support from the Tianjin Baodi Hospital.

References:

1. Nallamothu BK, Normand SL, Wang Y et al: Relation between door-to-balloon times and mortality after primary percutaneous coronary intervention over time: A retrospective study. Lancet, 2015; 385(9973): 1114–22
2. The Lancet: 40 years of percutaneous coronary intervention: Where next? Lancet, 2017; 390(10096): 715
3. Nallamothu BK, Bradley EH, Krumholz HM: Time to treatment in primary percutaneous coronary intervention. New Engl J Med, 2007; 357(16): 1631–38
4. Rezkalla SH, Stankowski RV, Hanna J, Kloner RA: Management of no-reflow phenomenon in the catheterization laboratory. JACC Cardiovasc Inter, 2017; 10(3): 215–23
5. Choo EH, Kim PJ, Chang K et al: The impact of no-reflow phenomena after primary percutaneous coronary intervention: A time-dependent analysis of mortality. Coron Artery Dis, 2014; 25(5): 392–98
6. Resnic FS, Wainstein M, Lee MK et al: No-reflow is an independent predictor of death and myocardial infarction after percutaneous coronary intervention. Am Heart J, 2003; 145(1): 42–46
7. Gorenek B: Management of cardiac arrythmias in post-PCI patients. Springer Milan, 2005; 231–39
8. Ndrepepa G, Tiroch K, Fusaro M et al: 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. J Am Coll Cardiol, 2010; 55(21): 2383–89

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]
10. Wang Z, Ren L, Liu N et al: Association of monocyte count on admission with angiographic no-reflow after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. Kardiol Pol, 2016; 74(10): 1160–66

11. Luz A, Santos M, Rodrigues P et al: Preinfarction angina: clinical significance and relationship with total ischemic time in patients with ST-elevation myocardial infarction. Coron Artery Dis, 2015; 26(1): 22–29

12. Posa A, Pavo N, Hemetsberger R, Csonka C et al: Protective effect of ischemic preconditioning on ischemia/reperfusion-induced microvascular obstruction determined by on-line measurements of coronary pressure and blood flow in pigs. Thromb Haemost, 2010; 103(2): 450–60

13. Ahmed TA, Sorgdrager BJ, Cannegieter SC et al: Pre-infarction angina predicts thrombus burden in patients admitted for ST-segment elevation myocardial infarction. EuroIntervention, 2012; 7(12): 1396–405

14. Olson JD: D-dimer: An overview of hemostasis and fibrinolysis, assays, and clinical applications. Adv Clin Chem, 2015; 69: 1–46

15. Sodeck G, Domanovits H, Schillinger M et al: D-dimer in ruling out acute aortic dissection: A systematic review and prospective cohort study. Eur Heart J, 2007; 28(24): 3067–75

16. Akgul O, Uyarel H, Pusuroglu H et al., Predictive value of elevated D-dimer in patients undergoing primary angioplasty for ST elevation myocardial infarction. Blood Coagul Fibrinolysis, 2013; 24(7): 704–10

17. Erkol A, Oduncu V, Turan B et al: The value of plasma D-dimer level on admission in predicting no-reflow after primary percutaneous coronary intervention and long-term prognosis in patients with acute ST segment elevation myocardial infarction. J Thromb Thrombolysis, 2014; 38(3): 339–47

18. Niccoli G, Buzotta F, Galuito L, Crea F et al: Myocardial no-reflow in humans. J Am Coll Cardiol, 2009; 54(4): 281–92

19. Kloner RA: No-reflow phenomenon: Maintaining vascular integrity. J Cardiovasc Pharmacol Ther, 2011; 16(3–4): 244–50

20. Ito H: No-reflow phenomenon and prognosis in patients with acute myocardial infarction. Nat Clin Pract Cardiovasc Med, 2006; 3(9): 499–506

21. Solomon SD, Anavekar NS, Greaves S et al: Angina pectoris prior to myocardial infarction protects against subsequent left ventricular remodeling. J Am Coll Cardiol, 2004; 43(9): 1511–14

22. Reiter R, Henry TD, Traverse JH: Preinfarction angina reduces infarct size in ST-elevation myocardial infarction treated with percutaneous coronary intervention. Circ Cardiovasc Interv, 2013; 6(1): 52–58

23. Niccoli G, Scalone G, Cosentino N et al: Protective effect of pre-infarction angina on microvascular obstruction after primary percutaneous coronary intervention is blunted in humans by cardiovascular risk factors. Circ J, 2014; 78(8): 1935–41

24. Rezkalla SH, Kloner RA: Ischemic preconditioning and preinfarction angina in the clinical arena. Nat Clin Pract Cardiovasc Med, 2004; 1(2): 96–102

25. Bromage DJ, Pickard JM, Rossello C et al: Remote ischemic conditioning reduces infarct size in animal in vivo models of ischemia-reperfusion injury: A systematic review and meta-analysis. Cardiovasc Res, 2017; 113(3): 288–97

26. Orbegozo Cortés D, Su F, Santacruz C et al: Ischemic conditioning protects the microcirculation, preserves organ function, and prolongs survival in sepsis. Shock, 2016; 45(4): 419–27

27. Bouleti C, Mevot N, Germain S: The no-reflow phenomenon: State of the art. Arch Cardiovasc Dis, 2015; 108(12): 661–74

28. Karila-Cohen D, Czitrom D, Brochet E et al: Decreased no-reflow in patients with anterior myocardial infarction and pre-infarction angina. Eur Heart J, 1999; 20(23): 1724–30

29. Koenig W, Rothenbacher D, Hoffmeister A et al: Plasma fibrin D-dimer levels and risk of stable coronary artery disease: results of a large case-control study. Arterioscler Thromb Vasc Biol, 2001; 21(10): 1701–5

30. Ali NMA, Gameel FEMH, and Elsayid M, Babker AMAAA: Alterations in coagulation and thrombogenesis activity markers in patients with acute myocardial infarction. Open Journal of Blood Diseases, 2016; 6(1): 1–5

31. Iwakura K, Ito H, Kawano S et al: Predictive factors for development of the no-reflow phenomenon in patients with reperfused anterior wall acute myocardial infarction. J Am Coll Cardiol, 2001; 38(2): 472–77

32. Jaffe R, Charron T, Puley G et al: Microvascular obstruction and the no-reflow phenomenon after percutaneous coronary intervention. Circulation, 2008; 117(24): 3152–56

© Med Sci Monit, 2018; 24: 4528-4535

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)