RESEARCH ARTICLE

The relationship between serum rheumatoid factor level and no-reflow phenomenon in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

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Objective: This study aimed to evaluate the relationship between serum rheumatoid factor (RF) levels and no-reflow phenomenon in patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

Methods: This single-center, cross-sectional study included a total of 318 consecutive patients who were diagnosed with STEMI and underwent primary PCI within 12 hours of the onset of symptoms. Baseline serum RF levels of all patients were measured. The diagnosis of no-reflow phenomenon was defined as a flow of TIMI II or less without the presence of dissection, mechanical obstruction, significant residual stenosis, or other plausible causes. The patients were divided into reflow group ($n = 283$) and no-reflow group ($n = 46$) regarding the angiographic features of thrombolysis in myocardial infarction (TIMI) flow of the infarct-related artery.

Results: No-reflow phenomenon was observed in 13.8% of the patients. Median RF level was significantly higher in no-reflow group than in reflow group (18.5 (7.0-27.6) vs 8.0 (4.6-50.8), $P < .001$). Forward conditional logistic regression analysis demonstrated that body mass index (OR = 0.845, 95% CI: 0.765 to 0.933, $P = .001$), diabetes mellitus (OR = 5.257, 95% CI: 1.124 to 24.587, $P = .035$), baseline RF level (OR = 1.198, 95% CI: 1.108 to 1.295, $P < .001$), and SYNTAX score I (OR = 1.065, 95% CI: 1.025 to 1.107, $P = .001$) were the independent predictors of no-reflow phenomenon.

Conclusion: Baseline serum RF concentrations are independently associated with the no-reflow phenomenon in patients undergoing primary PCI for acute STEMI.

KEYWORDS

no-reflow phenomenon, primary percutaneous coronary intervention, Rheumatoid factor, ST-segment elevation myocardial infarction

1 | INTRODUCTION

Primary percutaneous coronary intervention (PCI) is still the gold standard treatment of ST-segment elevation myocardial infarction (STEMI).¹ It usually results in restoration of both infarct-related artery (IRA) patency and thrombolysis in myocardial infarction (TIMI)

flow III in most patients.² However, there remain a small proportion of patients who continue to exhibit overt impairment of myocardial reperfusion despite successful opening of the IRA.³ This phenomenon, which is called no-reflow,⁴ occurs in up to 2% and in 8% to 11.5% of patients undergoing elective and primary PCI, respectively.^{5,6} The pathophysiology of no-reflow phenomenon involves

atherothrombotic microembolization,^{7,8} inflammation,^{8,9} activation of neutrophils, and platelets,⁸ which cause releasing of oxygen-free radicals, proteolytic enzymes, and proinflammatory mediators that can cause tissue and endothelial damage, particularly in critically injured myocytes.¹⁰ In addition, coronary microvascular spasm and reperfusion injury,¹¹ as well as genetic predisposition,¹⁰ may play a part in the pathophysiology of no-reflow phenomenon. No-reflow phenomenon is indisputably associated with poor short- and long-term clinical outcomes and may negate the potential benefits of primary PCI in patients with STEMI.^{12,13} Early detection of no-reflow phenomenon, which may occur within 1-2 hours after completion of PCI, is essential because it is associated with reduced myocardial salvage, larger infarct size, and increased 5-year mortality.¹⁴ Clinically, it may present as recurrent angina, cardiogenic shock, arrhythmia, or acute dyspnea compatible with pulmonary edema secondary to heart failure.

Autoimmunity has been considered to contribute to atherosclerosis. In fact, it seems that both cellular and humoral immune systems are involved in the development and progression of atherosclerosis.¹⁵ Several studies have demonstrated autoimmunity-related microvascular dysfunction caused by increased sympathetic outflow,¹⁶ increased oxidative stress,¹⁷ increased endothelin-1 levels,¹⁸ and reduced bioavailability of nitric oxide in response to shear stress. Nevertheless, coronary flow reserve, which has been considered as a useful diagnostic index for both functional and physiologic assessment of coronary circulation,¹⁹ has been demonstrated to be impaired in several autoimmune diseases, including systemic sclerosis,²⁰ and rheumatoid arthritis (RA).²¹ Rheumatoid factor (RF), an antibody against the Fc portion of immunoglobulin G, has been implicated to have an association with atherosclerosis. Rheumatoid factor is observed not only in RA, but also in other rheumatic and inflammatory diseases, including Sjogren's syndrome, systemic lupus erythematosus, and polydermatomyositis. In addition, positive reactions of RF can be observed in up to 5% and in up to 25% of healthy young and elderly population, respectively. Rheumatoid factor is associated not only with an increased likelihood of developing coronary artery disease but also with an increased cardiovascular mortality in healthy subjects.²² Although the association between autoimmunity and no-reflow phenomenon has not been addressed in the literature, these patients demonstrate increased rates of poor coronary flow after elective and primary PCIs.²³ The aim of this study was to evaluate the relationship between baseline serum RF levels and no-reflow phenomenon in patients with acute STEMI undergoing primary PCI.

2 | METHODS

2.1 | Study population and design

This single-center, cross-sectional study included a total of 318 consecutive patients (267 male and 51 female; mean age: 55.8 ± 9.9 years) who were diagnosed with acute STEMI and underwent primary PCI at our clinic within 12 hours of onset of

symptoms. Patients with coronary artery bypass grafting, cardiogenic shock, stent thrombosis, acute or chronic infective or inflammatory disease, chronic autoimmune or connective tissue disease, neoplastic disease, moderate-severe chronic kidney disease (glomerular filtration rate <60 mL/min/1.73 m²), and chronic liver disease were excluded.

After detailed medical history, each patient underwent a targeted physical examination. Risk factors for coronary artery disease (CAD) were established. Venous blood samples to measure complete blood count, blood chemistry, lipid profile, high-sensitivity C-reactive protein (hs-CRP), high-sensitivity cardiac troponin T (hs-cTnT), and RF level were obtained from all of the patients on admission. 12-lead electrocardiograms (ECGs) were obtained at baseline, completion of PCI, and the 4th hours following PCI. Body mass indices were calculated using the formula: body mass index (BMI) = weight (kg)/height² (m²). Estimated glomerular filtration rate (eGFR) of each patient was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

All patients were given a therapy of 300 mg acetylsalicylic acid and a loading dose of clopidogrel prior PCI. They also received angiotensin-converting enzyme inhibitor, beta-blocker, statin, and heparin. Glycoprotein IIb/IIIa antagonists were not given to any patient prior PCI.

The study was conducted in accordance with the Declaration of Helsinki. An institutional ethics committee approved the study protocol and each participant provided a written informed consent.

2.2 | Identification of cardiovascular risk factors

Data concerning cardiovascular risk factors, including age, gender, hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HPL), and smoking status, were noted. Patients who were previously on oral antidiabetic and/or insulin therapy or those with fasting blood glucose, measured at least twice, ≥ 126 mg/dL were considered diabetic.²⁴ Patients who were previously on antihypertensive therapy or those with blood pressures, measured at least twice, $\geq 140/90$ mmHg were considered hypertensive.²⁵ The presence of HPL was considered when a measure of total cholesterol >200 mg/dL or low-density lipoprotein cholesterol (LDL-C) > 100 mg/dL was obtained or when the patient was previously on lipid-lowering medication in accordance with the "Adult Treatment Panel III" guideline.²⁶ Patients who were using tobacco products on admission to hospital and those who had quit smoking within the past month were considered smokers.

2.3 | Diagnosis of acute ST-segment elevation myocardial infarction

Diagnosis of STEMI was made in the presence of the following characteristics: typical type chest pain lasting more than 30 minutes, new onset or presumably new ST-segment elevation in two or more contiguous leads ≥ 0.2 mV in men and ≥ 0.15 mV in women with respect to J in V2 and V3 and ≥ 0.1 mV in other as well as elevation in myocardial enzymes and troponin.

TABLE 1 Baseline characteristics of the patients

Variable	Reflow group (n = 274)	No-reflow group (n = 44)	P value
Age (year)	55.3 ± 9.7	59.3 ± 10.2	.013
Gender, (male), n (%)	223 (81.4)	44 (100)	.002
BMI (kg/m ²)	28.1 ± 4.3	26.3 ± 5.5	.010
Heart Rate (bpm)	72 (49-119)	79 (56-91)	.078
SPB (mmHg)	113.5 ± 14.0	109.8 ± 2.8	.455
DPB (mmHg)	71.1 ± 9.2	72.8 ± 2.1	.612
HT, n (%)	105 (38.3)	10 (22.7)	.046
DM, n (%)	79 (28.8)	2 (4.5)	.001
HPL, n (%)	50 (18.2)	4 (9.1)	.133
Smoking, n (%)	126 (46.0)	32 (72.7)	.001
Hemoglobin (g/dL)	14.2 (10.1-18.1)	14.9 (13.2-16.3)	.005
Leukocyte count, × 10 ³ /μL	9.9 (4.4-25.4)	11.0 (7.0-18.6)	.004
Platelet count, × 10 ³ /μL	251 (155-509)	248 (183-392)	.650
eGFR (mL/min per 1.73 m ²)	98.4 (61.5-176.8)	103.4 (65.0-127.6)	.846
Triglyceride (mg/dL)	145 (47-734)	103 (60-306)	.023
Total cholesterol (mg/dL)	194.8 ± 44.2	193.1 ± 48.3	.820
HDL cholesterol (mg/dL)	38 (20-71)	40 (21-62)	.156
LDL cholesterol (mg/dL)	140 (42-292)	137 (72-192)	.825
Hs-CRP (mg/dL)	0.3 (0.0-14.1)	0.5 (0.1-2.5)	.028
Hs-cTnT (ng/mL)	0.09 (0.00-50.00)	0.37 (0.03-9.3)	<.001
RF (IU/mL)	8.0 (4.6-50.8)	18.5 (7.0-27.6)	<.001
Predischarge LVEF (%)	58 (31-73)	46 (36-79)	<.001
SYNTAX score I	20 (8-61)	33 (21-37)	<.001

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HT, hypertension; DM, diabetes mellitus; HPL, hyperlipidemia; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; Hs-CRP, high-sensitivity C-reactive protein; Hs-cTnT, high-sensitivity cardiac troponin T; RF, rheumatoid factor; LVEF, left ventricular ejection fraction; SYNTAX, Synergy Between PCI With TAXUS™ and Cardiac Surgery.

Data are presented as number (%), mean ± standard deviation, or median (minimum-maximum).

2.4 | Transthoracic echocardiographic examination

Each patient underwent transthoracic echocardiographic examination before discharge. Examinations were performed with the patient lying in the supine position or in the left decubitus position.

Measurements were obtained in accordance with the recommendations of the American Echocardiography Unit. Left ventricular ejection fraction (LVEF) was calculated according to Simpson's method.

2.5 | Coronary angiography and no-reflow phenomenon

Index coronary angiography procedures were performed using commercially available Siemens (Axiom Sensis XP, Berlin, Germany) device via the femoral approach. Informed consents were obtained routinely from all of the patients before the procedure. Primary PCI of the IRA was performed using standard conventional techniques. The diagnosis of no-reflow phenomenon was defined as a flow of TIMI II or less without the presence of dissection, mechanical obstruction, significant residual stenosis, or other plausible causes.⁵

2.6 | Blood samples and laboratory analysis

Venous blood samples to measure complete blood count, blood chemistry, lipid panel, high-sensitivity C-reactive protein (hs-CRP), high-sensitivity cardiac troponin T (hs-cTnT), and RF levels were obtained from all of the patients on admission. Routine blood chemistry and lipid parameters were measured with standard auto-analyzer. Blood counts were measured with a Sysmex K-1000 (Block Scientific, Bohemia, NY, USA) auto-analyzer within 5 minutes of sampling. Serum RF concentrations were measured using ELISA (Roche/Hitachi analyzer, Mannheim, Germany), and the normal range was defined as 5-20 IU/mL. Positive results were defined by the manufacturer's instructions (RF > 20 IU/mL). High-sensitivity C-reactive protein levels were measured using a commercial kit (Abbott, Aeroset, Holliston, Minn.). Serum concentrations of hs-cTnT were measured using an Elecsys 2010 analyzer (Cobas e 411; Elecsys, Roche Diagnostics, Mannheim, Germany).

2.7 | Statistical analysis

Data analyses were performed using SPSS version 22.0 statistical software package (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation or median (minimum-maximum). Categorical variables were expressed as number (percentage). Normal distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. The Chi-square test was used to compare categorical variables. The independent-samples *t* test or the Mann-Whitney *U* test was used to compare continuous variables depending on whether statistical assumptions were fulfilled or not. The correlation between variables was performed using the Spearman's rank-order correlation analysis. All significant parameters (*P* < .1) in the univariate analysis were selected for the multivariate model, and forward conditional logistic regression analysis was used to determine the independent predictors of no-reflow phenomenon. Odds ratio and 95% confidence interval of each independent variable were calculated. A two-tailed *P* value of <.05 was considered significant.

3 | RESULTS

This study included a total of 318 consecutive patients who were diagnosed with acute STEMI and underwent primary PCI. Consistent with the published data, no-reflow phenomenon was observed in 13.8% of the patients. Mean age was significantly higher in the no-reflow group than in reflow group (59.3 ± 10.2 vs 55.3 ± 9.7 , $P = .013$). Interestingly, all patients who developed no-reflow were males. Mean BMI was significantly lower in the no-reflow group than in reflow group (26.3 ± 5.5 vs 28.1 ± 4.3 , $P = .010$).

Regarding cardiovascular risk factors, prevalences of HT and DM were significantly lower in no-reflow group than in reflow group (%22.7 vs %38.3, $P = .046$ for HT; %4.5 vs %28.8, $P = .001$ for DM). However, the smoking ratio was significantly higher in the former (%72.7 vs %46.0, $P = .001$).

Medians of hemoglobin level and leukocyte count were significantly higher in no-reflow group than in reflow group (14.9 (13.2 - 16.3) vs 14.2 (10.1 - 18.1), $P = .005$ for hemoglobin level; 11.0 (7.0 - 18.6) vs 9.9 (4.4 - 25.4), $P = .004$ for leukocyte count). However, median triglyceride level was significantly lower in the former (103 (60 - 306) vs 145 (47 - 734), $P = .023$). Medians of hs-CRP, hs-cTnT, and RF were significantly higher in no-reflow group than in reflow group (0.5 (0.1 - 2.5) vs 0.3 (0.0 - 14.1), $P = .028$ for hs-CRP; 0.37 (0.03 - 9.3) vs 0.09 (0.00 - 50.00), $P < .001$ for hs-cTnT; 18.5 (7.0 - 27.6) vs 8.0 (4.6 - 50.8), $P < .001$ for RF). Median predischage LVEF was significantly lower in no-reflow group than in reflow group (46 (36 - 79) vs 58 (31 - 73), $P < .001$). Median SYNTAX score I was significantly higher in no-reflow group than in reflow group (33 (21 - 37) vs 20 (8 - 61), $P < .001$). Baseline characteristics of the patients are shown in Table 1.

Angiographic and procedural characteristics of study groups were similar (Table 2). Age, leukocyte count, platelet count, triglyceride level, HDL cholesterol level, hs-CRP, hs-cTnT, and LVEF were significantly associated with RF level ($P < .05$) (Table 3).

Forward conditional logistic regression analysis demonstrated that BMI (OR = 0.845, 95% CI: 0.765 to 0.933, $P = .001$), DM (OR = 5.257, 95% CI: 1.124 to 24.587, $P = .035$), baseline RF level (OR = 1.198, 95% CI: 1.108 to 1.295, $P < .001$), and SYNTAX score I (OR = 1.065, 95% CI: 1.025 to 1.107, $P = .001$) were the independent predictors of no-reflow phenomenon (Table 4).

4 | DISCUSSION

The major findings of this study include (i) patients with acute STEMI who developed no-reflow during primary PCI have significantly higher baseline RF levels, and (ii) baseline RF levels are independently associated with the no-reflow phenomenon in these patients. To the best of our knowledge, this is the first report in the literature demonstrating the association between RF concentration and no-reflow phenomenon in patients with acute STEMI undergoing primary PCI.

In the present study, no-reflow was identified by changes in TIMI flow in the epicardial artery, which directly affects

TABLE 2 Angiographic and procedural characteristics of the patients

Variable	Reflow group (n = 274)	No-reflow group (n = 44)	P value
LAD as IRA, n (%)	75 (27.4)	11 (25.0)	.401
Balloon predilatation, n (%)	66 (24.1)	12 (27.3)	.402
Balloon postdilatation, n (%)	68 (24.8)	14 (31.8)	.136
Initial TIMI flow 0, n (%)	84 (30.7)	12 (27.3)	.102
Thrombus aspiration, n (%)	11 (4.0)	2 (4.5)	.523
DES, n (%)	212 (77.4)	31 (70.5)	.457
Stent diameter (mm)	3.1 ± 0.5	3.2 ± 0.4	.391
Stent length (mm)	24.9 ± 8.4	22.2 ± 10.1	.071

LAD, left anterior descending artery; IRA, infarct-related artery; TIMI, thrombolysis in myocardial infarction; DES, drug-eluting stent.

Data are presented as number and (%) and mean $\pm$ standard deviation.

TABLE 3 Baseline characteristics significantly associated with rheumatoid factor

Variable	ρ^a	P value
Age (year)	0.172	.049
Leukocyte count, $\times 10^3/\mu\text{L}$	0.321	<.001
Platelet count, $\times 10^3/\mu\text{L}$	0.336	<.001
Triglyceride (mg/dL)	-0.191	.028
HDL cholesterol (mg/dL)	0.264	.002
hs-CRP (mg/dL)	0.457	<.001
hs-cTnT (ng/mL)	0.249	.004
Predischage LVEF (%)	-0.398	<.001

HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; hs-cTnT, high-sensitivity cardiac troponin T; LVEF, left ventricular ejection fraction.

^aSpearman's rank correlation coefficient.

TABLE 4 Independent predictors of no-reflow phenomenon

Variable	OR	95% CI	P
BMI	0.845	0.765-0.933	.001
DM	5.257	1.124-24.587	.035
RF level	1.198	1.108-1.295	<.001
SYNTAX score I	1.065	1.025-1.107	.001

OR, odds ratio; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; RF, rheumatoid factor; SYNTAX, Synergy Between PCI With TAXUS™ and Cardiac Surgery.

myocardial perfusion. Thrombolysis in myocardial infarction flow grade is a crude but accurate indicator for myocardial reperfusion if this is suboptimal (i.e., <3). Myocardial no-reflow carries a poor prognosis and an increased mortality rate. Thus, intraprocedural

measures that can prevent this phenomenon would be especially beneficial in patients at high risk. Preventive precautions may include pharmacologic agents such as glycoprotein IIb/IIIa inhibitors, adenosine, nitroprusside, and nicorandil as well as mechanical precautions such as thrombus aspiration. The complex and multifactorial mechanism of no-reflow phenomenon involves distal embolization of coronary thrombus,^{7,8} inflammation,^{8,9} activation of platelets,⁸ coronary microvascular spasm, and reperfusion injury.¹¹ It is possible that autoimmunity plays a role in this process. However, this is still uncertain. The findings of this study may be understood as follows. Several studies have demonstrated the potential association between RF and atherogenesis,^{22,27} along with the vigorous existing relationship between RA and accelerated cerebro-cardiovascular atherosclerotic process.²⁸ It is well recognized that increased RF is considered as a marker of disease activity and inflammation in patients with RA. Moreover, it is associated with disease progression,²⁹ extra-articular manifestations,³⁰ and cardiovascular disease.²² On the other hand, inflammation and leukocytosis have been linked to no-reflow phenomenon.^{8,9,31} Thus, increased inflammation in patients with increased RF levels is likely to contribute to no-reflow. Indeed, observations of positive associations of RF with hs-CRP and leukocyte count suggest that RF correlates with inflammation in the study population. An alternative explanation is that RF may directly mediate no-reflow through endothelial injury and microvascular dysfunction. Indeed, it has been previously suggested that atherosclerotic plaques contain immunoglobulins and complements suggesting an immune complex activity³² and that RF may play a direct pathogenic role in endothelial injury and cardiovascular disease through immune complex formation.^{15-18,20,21,33} Taken together, these data suggest that either through inflammation or endothelial damage or even immune complex formation increased RF concentrations may lead to an increased risk of no-reflow phenomenon in patients with acute STEMI undergoing primary PCI.

Several studies have investigated the predictors of no-reflow phenomenon in patients with acute STEMI undergoing primary PCI. Çelik et al³⁴ recently demonstrated that female gender, pain to balloon time, high TIMI thrombus grade, tirofiban administration, mean platelet volume, and platelet-lymphocyte ratio are independent predictors of no-reflow after primary PCI in young patients. In addition, Wang et al³⁵ revealed that monocyte count on admission and low hemoglobin concentration are independent clinical predictors of no-reflow following primary PCI in patients with STEMI. Şahin et al³⁶ reported that age, DM, acute anterior STEMI, the involvement of left main coronary artery or left anterior descending artery, and thrombus grade are independently associated with no-reflow in the same population.

In our study, no-reflow phenomenon was independently associated with BMI, DM, RF level, and SYNTAX score I. Previous studies demonstrated contradictory results regarding the impact of BMI on the no-reflow phenomenon. Harrison et al³⁷ revealed that patients who presented with acute myocardial infarction and developed no-reflow during PCI had significantly lower BMI. On the other hand,

Soeda et al³⁸ reported that BMI was not different between patients with reflow and no-reflow. In this study, BMI was independently associated with the no-reflow phenomenon.

Iwakura et al³⁹ reported that there was no difference in glycosylated hemoglobin or in the incidence of DM between reflow and no-reflow groups. In addition, Harrison et al³⁷ also revealed that the incidence of DM between reflow and no-reflow groups was similar. However, it was previously reported that despite similar high rates of TIMI flow grade 3 after primary PCI in patients with and without DM, patients with DM were more likely to have abnormal myocardial perfusion.⁴⁰ Unlike previous studies, DM was independently associated with the no-reflow phenomenon in this study.

In the present study, patients who developed no-reflow had significantly higher median SYNTAX score I. Moreover, this score was an independent predictor of myocardial no-reflow in these patients. Magro et al⁴¹ revealed that SYNTAX score was an independent predictor of myocardial no-reflow in patients with STEMI and that a score >21 carries a double risk for developing no-reflow. Şahin et al³⁶ reported similar findings.

Taken together with the published data, this study raises the importance of the potential role of autoimmunity in the pathophysiology of coronary circulation and no-reflow phenomenon. However, it did not determine the exact mechanism of RF in the pathogenesis of this phenomenon.

5 | LIMITATIONS OF THE STUDY

This was a single-center study which included a relatively small sample size. A multicenter study involving more patients could have more significant results and data. Some diseases may have not been recognized in the study group. Only angiographic parameters were used in determining no-reflow. However, the microcirculation was not directly evaluated, for example, by contrast echocardiography. ST-segment resolution as another measure of no-reflow was not available in all patients.

6 | CONCLUSION

Rheumatoid factor concentrations are independently associated with the no-reflow phenomenon in patients undergoing primary PCI for acute STEMI.

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REFERENCES

1. American College of Emergency P, Society for Cardiovascular A, Interventions, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report

- of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;61:485-510.
2. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:e362-425.
 3. Sorajja P, Gersh BJ, Costantini C, et al. Combined prognostic utility of ST-segment recovery and myocardial blush after primary percutaneous coronary intervention in acute myocardial infarction. *Eur Heart J*. 2005;26:667-674.
 4. Yip HK, Chen MC, Chang HW, et al. Angiographic morphologic features of infarct-related arteries and timely reperfusion in acute myocardial infarction: predictors of slow-flow and no-reflow phenomenon. *Chest*. 2002;122:1322-1332.
 5. Piana RN, Paik GY, Moscucci M, et al. Incidence and treatment of 'no-reflow' after percutaneous coronary intervention. *Circulation*. 1994;89:2514-2518.
 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;145:42-46.
 7. Heusch G, Schulz R, Haude M, Erbel R. Coronary microembolization. *J Mol Cell Cardiol*. 2004;37:23-31.
 8. Skyschally A, Leineweber K, Gres P, Haude M, Erbel R, Heusch G. Coronary microembolization. *Basic Res Cardiol*. 2006;101:373-382.
 9. Furuichi K, Wada T, Iwata Y, et al. Interleukin-1-dependent sequential chemokine expression and inflammatory cell infiltration in ischemia-reperfusion injury. *Crit Care Med*. 2006;34:2447-2455.
 10. Celik T, Balta S, Mikhailidis DP, et al. The relation between no-reflow phenomenon and complete blood count parameters. *Angiology*. 2017;68:381-388.
 11. Carden DL, Granger DN. Pathophysiology of ischaemia-reperfusion injury. *J Pathol*. 2000;190:255-266.
 12. Jaffe R, Dick A, Strauss BH. Prevention and treatment of microvascular obstruction-related myocardial injury and coronary no-reflow following percutaneous coronary intervention: a systematic approach. *JACC Cardiovasc Interv*. 2010;3:695-704.
 13. Brosh D, Assali AR, Mager A, et al. Effect of no-reflow during primary percutaneous coronary intervention for acute myocardial infarction on six-month mortality. *Am J Cardiol*. 2007;99:442-445.
 14. Ndrepepa G, Tiroch K, Fusaro M, et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. *J Am Coll Cardiol*. 2010;55:2383-2389.
 15. Sherer Y, Shoenfeld Y. Atherosclerosis. *Ann Rheum Dis*. 2002;61:97-99.
 16. Harle P, Straub RH, Wiest R, et al. Increase of sympathetic outflow measured by neuropeptide Y and decrease of the hypothalamic-pituitary-adrenal axis tone in patients with systemic lupus erythematosus and rheumatoid arthritis: another example of uncoupling of response systems. *Ann Rheum Dis*. 2006;65:51-56.
 17. Zalba G, Beaumont J, San Jose G, Fortuno A, Fortuno MA, Diez J. Vascular oxidant stress: molecular mechanisms and pathophysiological implications. *J Physiol Biochem*. 2000;56:57-64.
 18. Yoshio T, Masuyama J, Mimori A, Takeda A, Minota S, Kano S. Endothelin-1 release from cultured endothelial cells induced by sera from patients with systemic lupus erythematosus. *Ann Rheum Dis*. 1995;54:361-365.
 19. Hirata K, Amudha K, Elina R, et al. Measurement of coronary vasomotor function: getting to the heart of the matter in cardiovascular research. *Clin Sci (Lond)*. 2004;107:449-460.
 20. Montisci R, Vacca A, Garau P, et al. Detection of early impairment of coronary flow reserve in patients with systemic sclerosis. *Ann Rheum Dis*. 2003;62:890-893.
 21. Ciftci O, Yilmaz S, Topcu S, et al. Impaired coronary microvascular function and increased intima-media thickness in rheumatoid arthritis. *Atherosclerosis*. 2008;198:332-337.
 22. Edwards CJ, Syddall H, Goswami R, et al. The autoantibody rheumatoid factor may be an independent risk factor for ischaemic heart disease in men. *Heart*. 2007;93:1263-1267.
 23. Durante A, Bronzato S. The increased cardiovascular risk in patients affected by autoimmune diseases: review of the various manifestations. *J Clin Med Res*. 2015;7:379-384.
 24. Expert Committee on the D, Classification of Diabetes M. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2003;26(Suppl 1):S5-20.
 25. Cuddy ML. Treatment of hypertension: guidelines from JNC 7 (the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure 1). *Journal of Practical Nursing*. 2005;55:17-21; quiz 22-13.
 26. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment Panel III) final report. *Circulation*. 2002;106:3143-3421.
 27. Grainger DJ, Bethell HW. High titres of serum antinuclear antibodies, mostly directed against nucleolar antigens, are associated with the presence of coronary atherosclerosis. *Ann Rheum Dis*. 2002;61:110-114.
 28. Wolfe F, Freundlich B, Straus WL. Increase in cardiovascular and cerebrovascular disease prevalence in rheumatoid arthritis. *J Rheumatol*. 2003;30:36-40.
 29. Aletaha D, Alasti F, Smolen JS. Rheumatoid factor determines structural progression of rheumatoid arthritis dependent and independent of disease activity. *Ann Rheum Dis*. 2013;72:875-880.
 30. Turesson C, Jacobsson LT, Sturfelt G, Matteson EL, Mathsson L, Ronnelid J. Rheumatoid factor and antibodies to cyclic citrullinated peptides are associated with severe extra-articular manifestations in rheumatoid arthritis. *Ann Rheum Dis*. 2007;66:59-64.
 31. Kato H, Yamakawa M, Ogino T. Complement mediated vascular endothelial injury in rheumatoid nodules: a histopathological and immunohistochemical study. *J Rheumatol*. 2000;27:1839-1847.
 32. Wick G, Knoflach M, Xu Q. Autoimmune and inflammatory mechanisms in atherosclerosis. *Annu Rev Immunol*. 2004;22:361-403.
 33. Hjeltne G, Hollan I, Forre O, Wiik A, Mikkelsen K, Agewall S. Anti-CCP and RF IgM: predictors of impaired endothelial function in rheumatoid arthritis patients. *Scand J Rheumatol*. 2011;40:422-427.
 34. Celik T, Balta S, Ozturk C, et al. Predictors of no-reflow phenomenon in young patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Angiology*. 2016;67:683-689.
 35. Wang Z, Ren L, Liu N, Lei L, Ye H, Peng J. 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;74:1160-1166.
 36. Sahin DY, Gur M, Elbasan Z, et al. 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.
 37. Harrison RW, Aggarwal A, Ou FS, et al. Incidence and outcomes of no-reflow phenomenon during percutaneous coronary intervention among patients with acute myocardial infarction. *Am J Cardiol*. 2013;111:178-184.
 38. Soeda T, Higuma T, Abe N, et al. Morphological predictors for no reflow phenomenon after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction caused by plaque rupture. *Eur Heart J Cardiovasc Imaging*. 2017;18:103-110.

39. Iwakura K, Ito H, Ikushima M, et al. Association between hyperglycemia and the no-reflow phenomenon in patients with acute myocardial infarction. *J Am Coll Cardiol*. 2003;41:1-7.
40. Prasad A, Stone GW, Stuckey TD, et al. Impact of diabetes mellitus on myocardial perfusion after primary angioplasty in patients with acute myocardial infarction. *J Am Coll Cardiol*. 2005;45:508-514.
41. Magro M, Nauta ST, Simsek C, et al. 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.

How to cite this article: Quisi A, Alici G. The relationship between serum rheumatoid factor level and no-reflow phenomenon in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *J Clin Lab Anal*. 2018;32:e22598. <https://doi.org/10.1002/jcla.22598>