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PCI

Renal Dysfunction on Admission Predicts No-Reflow Phenomenon in Patients Undergoing Manual Thrombus Aspiration during Primary Percutaneous Coronary Intervention

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Background: No-reflow is a frequent complication during percutaneous coronary intervention (PCI) for acute ST segment elevation myocardial infarction (STEMI). Available data is limited regarding its impact on short-term outcomes in patients undergoing manual thrombus aspiration. Renal impairment is also associated with higher complication rates in STEMI. Herein, we aimed to evaluate the impact of baseline renal dysfunction on the no-reflow phenomenon and the association of no-reflow phenomenon with early clinical outcomes.

Methods: A total of 94 consecutive STEMI patients who underwent primary stent-based PCI and thrombus aspiration were enrolled. No-reflow was established by the use of angiographic and electrocardiographic reperfusion criteria, respectively. Additionally angiographic and clinical follow-up data were also recorded.

Results: In our study, the no-reflow phenomenon was observed in 10 patients (11%) angiographically and in 23 patients (24%) electrocardiographically. Whereas, the the estimated glomerular filtration rate (eGFR) [odds ratio (OR) 10.4], hypertension (OR 6.2), previous MI (OR 6.5), previous PCI history, (OR 4.2), predilatation (OR 7.2), final balloon pressure (OR 0.9) were found to be the significant predictors of angiographic no-reflow, only reperfusion time was the predictor of electrocardiographic no-reflow (OR 1.12) at univariate analysis. After adjustment, lower eGFR (OR 14.8) was found to be the independent predictor for angiographic no-reflow. In-hospital mortality was more common in patients with either no-reflow condition separately.

Conclusions: Longer ischemic time and lower initial eGFR values were associated with no-reflow phenomenon. Irrespective of poor reperfusion criteria, no-reflow phenomenon is associated with in-hospital outcome. Future efforts should be made to reduce the incidence of no-reflow especially in patients with lower initial eGFR values.

Key Words: Acute myocardial infarction • Glomerular filtration rate • No-reflow phenomenon • Primary percutaneous coronary intervention

INTRODUCTION

Although immediate restoration of normal blood flow in the infarct-related artery (IRA) is the primary aim of primary percutaneous coronary intervention (PCI), achievement of thrombolysis in myocardial infarction (TIMI) grade 3 flow can't be sufficient to ensure myocardial salvage.[1] Micro-vascular damage, however, is often present despite coronary artery recanalization. This pathologic process, namely 'no-reflow phenomenon',

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may limit the benefits of reperfusion therapy.[2] Thrombus aspiration has emerged as a valuable tool in avoiding distal thrombus embolization and no-reflow phenomenon during primary PCI, improving final TIMI flow.[3] It was pointed that electrocardiographic 'no-reflow' despite TIMI grade 3 flow occurred in a third of patients after reperfusion therapy and it was associated with higher incidence of congestive heart failure and left ventricular dysfunction.[2] Earlier clinical studies have delineated that no-reflow predicts short and long-term adverse clinical outcomes in patients presenting with acute myocardial infarction (AMI).[4,5] In the presence of AMI, reduced renal function on presentation is shown to be associated with 'no-reflow' and it has been found that not only severe, but also mild-to-moderate renal impairment are associated with a higher mortality in the setting of AMI.[6] Accordingly, we aimed to investigate the impact of admission estimated glomerular filtration rates (e-GFR) on the development of poor myocardial perfusion in patients undergoing manual thrombus aspiration presenting with AMI; as well as to evaluate the association of short-term adverse events with poor myocardial perfusion after primary PCI.

MATERIALS AND METHODS

Study population

We selected ST-segment elevation MI (STEMI) patients who were consecutively treated with manual aspiration during primary PCI in our catheterization laboratory between January 2009 and August 2013. We evaluated the same patients by angiographic and electrocardiographic reperfusion criteria separately. Achieving TIMI grade 3 flow at completion (angiographic) and at least 50% resolution of St-segment at 90 minutes of the procedures were (electrocardiographic) identified as good flow respectively. All clinical, demographic, angiographic, information about death, adverse events and prognostic data were obtained from hospital files and computer records. In hospital and 30-day period events (all cause death, re-infarct, stent thrombosis, and post discharge hospitalization) were recorded.

The diagnosis of AMI was established by using American College of Cardiology/European Society of Cardiology criteria.[7] STEMI patients with ischemic symptoms for less than 12 hours and ongoing ischemia more than 12 hours were both included in our study group. Reperfusion time was defined as the time from onset of symptoms to first balloon dilatation. Pre-infarction angina was defined as cardiac symptoms for < 30 min that occurred within 2 days before infarct onset. Renal dysfunction was defined as eGFR less than 90 ml/min/1.73 m^2. The e-GFR on admission was calculated according to modification of diet in renal disease (MDRD) formula.[8] Anemia was defined as baseline hemoglobin levels < 13 mg/dl in males and < 12 mg/dl in females. Re-infarction was defined as the recurrence of typical ischemic symptoms and new electrocardiographic changes with a new elevation of the creatine kinase MB fraction levels > 2 times the upper limit of normal or by ≥ 50% above a previously elevated level. Revascularization was defined as repeated PCI or bypass grafting of not only IRA but also non-IRA, driven by ischemic symptoms (stable/unstable angina or re-infarction) or detection of ischemia by non-invasive tests.

Coronary angiography and percutaneous coronary intervention procedure

Upon admission, all the patients received heparin, nitroglycerine, a loading-dose of 300 mg and maintenance dose of 100 mg a day aspirin; additionally they received clopidogrel with a starting dose of 600 mg; and a maintenance dose of 75 mg. Primary PCI was performed with all possible speed. The use of other medications, including glycoprotein IIb/IIIa inhibitor receptor antagonists, was left to the discretion of the attending operator.

Coronary angiographic data were quantitatively analyzed. Greater than 70% diameter stenosis in one, two, or three coronary arteries was defined as one, two, or three-vessel disease, respectively. Anterograde coronary flow was graded using the standard TIMI criteria.[9] Thrombus-aspirating device; The Diver CE (Invatec, Brescia, Italy) is a rapid-exchange, 6-F compatible, thrombus-aspirating catheter, whose properties were described in previous publications.[3] After placement of the guide wire, the culprit lesion was aspirated several times by the Diver CE (Invatec), then direct stent implantation was attempted on all patients with or without pre-dilation. The success of the intervention was defined as the renewed establishment of TIMI grade 3 flow in the IRA with a residual stenosis less than 20%.[9]

Patients with culprit lesion in the left main coronary artery, left main stenosis greater than 50%, presence of any chronic inflammatory-autoimmune disease, known malignancy, and patients undergoing dialysis were excluded from this study. The study protocol was approved by the ethics committee of our institution.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD) or median (interquartile range) depending on normality test results, assessed using the Kolmogorov-Smirnov test. Categorical variables are expressed as number and percentage of patients and compared using Chi square and Fischer's exact tests. Group means for continuous variables were compared using the Student's t-test or the Wilcoxon test as appropriate. Multivariable logistic regression analysis was applied to identify independent predictors of angiographic and electrocardiographic no-reflow. Within this scope, variables for which the unadjusted p value of less than 0.10 at univariate analysis and variables previously shown to be identified as potential risk factors for the prediction of poor myocardial perfusion were also included by using enter method in the logistic regression model. The Statistical Package for Social Sciences (IBM, Chicago, Illinois, USA) version 20 was used for statistical analysis. A two-tailed p value of < 0.05 was considered statistically significant.

RESULTS

This study included 94 patients (age 58.8 ± 13.4 years, 83% men) with acute STEMI treated with manual aspiration during primary PCI. The incidence of no-reflow was 11% (n = 10, age 63 ± 15 years) angiographically and 24% (n = 23, mean age 56 ± 14years) electrocardiographically. Overlapping subjects who had both no-reflow conditions was not high, with only 6 (6%) patients. The baseline clinical characteristics of the study patients are summarized in Table 1.

Table 1. Baseline clinical and demographic characteristics of the study patients (N = 94)

Variable	All patients (N = 94)	Angiographic reperfusion		p value	Electrocardiographic reperfusion		p value
		No-reflow (n = 10)	Good reflow (n = 84)		No reflow (n = 23)	Good reflow (n = 71)	
Age, years	58.8 ± 13.4	63 ± 15	58 ± 13	0.3	56 ± 14	60 ± 13	0.3
Age > 70 y, n(%)	22 (23)	4 (40)	18 (21)	0.2	5 (22)	17 (24)	0.8
Male gender, n (%)	78 (83)	8 (80)	70 (83)	0.67	17 (74)	61 (86)	0.2
SBP, mmhg	109.3 ± 24.4	90 ± 20	112 ± 24	**0.008**	110 ± 31	109 ± 22	0.8
Blood glucose, mg/dl	155.4 ± 104.4	141 ± 73	157 ± 108	0.6	171 ± 150	150 ± 85	0.4
Diabetes mellitus, n (%)	29 (31)	2 (20)	27 (32)	0.72	6 (26)	23 (32)	0.6
Hypertension, n (%)	41 (44)	8 (80)	33 (39)	**0.02**	13 (57)	28 (39)	0.2
Smoking, n (%)	54 (57)	3 (30)	51 (61)	0.09	11 (48)	43 (61)	0.3
Family history of CAD, n (%)	37 (39)	5 (50)	32 (38)	0.5	5 (22)	32 (45)	**0.04**
Pre-infarct angina, n (%)	32 (34)	3 (30)	29 (34)	0.9	5 (22)	27 (38)	0.2
Previous MI, n (%)	29 (31)	7 (70)	22 (26)	**0.009**	7 (30)	22 (31)	0.9
PCI history (%)	37 (39)	7 (70)	30 (36)	**0.046**	8 (35)	29 (41)	0.6
Killip class							
Class 1, n (%)	81 (86)	7 (70)	74 (88)	0.14	5 (22)	8 (11)	0.3
Class 2-3, n (%)	13 (14)	3 (30)	10 (12)				
Anemia, n (%)	37 (39)	6 (60)	31 (39)	0.3	11 (50)	26 (38)	0.3
Hemoglobin, g/dl	13 ± 2	12 ± 2	13 ± 2	0.07	12 ± 2	13 ± 2	0.2
Total cholesterol, mg/dL	165.6 ± 43.3	170 ± 58	165 ± 42	0.7	161 ± 47	167 ± 42	0.5
LDL-C, mg/dL	103 ± 39.6	96 ± 41	104 ± 40	0.5	92 ± 34	107 ± 41	0.1
HDL-C, mg/dL	37 ± 16	33 ± 9	38 ± 17	0.4	35 ± 13	38 ± 17	0.4
Triglyceride, mg/dL	142 ± 86	148 ± 119	141 ± 82	0.8	155 ± 92	138 ± 84	0.4
eGFR ml/min/1.73 m^2, n (%)	86.8 ± 26.7	65 ± 38	90 ± 24	**0.005**	89 ± 31	86 ± 25	0.7
eGFR < 60 ml/min/1.73 m^2, n (%)	16 (17)	6 (60)	10 (13)	**0.002**	4 (18)	12 (17)	0.9

CAD, coronary artery disease; eGFR, glomerular filtration rate; HDL-C, high-density lipoprotein; LDL-C, low-density lipoprotein-cholesterol; MI, miyocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure.

No statistically significant difference was observed except for family history of coronary artery disease between no-reflow and good-reflow electrocardiographically (22% vs. 45%, p = 0.04). No-reflow patients had lower blood pressure at admission (90 ± 20 vs. 112 ± 24 mmhg, p = 0.008), and more history of hypertension (80% vs. 39%, p = 0.02), previous myocardial infarction (MI), (70% vs. 26%, p = 0.009) and previous PCI (70% vs. 36%, p = 0.05) compared to good reflow patients angiographically. Renal disfunction was also higher in no-reflow patients than good reflow patients angiographically (eGFR < 60 ml/min/1.73 m^2, 60% vs. 13%, p = 0.002 and 65 ± 38 vs. 90 ± 24 ml/min/1.73 m^2, p = 0.005).

While longer reperfusion time was the only significant parameter (11 ± 10 vs. 4 ± 5 hours, p < 0.001) between no-reflow and good reflow patients electrocardiographically; the comparison of angiographic, echocardiographic and procedural characteristics showed no statistically significant difference except for lower final balloon pressure (10 ± 8 vs. 14 ± 5 atm, p = 0.02) and higher rate of predilatation (90% vs. 55%, p = 0.04) between no-reflow and good reflow patients angiographically (Table 2). Overall, tirofiban use was 63% in our study patients and its use tended to be higher in only no-reflow patients compared to good reflow patients angiographically (90% vs. 59%, p = 0.08).

The effects of different variables on myocardial perfusion were analyzed by using univariate and multivariate logistic regression analyses as shown in Table 3. Whereas the e-GFR [odds ratio (OR) 10.4, 95% confidence interval (CI) 2.5-43, p = 0.001], hypertension (OR: 6.2, 95% CI: 1.2-30.9, p = 0.03), previous MI (OR: 6.5, 95% CI: 1.6-27.7, p = 0.01), PCI history, (OR: 4.2, 95% CI: 1.0-17.4, p = 0.04), predilatation (OR: 7.2, 95% CI: 0.9-59, p = 0.06), final balloon pressure (OR: 0.9, 95% CI: 0.8-0.99, p = 0.04) were found to be predictors of poor myocardial perfusion angiographically, only the reperfusion time was the predictor of no-reflow electrocardiographically (OR: 1.12, 95% CI: 1-1.22, p = 0.002) by univariate analysis. After multivariate analyses, the eGFR lower than 60 ml/min/1.73 m^2 (OR: 14.8, 95% CI: 1.9-116, p = 0.01) for no-reflow angiographically found to be the only independent predictor of poor myocardial perfusion (Table 3). In hospital and post discharge 30 day period major adverse cardiac events are given in Table 4. The number of in hospital deaths was significantly worse in both electrocardiographic and angiographic group of no-reflow patients severally.

Table 2. Angiographic and echocardiographic data of the study patients

Variable	All patients (N = 94)	Angiographic reperfusion		p value	Electrocardiographic reperfusion		p value
		No-reflow (n = 10)	Good reflow (n = 84)		No-reflow (n = 23)	Good reflow (n = 71)	
IRA							
LAD, n(%)	29 (31)	4 (40)	25 (30)		10 (43)	19 (27)	
RCA, n (%)	12 (13)	5 (50)	40 (48)	0.6	9 (39)	36 (50)	0.5
CX, n (%)	45 (48)	0 (0)	12 (14)		2 (9)	10 (14)	
SVG, n (%)	8 (8)	1 (10)	7 (8)		2 (9)	6 (9)	
MVD, n(%)	83 (88.3)	10 (100)	73 (87)	0.6	20 (87)	63 (88)	0.9
Pain to balloon time (h)	6 ± 7.4	5.4 ± 4	6.1 ± 7.7	0.8	11 ± 10	4 ± 5	**< 0.001**
Reperfusion time > 4 h, n (%)	32 (34)	4 (40)	28 (33)	0.73	15 (65)	17 (24)	**< 0.001**
Preprocedural TIMI 0/1, n (%)	92 (98)	10 (100)	82 (97)	0.9	21 (91)	71 (100)	*0.06*
Tirofiban use, n (%)	59 (63)	9 (90)	50 (59)	*0.08*	17 (74)	42 (59)	0.2
Stent diameter (mm)	3.3 ± 0.5	3.4 ± 0.4	3.3 ± 0.5	0.7	3.5 ± 0.5	3.3 ± 0.5	0.2
Stent length (mm)	19 ± 6	20 ± 7	19 ± 6	0.8	21 ± 6	19 ± 6	0.2
Final balloon pressure (atm)	14 ± 5.3	10 ± 8	14 ± 5	**0.02**	13 ± 6	14 ± 5	0.2
Predilatation (%)	55 (58.5)	9 (90)	46 (55)	**0.04**	13 (59)	42 (59)	0.9
LVEF (%)	42.6 ± 6.8	40 ± 10	43 ± 6	0.16	41 ± 8	43 ± 6	0.3
LVEF (< 35), n (%)	9 (10)	1 (10)	8 (9)	0.9	4 (17)	5 (7)	0.2

CX, circumferential artery; IRA, infarct related artery; LAD, left anterior descending coronary artery; LVEF, admission left ventricular ejection fraction; MVD, multivessel disease; RCA, right coronary artery; SVG, saphenous vein graft; TIMI, thrombolysis in myocardial infarction.

Table 3. Independent predictors of angiographic and electrographic no-reflow

Variables	Angiographic reperfusion No-reflow				Electrocardiographic reperfusion No-reflow			
	Univariate		Multivariate*		Univariate		Multivariate*	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
GFR < 60 ml/min/1.73 m	10.4 (2.5-43)	**< 0.001**	14.8 (1.9-116)	**0.01**	0.9 (0.3-3.5)	0.9	-	-
Anemia	2.3 (0.6-9)	0.2	-	-	1.6 (0.6-4.2)	0.33	-	-
Age (per year)	1.02 (0.97-1.07)	0.33	-	-	0.98 (0.94-1)	0.3	-	-
Diabetes mellitus	0.5 (0.1-2.6)	0.43	-	-	1.3 (0.4-3.9)	0.5	-	-
Hypertension	6.2 (1.2-30.9)	**0.03**	10.5 (0.9-121)	*0.06*	0.5 (0.2-1.2)	0.15	-	-
Smoking	0.28 (0.07-1.15)	*0.08*	0.2 (0.02-1.9)	0.17	1.67 (0.6-4.3)	0.28	-	-
Previous MI	6.5 (1.6-27.7)	**0.01**	4.8 (0.4-56)	0.21	1.02 (0.3-2.8)	0.9	-	-
PCI history	4.2 (1.0-17.4)	**0.04**	0.3 (0.02-6)	0.48	1.3 (0.5-3.4)	0.6	-	-
Killip class > 1	3.1 (0.7-14)	0.14	3.4 (0.2-35)	0.3	2.1 (0.6-7.5)	0.2	-	-
Pain to balloon time	0.99 (0.9-1.1)	0.8	-	-	1.12 (1-1.22)	**0.002**	1.12 (1-1.22)	**0.002**
Tirofiban use	0.16 (0.02-1.3)	*0.09*	0.08 (0.06-1.2)	*0.07*	0.2 (0.7-5.5)	0.2	-	-
Predilatation	7.2 (0.9-59)	0.06	11 (0.6-189)	*0.09*	1 (0.4-2.6)	0.9	-	-
Stent diameter	1.4 (0.2-8.6)	0.7	-	-	2.1 (0.6-6.9)	0.2	-	-
Stent length	1.01 (0.8-1.2)	0.8	-	-	1.02 (0.9-1.1)	0.2	-	-
Final balloon pressure	0.9 (0.8-0.99)	**0.04**	0.9 (0.8-1.1)	0.6	0.9 (0.86-1)	0.18	-	-

CI, confidence interval; eGFR, estimated glomerular filtration rate; MI,miyocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention.

* Adjusted for killip class, eGFR, hypertension, smoking, previous MI and intervention history, tirofiban use, predilatation, final balloon pressure and pain to balloon time.

Table 4. In-hospital and 30-day period clinical outcome data of the study population

	Patients (N = 94)	Angiographic reperfusion		p value	Electrocardiographic reperfusion		p value
		No reflow (n = 10)	Good reflow (n = 84)		No-reflow (n = 23)	Good reflow (n = 71)	
Inhospital							
Death, n (%)	10 (10)	4 (40)	6 (7)	**0.01**	7 (30)	3 (4)	**0.002**
Re-MI, n (%)	16 (17)	4 (40)	12 (14)	0.06	8 (35)	8 (11)	0.02
Stent thrombosis, n (%)	16 (17)	4 (40)	12 (14)	0.06	8 (35)	8 (11)	0.02
30 days							
Hospitalization, n (%)	14 (15)	2 (20)	12 (14)	0.6	2 (9)	12 (17)	0.5
Death, n (%)	1 (1)	1 (10)	0 (0)	0.1	1 (4)	0 (0)	0.2
Re-MI, n (%)	7 (7)	2 (20)	5 (6)	0.2	3 (13)	9 (12)	0.9
Stent thrombosis, n (%)	7 (7)	2 (20)	5 (6)	0.2	2 (9)	5 (7)	0.9
Composite end point, n(%)	12 (13)	2 (20)	10 (12)	0.6	3 (13)	9 (12)	0.9

Re-MI, recurrent miyocardial infarction; ST, stent thrombosis.

DISCUSSION

This study demonstrates that while the in-hospital death rate is higher with both angiographic or electrocardiographic diagnosed no-reflow, and STEMI patient groups treated with manual thrombus aspiration during PCI, no significant adverse event was observed at post-discharge 30-day period. Admission e-GFR lower than 60 ml/min/1.73 m^2 and longer reperfusion time were independent predictors of no-reflow.

As conditions promoting coagulation, may contribute to the progression of arteriosclerosis and a worse prognosis,[10] we speculated that these strong relationships between the no-reflow phenomenon and these in-

dependent predictors may indicate the presence of highly organized thrombus burden with a higher propensity for distal and micro embolization. That can be a reasonable explanation for in-hospital adverse events. Despite numerous advances in PCI technique, devices, and adjunct pharmacology over the past decades, the incidence of no-reflow after primary PCI remains relatively common. The rates of no-reflow after primary PCI reported in previous studies varied from 2.3 to 39.9% on the basis of angiographic criteria.[6,11,12] We observed the rate of no-flow of 11% after manual thrombus aspiration angiographically. In the REMEDIA trial,[13] manual thrombus aspiration was associated with better angiographic and electrocardiographic myocardial reperfusion rates compared with those achieved by standard PCI. But data coming from larger multicenter trials and studies using more complex devices is diverse.[14,16] Those differences in both the devices and the populations studied could explain such divergences. Although no-reflow is associated with short and long-term adverse clinical outcomes in the clinical setting of AMI, there is limited data about the impact of poor myocardial perfusion on short-term outcomes concerning in STEMI patients treated with manual aspiration.[4,5,17] We demonstrated the importance of either described no-reflow criterion on early outcomes in STEMI patients treated with manual aspiration during PCI.

It remains unclear whether the increased mortality in patients with no-reflow after primary PCI is directly caused by the lack of blood flow, or whether it is due to the underlying predisposing factors that caused the no-reflow phenomenon. The observation that no-reflow is significantly associated with mortality only in the hospitalization period after PCI, but not after discharge, is reasonably consistent with a causal effect. Previous studies have demonstrated that high thrombus burden assessed with various scores, increases the risk of distal embolization and no-reflow.[18,19] We have extended these findings by showing that predilatation and lower final balloon pressures in the culprit lesions were associated with angiographic no-reflow in our study. Compressing thrombus material inadequately to the vessel wall may cause distal embolization of thrombi and atherosclerotic gruel, which than activates platelets and inflammatory cells to induce vasospasms in combination with mechanical plugging of the micro-circulation.[20]

In our angiographic no-reflow patients, previous MI and coronary interventions occurred more frequently. However, no difference in stent length and diameter was detected,[21] which varies from previously described associations between the complexity of a lesion and no-reflow in patients with STEMI. This may be partly due to the different clinical and angiographic characteristics of our study patients. Genetic predisposition to the hypercoagulable state, acquired risk factors such as diabetes, hypertension, smoking and hypercholesterolemia might modulate the individual response to myocardial injury.[22]

In addition to distal embolization, poor myocardial perfusion in patients with STEMI may develop due to in situ thrombosis. Individual susceptibility of coronary microcirculation to injury and micro vascular damage is one of the main pathophysiological mechanisms of no-reflow. The divergence in mortality among patients with TIMI grade 3 flow is also associated with degree of micro vascular dysfunction and subsequent impairment of tissue perfusion. This pathologic process may limit the benefits of reperfusion therapy despite coronary artery recanalization.[2] Propitiously, Stone et al.[23] showed that although angiographic recanalization rates were similar, the rates of sub-acute thrombosis and recurrent ischemia decreased with the use of abciximab during the first several weeks after primary percutaneous transluminal coronary angioplasty in STEMI patients. By observing a 13% difference in the no-reflow success rate between angiographic and electrocardiographic reperfusion groups, we believe that electrocardiographic no-flow criteria is more sensitive than angiographic no-flow criteria in detecting micro vascular dysfunction at the cellular level. When the desired coronary flow is maintained mechanically after a critical time period, inadequate blood supply at the cellular level can occur due to micro-vascular dysfunction. In the electrocardiographic no-reflow group, patients with ongoing ischemia were more frequently recanalized twelve hours after onset of their complaints. The process of inflammation due to this prolonged reperfusion time by generation of free radicals and complement activation, endothelial injury, plugging of capillaries by neutrophils and microthrombi, increases cellular damage.[24] This pathological process can effect reperfusion at the microvascular level after a critical time delay irrespective of renal impairment. That

can be the cause of the different risk predictors between the electrocardiographic and the angiographically no-reflow condition as the number of overlapping subjects who had both no-reflow criterion was not high with only 6 (6%) patients. Also, the rate of periprocedural glycoprotein IIb/IIIa inhibitor use was lower in our study population compared with the rates in previous studies.[4,6,11] If tirofiban had been used more frequently, no-reflow rates could be reduced at least in electrocardiographic reperfusion patients.

Renal impairment is associated with hypercoagulable states. Therefore, reflecting the severity of the hypercoagulable state, admission eGFR lower than 60 ml/min/1.73 m^2 might be valuable as a predictor of distal embolization and/or no-reflow in patients with STEMI. Many clinical studies have showed that patients with baseline renal dysfunction have increased cardiovascular risk and correlate with a major decrease in life expectancy after the procedure.[25] Baseline renal dysfunction, analyzed according to MDRD equation, was an independent predictor of in-hospital mortality in STEMI patients undergoing successful primary PCI.[26] In the Heart Institute of Japan Acute Myocardial Infarction Registry, decreased GFR was associated with the risk of unsuccessful primary PCI, and unsuccessful PCI was associated with poor long-term survival in patients with GFR lower than 30 ml/min/1.73 m^2.[10] For an unfavorable result, failure to cross the guide wire was the most common reason (40%) followed by no-reflow on the final angiogram (20%). Assali and coworkers[27] analyzed the outcomes of AMI patients with impaired renal function tests treated using primary PCI to determine factors associated with increased mortality. As the degree of renal function worsened, 30-day period mortality was gradually decreasing. They concluded that the degree of renal impairment before/after the procedure, measures of PCI complexity and the extent of coronary artery disease were altogether related to 30-day mortality. We observed no adverse 30-day outcomes in our study. Not severely but mildly impaired renal function and the small sample size can be responsible for our observation. We found that the admission eGFR value lower than 60 ml/min/1.73 m^2 was an independent predictor of angiographic no-flow, and this poor perfusion criteria was associated with a worsening of hospital outcomes. This is concordant with the study of Dragu and et al.,[25] in which they investigated the effect of different myocardial reperfusion modalities in patients with STEMI and renal failure, and mentioned thrombolytic therapy to be the preferred modality of reperfusion therapy due to lower mortality rate in these patients with high thrombotic burden. These findings have suggested that baseline renal dysfunction may play a significant role in the development of poor myocardial reperfusion in STEMI patients due to high thrombotic burden, even when treated with manual aspiration during primary PCI.

The main limitation of this study is its relatively small sample size and its single center retrospective design. Despite adjustment for statistically significant clinical variables, the presence of residual confounding from unmeasured variables is still possible. Nevertheless by adding accepted confounding variables to our final adjustment models, it was minimized. There was a low rate of glycoprotein IIb/IIIa inhibitor use in the study population, which is inconsistent with no-reflow prevention efforts. We didn't exclude patients with previously known chronic kidney disease so we can't comment on whether lower admission eGFR values were linked to acute MI. Incidence of contrast induced nephropathy which might also impact on in-hospital and 30-day outcomes wasn't investigated in this study. Finally, lack of quantitative data for infarct size by using magnetic resonance imaging or nuclear tests, GRACE or TIMI scores may be further limited during evaluation of the early outcomes. Consequently, our study results cannot be generalized to the overall population of patients undergoing primary PCI.

CONCLUSIONS

In conclusion, the results of the current study provide further evidence that no-reflow even after thrombus aspiration during primary PCI is common. Not only admission eGFR lower than 60 ml/min/1.73 m^2 but also longer reperfusion time, separately might be a selection criteria for more aggressive, complementary and different treatment strategies to improve macro and micro vascular reperfusion. These findings suggest that continued efforts to reduce complications are warranted especially in patients with renal dysfunction.

ANY RELATIONSHIP WITH INDUSTRY

No.

CONFLICT INTEREST

No.

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