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# Mild to Moderate Renal Impairment Is Associated With No-Reflow Phenomenon After Primary Percutaneous Coronary Intervention in Acute Myocardial Infarction

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**Abstract**

We investigated whether admission estimated glomerular filtration rate (eGFR) values are associated with no-reflow phenomenon in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (pPCI). Patients (n = 673; 59 ± 13 years; 77.1% men) were stratified into 3 groups according to eGFR at admission: normal renal function (eGFR ≥ 90 mL/min/1.73 $m^2$), mild renal impairment (eGFR 60-89 mL/min/1.73 $m^2$), and moderate renal impairment (eGFR 30-59 mL/min/1.73 $m^2$). No-reflow phenomenon was defined as thrombolysis in myocardial infarction flow grade <3 after pPCI. The rate of no-reflow gradually increased from the normal renal function group to the moderate impaired renal function group ($P < .001$). Multivariate analysis showed that eGFR (odds ratio [OR] 0.942, $P < .001$), Killip ≥2 class (OR 3.968, $P = .008$), left ventricular ejection fraction (OR 0.959, $P = .034$), and early patency of infarct vessel (OR 0.186, $P < .001$) were independent predictors of no-reflow phenomenon. Mild to moderate renal impairment at admission is independently associated with no-reflow phenomenon after pPCI.

**Keywords**

estimated glomerular filtration rate, no-reflow phenomenon, acute myocardial infarction, primary percutaneous coronary intervention

## Introduction

Early reperfusion with primary percutaneous coronary intervention (pPCI) significantly improves the survival of patients with ST-segment elevation myocardial infarction (STEMI).[1] However, no-reflow phenomenon defined as incomplete reperfusion at the microvascular level despite adequate patency of the occluded artery remains an important limitation of the procedure, which is associated with larger infarct size, worse functional recovery, higher incidence of complications, and increasing early and late mortality and morbidity in patients with STEMI.[2-5] The pathophysiological mechanisms of no-reflow phenomenon have not been fully understood and its etiology appears to be multifactorial. These factors include ischemic endothelial damage, oxidative stress, microvascular leukocytes and platelet plugging, and complex interactions between leukocytes and platelets induced by the inflammatory process.[6-8] Several studies have shown that biomarkers and other easily available clinical parameters can predict the risk of no-reflow phenomenon and may also suggest what mechanisms are involved.

Mild renal impairment (estimated glomerular filtration rate [eGFR] = 60-89 mL/min/1.73 $m^2$), a level commonly considered clinically insignificant by cardiologists, was a strong independent risk factor for early and late mortality in patients with STEMI treated with pPCI.[9,10] Similarly, moderate renal insufficiency (eGFR of 30-59 mL/min/1.73 $m^2$) in patients with STEMI is an important predictor of short- and long-term worse clinical outcomes.[11,12] The mechanisms involved in the atherosclerotic process, in particular endothelial dysfunction, oxidative stress and vascular inflammation, could affect renal function, resulting in a possible decrease in the eGFR.[13]

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We assessed the relationship between mild to moderate renal impairment and the no-reflow phenomenon in patients who underwent pPCI for acute STEMI.

## Methods

### Patients

From the August 2012 to April 2014, 696 consecutive patients with STEMI (within 12 hours of symptoms onset) were admitted to this study. Medical treatment was decided in 3 patients because of distal lesion at a thin vessel. In all, 12 patients with severe renal impairment (eGFR < 30 mL/min/1.73 $m^2$) were excluded from study. In addition, 15 patients were excluded because of urgent coronary artery bypass graft surgery due to failed pPCI or coronary anatomy, which is not amenable to pPCI. Thus, 673 patients were included in the analyses of the present study.

The STEMI was considered when patients had symptoms of acute myocardial infarction lasting ≥30 minutes and accompanied by >1 mm (0.1 mV) ST-segment elevation in ≥2 contiguous leads (or reciprocal ST depression ≥ 1 mm in V1 or V2 for true posterior infarct) or presumably new onset left bundle branch block and later confirmed by cardiac markers (eg, troponin T) increase.

Patients who presented >12 hours from the onset of symptoms with cardiogenic shock on admission and taking fibrinolytic agents before pPCI were excluded. Additionally, patients with acute or chronic infection/inflammation, severe renal disease (eGFR < 30 mL/min/1.73 $m^2$), severe chronic heart failure, or a history of malignancy were excluded.

The study protocol was approved by the local ethics committee. Informed consent was obtained from all patients before enrollment.

### Laboratory and Echocardiographic Analyses

On admission, peripheral blood samples were obtained before administration of any medication. Peak troponin T was obtained during the hospital stay. High-sensitivity C-reactive protein (hsCRP) levels were also measured using an immunoturbidimetric assay (Integra 800; Roche, Lewes, Sussex, United Kingdom).

Kidney disease was classified according to the Kidney Disease Outcome Quality Initiative guidelines.[14] The eGFR values were calculated using the Modification of Diet in Renal Disease formula[15] and utilizing the serum creatinine level measured on admission. Patients were stratified into 3 groups according to eGFR: normal renal function (eGFR ≥ 90 mL/min/1.73 $m^2$), mild renal impairment (eGFR 60-89 mL/min/1.73 $m^2$), and moderate renal impairment (eGFR 30-59 mL/min/1.73 $m^2$).

Standard 2-dimensional echocardiography was performed in all patients within 48 hours of admission (Vivid 3; GE Medical System, Horten, Norway). Left ventricular ejection fraction (LVEF) was assessed using the modified Simpson method.

### Medical Therapy

All patients received oral aspirin (300 mg), clopidogrel (600 mg), and intravenous unfractionated heparin (5.000 U) immediately after arrival in the emergency service. Intravenous heparin was continued and adjusted to achieve a target-activated clotting time of 200 to 300 seconds during the pPCI. A glycoprotein IIb/IIIa inhibitor (tirofiban) was used at the operator's discretion. Additional medical therapies including β-blockers, nitrates, calcium antagonists, angiotensin-converting enzyme inhibitors/angiotensin receptor blockades, and statins were administered at the decision of the coronary care unit physicians.

### Coronary Angiography and Interventions

All patients underwent baseline coronary angiography using standard techniques (Axiom Artis zee 2011; Siemens, Munich, Germany). The pPCI procedures were performed according to the standard femoral approach with a 6F-guiding catheter (Launcher; Medtronic, Minneapolis, Minnesota). The use of balloon predilatation or postdilatation, thrombus aspiration device, and the type of stents (bare metal or drug eluting) was left to the treating physician's discretion. All angiograms were analyzed by 2 independent experienced interventional cardiologists using a validated quantitative coronary angiographic software system (Axiom Sensis XP; Siemens). Coronary blood flow patterns before and after pPCI were assessed according to the thrombolysis in myocardial infarction (TIMI) flow scale, using grades 0, 1, 2, and 3.[16] The no-reflow phenomenon after pPCI was defined as TIMI flow grade <3 without evidence of dissection, stenosis, or vasospasm.[17]

Multivessel disease (MVD) was defined by visual assessment as the presence of at least 1 lesion with stenosis ≥50% in ≥1 major coronary artery or its major branch, remote from the infarct artery, and further subclassified as 2- or 3-vessel disease.

Preinterventional syntax score for each patient was also calculated by scoring all coronary lesions with a stenosis ≥50%, in vessels ≥1.5 mm, using the online calculator version 2.1 at www.syntaxscore.com.

### Statistical Analysis

Categorical variables are expressed as numbers and percentages and continuous variables as mean ± standard deviation or median (interquartile range). Continuous variables were compared using Student unpaired *t* tests or Mann-Whitney nonparametric *U* tests. The baseline characteristics of the groups were compared by 1-way analysis of variance for continuous variables and by the chi-square statistic for noncontinuous variables. Separate logistic regression analyses were performed to identify independent predictors of no-reflow phenomenon using all clinical variables. All significant parameters in the univariate analysis were entered into a multivariate logistic regression analysis to identify independent predictors of no-reflow phenomenon. All statistical analyses were performed using SPSS 18.0 (SPSS Inc, Chicago, Illinois), and a 2-tailed $P < .05$ was considered significant. Receiver–operating characteristics (ROC) curve analysis was performed to demonstrate the sensitivity and specificity of admission eGFR optimal cutoff value for predicting no-flow phenomenon following pPCI in patients with STEMI.

**Table 1.** Baseline Clinical and Laboratory Characteristics of the Study Groups.[a]

| | Renal Impairment | | | |
|---|---|---|---|---|
| | None (eGFR ≥ 90 mL/min/1.73 $m^2$; n = 162) | Mild (eGFR 60-89 mL/min/1.73 $m^2$; n = 350) | Moderate (eGFR 30-59 mL/min/1.73 $m^2$; n = 161) | *P* |
| Age, years | 50 ± 10 | 59 ± 11 | 69 ± 11 | <.001 |
| Female gender, n (%) | 32 (19.8) | 66 (18.9) | 56 (34.8) | <.001 |
| Body mass index, kg/$m^2$ | 27.9 ± 4.5 | 27.3 ± 3.8 | 27.6 ± 4.4 | .416 |
| Hypertension, n (%) | 39 (24.1) | 119 (34.0) | 82 (50.9) | <.001 |
| Diabetes mellitus, n (%) | 40 (24.7) | 85 (24.3) | 60 (37.3) | .006 |
| Smoker, n (%) | 114 (70.4) | 192 (54.9) | 49 (30.4) | <.001 |
| Hypercholesterolemia, n (%) | 60 (37.0) | 132 (37.7) | 48 (29.8) | .384 |
| Prior coronary artery bypass grafting, n (%) | 6 (3.7) | 6 (1.7) | 9 (5.6) | .057 |
| Prior myocardial infarction, n (%) | 5 (3.1) | 15 (4.3) | 9 (5.6) | .541 |
| Systolic blood pressure, mm Hg | 126 ± 21 | 127 ± 23 | 123 ± 28 | .177 |
| Diastolic blood pressure, mm Hg | 77 ± 13 | 78 ± 13 | 76 ± 13 | .669 |
| Heart rate, beats/min | 80 ± 14 | 78 ± 14 | 81 ± 14 | .157 |
| Anterior myocardial infarction, n (%) | 70 (43.2) | 146 (41.7) | 71 (44.1) | .709 |
| Killip class ≥ 2 at admission, n (%) | 1 (0.6) | 21 (6.0) | 26 (16.1) | <.001 |
| Left ventricular ejection fraction, % | 47 ± 9 | 46 ± 10 | 41 ± 10 | <.001 |
| Symptoms to intervention (h), n (%) | | | | |
| <6 | 134 (82.7) | 285 (81.4) | 119 (73.9) | .086 |
| ≥6 | 28 (17.3) | 65 (18.6) | 42 (26.1) | |
| Prior medications, % | | | | |
| Aspirin | 9.6 | 11.5 | 17.1 | .556 |
| Clopidogrel | 0 | 3.9 | 2.9 | .363 |
| Angiotensin–aldosterone antagonists | 29.8 | 32.3 | 34.3 | .722 |
| β-Blockers | 3.8 | 7.7 | 14.3 | .206 |
| Statin | 3.8 | 2.9 | 5.7 | .705 |
| Serum glucose, mg/dL | 138 ± 72 | 139 ± 68 | 164 ± 92 | <.001 |
| Creatinine, mg/dL | 0.87 ± 0.1 | 1.04 ± 0.14 | 1.32 ± 0.22 | <.001 |
| Glomerular filtration rate, mL/min/1.73 $m^2$ | 97.7 ± 6.1 | 74.1 ± 8.6 | 50.3 ± 7.7 | <.001 |
| Peak troponin-T, ng/mL | 1287 (540-3259) | 1712 (565-3830) | 1726 (695-5374) | .028 |
| Total cholesterol, mg/dL | 199 ± 43 | 194 ± 45 | 190 ± 42 | .166 |
| Triglyceride, mg/dL | 165 ± 85 | 155 ± 87 | 145 ± 79 | .133 |
| High-density lipoprotein cholesterol, mg/dL | 39 ± 9 | 41 ± 9 | 40 ± 10 | .058 |
| Low-density lipoprotein cholesterol, mg/dL | 124 ± 34 | 124 ± 39 | 117 ± 38 | .173 |
| Uric acid, mg/dL | 4.99 ± 1.25 | 5.42 ± 1.43 | 6.43 ± 1.74 | <.001 |
| High-sensitivity C-reactive protein, mg/L | 6.41 ± 3.64 | 6.77 ± 4.34 | 8.16 ± 3.83 | .005 |
| Hemoglobin, g/dL | 14.6 ± 1.6 | 14.4 ± 1.5 | 13.5 ± 2.0 | <.001 |
| White blood cell count, $\times 10^9$/L | 12.0 ± 3.6 | 11.4 ± 3.2 | 11.9 ± 3.6 | .119 |
| Platelet count, $\times 10^9$/L | 241 ± 66 | 240 ± 62 | 244 ± 84 | .876 |

Abbreviation: eGFR, estimated glomerular filtration rate.

## Results

The mean eGFR was 74.1 (±18.2) mL/min/1.73 $m^2$. The normal renal function group was composed of 162 patients with eGFR ≥90 mL/min/1.73 $m^2$, the mild renal impairment group of 350 patients with eGFR 60 to 89 mL/min/1.73 $m^2$, and the moderate renal impairment group of 161 patients with eGFR 30 to 59 mL/min/1.73 $m^2$. The no-reflow phenomenon was diagnosed in 116 (17.2%) patients of the 673 patients.

Baseline clinical and laboratory characteristics of the study populations according to severity of renal impairment are summarized in Table 1. Age, prevalence of Killip ≥2 at admission gradually increased, and the prevalence of smoking gradually decreased from the normal renal function group to the moderate renal impairment group. Patients with moderate renal dysfunction had a higher prevalence of female gender, a history of diabetes mellitus, and had lower LVEF. Serum creatinine, uric acid, and hsCRP levels progressively increased from the normal renal function to the moderate renal impairment group. Additionally, serum glucose levels were significantly higher, and hemoglobin levels were significantly lower in patients with moderate renal impairment than in the other groups. Patients in the normal renal function had lower peak troponin T levels compared with patients in the mild and moderate renal impairment groups. Medical treatment before or during the procedure was similar for the 3 groups.

The angiographic and procedural characteristics across the 3 groups are presented in Table 2. Patients with mild to moderate

**Table 2.** Comparison of Angiographic and Procedural Findings of the Groups.[a]

| Variable | Renal Impairment | | | P |
|---|---|---|---|---|
| | None (eGFR ≥ 90 mL/min/1.73 $m^2$; n = 162) | Mild (eGFR 60-89 mL/min/1.73 $m^2$; n = 350) | Moderate (eGFR 30-59 mL/min/1.73 $m^2$; n = 161) | |
| Infarct-related coronary artery, n (%) | | | | |
| Left anterior descending | 73 (45.1) | 152 (43.4) | 76 (47.2) | .878 |
| Left circumflex | 30 (18.5) | 56 (16.0) | 22 (13.7) | |
| Right | 59 (36.4) | 140 (40.0) | 63 (39.1) | |
| Left main | 0 (0) | 2 (0.6) | 0 (0) | |
| Multivessel disease | 62 (38.3) | 178 (50.9) | 97 (60.2) | <.001 |
| Chronic total occlusion | 10 (6.2) | 40 (11.4) | 43 (26.7) | <.001 |
| Number of diseased vessel | 1.52 ± 0.73 | 1.70 ± 0.78 | 1.86 ± 0.79 | .001 |
| One, n (%) | 100 (61.7) | 173 (49.4) | 64 (39.8) | .003 |
| Two, n (%) | 39 (24.1) | 107 (30.6) | 56 (34.8) | |
| Three, n (%) | 23 (14.2) | 70 (20.0) | 41 (25.5) | |
| Syntax score | 14.7 ± 8.1 | 15.6 ± 8.4 | 18.8 ± 9.5 | <.001 |
| Procedure, n (%) | | | | |
| Balloon angioplasty | 5 (3.1) | 22 (6.3) | 22 (13.7) | .001 |
| Balloon + stenting | 67 (41.4) | 158 (45.1) | 74 (46.0) | |
| Stenting without balloon predilatation | 90 (55.6) | 170 (48.6) | 64 (40.0) | |
| Stent implantation | 157 (97.0) | 328 (93.7) | 139 (86.4) | .001 |
| Total stent length, mm | 23.1 ± 10.2 | 23.4 ± 10.7 | 24.5 ± 11.0 | .519 |
| Stent diameter, mm | 3.15 ± 0.43 | 3.22 ± 0.40 | 3.15 ± 0.40 | .087 |
| Number of used stent | 1.27 ± 0.49 | 1.29 ± 0.55 | 1.29 ± 0.55 | .916 |
| Early patency of culprit vessel, n (%) | 60 (37.0) | 140 (40.0) | 57 (35.4) | .575 |
| No-reflow phenomenon, n (%) | 5 (3.1) | 49 (14.0) | 62 (38.5) | <.001 |
| Thrombus aspiration, n (%) | 16 (10.0) | 40 (11.4) | 22 (13.7) | .284 |
| Tirofiban therapy, n (%) | 8 (51.9) | 175 (50.0) | 69 (42.9) | .214 |
| In-hospital mortality, n (%) | 1 (0.6) | 7 (2.0) | 21 (13.0) | <.001 |

Abbreviation: eGFR, estimated glomerular filtration rate.

renal impairment were more likely to have MVD and chronic total occlusion remote from the culprit vessel. In addition, these patients had higher number of diseased vessel and higher syntax scores. Patients with normal renal function had a higher prevalence of coronary stenting without balloon predilatation. The rate of no-reflow phenomenon was gradually increased from the normal renal function group to the moderate impaired renal function group (3.1%, 14%, and 38.5%, respectively, $P < .001$). In the overall population, patients with mild to moderate renal impairment showed significantly higher in-hospital mortality than those of patients with normal renal function (2% and 13% vs 0.6%, respectively, $P < .001$).

The patients were divided into 2 groups according to whether no-reflow phenomenon was present. Compared with normal-reflow patients, no-reflow patients were older, had a higher rate of female gender, diabetes mellitus, Killip ≥2 class at presentation, MVD, chronic total occlusion, and lower rate of early patency of culprit vessel (TIMI 2/3). Serum glucose, creatinine, hsCRP, peak troponin T, and uric acid levels were higher, while hemoglobin levels were lower in patients with no-reflow than the normal-reflow group. The eGFR values were lower in the no-reflow group compared to the normal-reflow group (59 ± 16 vs 77 ± 17, $P < .001$; Table 3 and Figure 1). Additionally, the syntax score was higher, LVEF was lower in the no-reflow group than in the normal-reflow group. In patients with no-reflow phenomenon showed significantly higher in-hospital mortality than those of patients with normal-reflow (17.2% vs 1.6%, $P < .001$).

The ROC analysis was performed to determine the cutoff value of eGFR to predict the no-reflow versus normal-reflow. The area under the ROC curve for eGFR was 0.78, and an eGFR of 64.9 or lower predicted no-reflow phenomenon with a sensitivity of 75% and specificity of 68% (Figure 2).

Multivariate logistic regression analysis showed that admission eGFR (odds ratio [OR] 0.942, 95% confidence interval [CI] 0.917-0.967, $P < .001$), Killip ≥ 2 class at presentation (OR 3.968, 95% CI 1.434-10.989, $P = .008$), LVEF (OR 0.959, 95% CI 0.922-0.997, $P = .034$), and early patency of infarct vessel (OR 0.186, 95% CI 0.076-0.454, $P < .001$) were independent predictors of no-reflow phenomenon after pPCI in STEMI (Table 4).

## Discussion

The present study demonstrated that no-reflow phenomenon after pPCI for STEMI can be predicted by the eGFR on admission. The cutoff value of eGFR obtained by the ROC curve analysis for the prediction of no-reflow phenomenon was 64.9 mL/min/1.73 $m^2$ (sensitivity: 75% and specificity: 68%). In addition, in-hospital mortality was higher in patients with

**Table 3.** Comparison of Characteristics of Patients With Normal-Reflow and No-Reflow.

| Variable | Normal-Reflow (n = 557) | No-Reflow (n = 116) | P |
|---|---|---|---|
| Age, years | 57 ± 12 | 69 ± 13 | <.001 |
| Female gender, n (%) | 111 (19.9) | 43 (37.1) | <.001 |
| Body mass index, kg/m$^2$ | 28 ± 4 | 27 ± 4 | .173 |
| Hypertension, n (%) | 190 (34.1) | 50 (43.1) | .066 |
| Diabetes mellitus, n (%) | 144 (25.9) | 41 (35.3) | .037 |
| Smoker, n (%) | 321 (57.6) | 34 (29.3) | <.001 |
| Killip ≥ 2 class at admission, n (%) | 18 (3.2) | 30 (25.9) | <.001 |
| Left ventricular ejection fraction (%) | 47 ± 9 | 39 ± 10 | <.001 |
| Glucose, mg/dL | 142 ± 74 | 158 ± 83 | .033 |
| Creatinine, mg/dL | 1.04 ± 0.20 | 1.19 ± 0.27 | <.001 |
| Glomerular filtration rate, mL/min/1.73 m$^2$ | 77 ± 17 | 59 ± 16 | <.001 |
| Uric acid, mg/dL | 5.49 ± 1.51 | 5.88 ± 1.74 | .017 |
| Peak troponin-T, ng/mL | 1430 (528-3602) | 2288 (1050-6271) | <.001 |
| High-sensitivity C-reactive protein, mg/L | 6.8 ± 4.1 | 8.1 ± 3.9 | .015 |
| Hemoglobin, g/dL | 14.4 ± 1.6 | 13.4 ± 2.1 | <.001 |
| White blood cell count, ×10$^9$/L | 11.5 ± 3.4 | 12 ± 3.8 | .123 |
| Syntax score | 15 ± 8 | 22 ± 9 | <.001 |
| Chronic total occlusion, n (%) | 67 (12.0) | 26 (22.4) | .003 |
| Multivessel disease, n (%) | 262 (47) | 75 (64.7) | .001 |
| Early patency of infarct vessel, n (%) | 241 (43.3) | 16 (13.8) | <.001 |
| Stent implantation, n (%) | 541 (97.1) | 83 (71.5) | <.001 |
| Total stent length, mm | 23 ± 10 | 26 ± 12 | .112 |
| Stent diameter, mm | 3.1 ± 0.4 | 3.2 ± 0.4 | .590 |
| In hospital mortality, n (%) | 9 (1.6) | 20 (17.2) | <.001 |

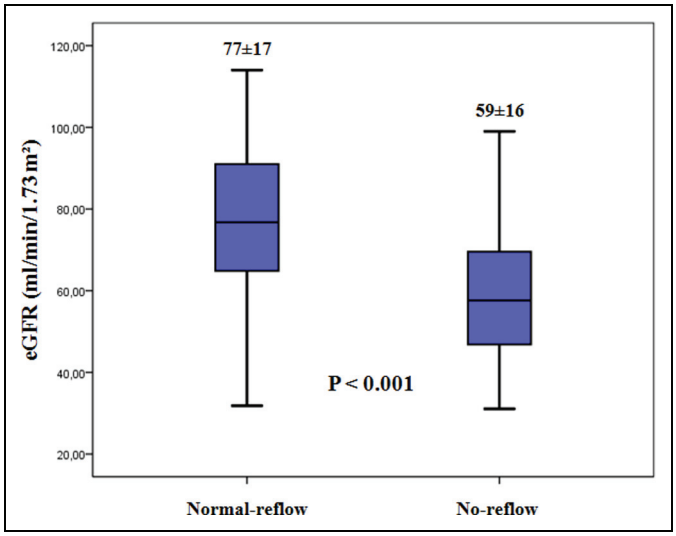


**Figure 1.** Comparison of estimated glomerular filtration rate (eGFR) values in patients with and without no-reflow.

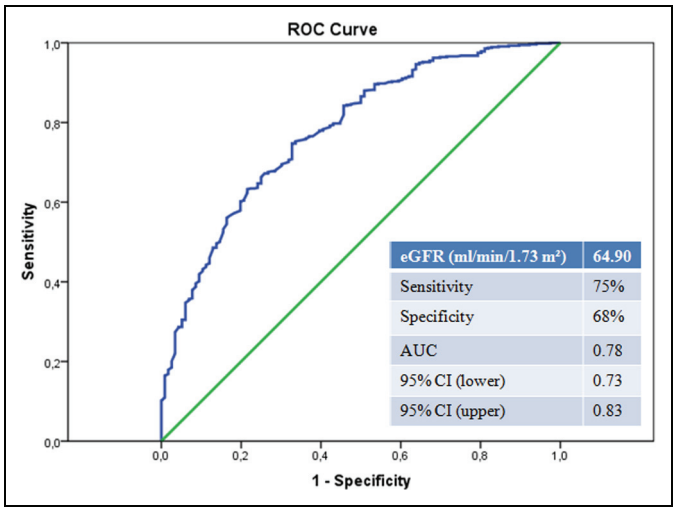


**Figure 2.** Receiver–operating characteristics (ROC) curve analyses of estimated glomerular filtration rate (eGFR) values for predicting the angiographic no-reflow phenomenon. Area under curve (AUC): 0.78 (0.73-0.83).

mild to moderate (especially moderate) renal impairment and no-reflow phenomenon.

The no-reflow phenomenon may be defined as incomplete reperfusion at the microvascular level despite adequate recanalization of the occluded artery.[18] The pathophysiology of no-reflow phenomenon has not been fully clarified yet. This pathological process can be accelerated by coronary reperfusion, which gives rise to tissue edema, endothelial injury, plugging of capillaries by neutrophils and microthrombi, and inflammation due to generation of free radicals and complement activation.[19] Clinical outcomes are similar for patients with either a TIMI 2 or TIMI 0/1 flow and are worse than those for patients with a TIMI flow grade 3.[20] The patients with no-reflow phenomenon displayed a higher prevalence of early and late morbidity and mortality.[5,21]

Chronic kidney disease is a major risk factor for worse cardiovascular outcome; however, renal function is often estimated on the basis of serum creatinine levels, and advanced renal impairment may be hidden behind near normal creatinine levels. Mild to moderate renal impairment (eGFR of 30-89 mL/min/1.73 m$^2$) is an important predictor of short- and long-term poor clinical outcomes including mortality in patients with acute STEMI treated with pPCI.[9-12] The mechanisms involved in the atherosclerotic process, in particular endothelial dysfunction, oxidative stress, and vascular inflammation, could affect kidney function, resulting in a possible decrease in eGFR.[13]

Although the association between decreased eGFR and no-reflow phenomenon is not completely understood, several mechanisms may be involved. Previous studies have studied the association between eGFR and endothelial dysfunction.[14,22-25] Renal impairment is significantly associated with endothelial dysfunction.[14,22,23] Kielstein et al[24] have found

**Table 4.** Univariate and Multivariate Predictors of No-Reflow Phenomenon.

| | Univariate Analysis | | Mulivariate Analysis | |
|---|---|---|---|---|
| Variable | Odds Ratio, 95% CI | *P* | Odds Ratio, 95% CI | *P* |
| Age | 1.083 (1.063-1.103) | <.001 | 1.014 (0.979-1.051) | .435 |
| Female gender | 2.367 (1.539-3.640) | <.001 | 1.013 (0.448-2.287) | .976 |
| Hypertension | 0.683 (0.455-1.027) | .067 | | |
| Diabetes mellitus | 1.567 (1.024-2.398) | .038 | 1.119 (0.467-2.682) | .801 |
| Smoking | 0.305 (0.198-0.470) | <.001 | 0.723 (0.324-1.612) | .428 |
| Left ventricular ejection fraction | 0.927 (0.906-0.948) | <.001 | 0.959 (0.922-0.997) | .034 |
| Hemoglobin | 0.756 (0.679-0.842) | <.001 | 0.928 (0.758-1.136) | .467 |
| Estimated glomerular filtration rate | 0.935 (0.922-0.049) | <.001 | 0.942 (0.917-0.967) | <.001 |
| Serum glucose | 1.003 (1.000-1.005) | .034 | 0.999 (0.994-1.004) | .772 |
| Uric acid | 1.165 (1.027-1.323) | .018 | 1.345 (1.058-1.712) | .015 |
| Early patency of infarct artery | 0.209 (0.120-0.364) | <.001 | 0.186 (0.076-0.454) | <.001 |
| Killip $\geq$ 2 class at presentation | 10 416 (5.586-19.607) | <.001 | 3.968 (1.434-10.989) | .008 |
| Syntax score | 1.088 (1.062-1.115) | <.001 | 1.008 (0.963-1.055) | .736 |
| High-sensitivity C-reactive protein | 1.077 (1.013-1.145) | .017 | 1.048 (0.964-1.138) | .270 |

Abbreviation: CI, confidence interval.

higher levels of asymmetric dimethylarginine (which is a marker of endothelial dysfunction) in patients who have end-stage renal disease. Astrup et al[25] demonstrated a significant relationship between endothelial dysfunction and GFR in patients who have diabetic nephropathy. In another study,[26] high-admission asymmetric dimethylarginine levels were found to be associated with impaired myocardial perfusion in patients with STEMI undergoing pPCI.

Patients with chronic kidney disease experience persisting inflammation.[27] Several studies have shown a relationship between no-reflow phenomenon and increased inflammatory activity.[28-30] Renal impairment is an inflammatory state,[31,32] and in this setting may predispose to the development of no-reflow phenomenon.

The mechanisms underlying abnormalities in chronic renal impairment are complicated, and several factors contribute to their pathogenesis. Of these factors, oxidative stress is considered to play a key role in the progression of renal impairment.[33,34] Gür et al[7] have shown that impaired oxidative stress has associated with no-reflow phenomenon in patients with STEMI.

Finally, decreased eGFR associated with enhanced platelet activity and coagulability may contribute to pathogenesis of no-reflow phenomenon. Landray et al[35] demonstrated that chronic kidney disease is associated with low-grade inflammation, endothelial dysfunction, and platelet activation, even among patients with moderate renal impairment. It was shown that there is a relationship between increased platelet activity and no-reflow phenomenon.[36] As a result, all of the above-mentioned factors may explain the relationship between decreased eGFR and no-reflow in patients with STEMI treated with pPCI.

Several studies reported protective effects of statin therapy on kidney function.[37-39] In addition to their lipid-lowering effects, statins induce a variety of pleiotropic actions such as anti-inflammatory effects and it was speculated that, given the vascular nature of contrast-induced nephropathy (CIN), they may have renoprotective effects. Gandhi et al[40] reported that statin therapy was effective at reducing the risk of contrast-induced acute kidney injury. In our study population, statin use was similar within study groups but we did not evaluate the effect of statin use in renal function and no-reflow phenomenon.

There are several limitations of our study. First, the assessment of eGFR was based on a single serum creatinine measurement at the time of hospital admission. This measurement could have been affected by hemodynamic instability in some patients. Second, we did not assess the association between final TIMI flow and other angiographic surrogate markers of myocardial perfusion (eg, myocardial blush and TIMI frame count). Third, we did not measure oxidative stress status. Finally, we did not consider CIN or differences between groups (eg, those who were on statins or not; tirofiban during pPCI).

Mild to moderate renal impairment at admission is independently associated with no-reflow phenomenon following pPCI in patients with acute STEMI together with lower LVEF, higher Killip class at presentation, and absence of early patency of infarct vessel.

## Authors' Note

All authors have substantial contributions to conception and design, or acquisition of data, and analysis and interpretation of data; drafting the article and revising it critically for important intellectual content; and final approval of the version to be published.

## Declaration of Conflicting Interests

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