Original Article

The Usefulness of the Metabolic Syndrome Score in Predicting the Angiographic Outcome in Patients With STEMI Treated With Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: The relationship between metabolic syndrome (MS) and the MS score and the angiographic outcome of primary percutaneous coronary intervention (PPCI) for ST-segment-elevation myocardial infarction (STEMI) is still unclear. We aimed to examine the association between angiographic outcomes including angiographic no-reflow and MS.

Methods: We prospectively included 100 patients with STEMI treated with PPCI. Angiographic no-reflow was defined as a thrombolysis in myocardial infarction (TIMI) risk score of below 3 or a TIMI risk score of 3 with a myocardial blushing grade (MBG) of 0 to 1 in the absence of mechanical complications. MS was defined based on the National Cholesterol Education Program criteria. The MS score was defined as the number of MS components present.

Results: Totally, 26 patients (26%) developed no-reflow. The patients with no-reflow had a higher prevalence of MS, a higher level of triglycerides, a lower level of high-density lipoprotein, and a higher fasting blood glucose level. The fasting blood glucose level and the time from symptom onset to wire crossing were independent predictors of the no-reflow phenomenon (OR, 1.225; 95% CI, 1.105 to 2.854; P<0.001) and (OR, 1.049; 95% CI, 1.026 to 1.073; P<0.001).

There were significant negative correlations between the MS score and both the post-intervention TIMI flow grade and MBG (P<0.001 for both).

Conclusions: MS plays an important role in the development of no-reflow in STEMI patients treated with PPCI with significant negative correlations between the MS score and both the post-intervention TIMI flow grade and MBG. ***(Iranian Heart Journal 2021; 22(4): 80-89)***

KEYWORDS: Metabolic syndrome score, No-reflow, Myocardial infarction

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Received: December 15, 2020 **Accepted:** August 11, 2021

Primary percutaneous coronary intervention (PPCI) is the preferred reperfusion strategy for patients with acute ST-segment-elevation myocardial infarction (STEMI). [1] However, myocardial tissue could fail to restore normal perfusion despite the opening of the occluded infarct-related artery; and this phenomenon is called "the coronary no-reflow". [2] The incidence of no-reflow is about 30% of all STEMI

patients treated with PPCI, and it occurs when the thrombolysis in myocardial infarction risk score (TIMI) is below 3 and the myocardial blushing grade (MBG) is less than 3 in the infarct-related artery. [3] No-reflow is associated with an increased incidence of congestive heart failure, re-infarction, and death. Nonetheless, the exact pathophysiology is not well understood, and there is no definite effective treatment for this phenomenon. [4]

The prediction of the occurrence of no-reflow is important in STEMI patients. Delayed presentation and large thrombus burden are well accepted angiographic risks for no-reflow. [5] Clinical predictors include hypertension, hyperlipidemia, diabetes mellitus, and inflammatory and prothrombotic markers. [6] Those risk factors represent the major components of metabolic syndrome (MS). [7] Several previous studies have shown that the presence of MS in STEMI patients is associated with long-term poor clinical outcomes, [8, 9] but previous data indicated that the risks associated with MS were not beyond the risks of its components. [10] To overcome the limitations of traditional binary MS, researchers developed a severity score that depends on the number of the components of MS. [11] The use of the MS severity score provides additional predictive powers beyond the individual MS components. [12]

This study aimed to assess the association between MS and no-reflow and to determine the impact of the MS score on the immediate angiographic outcome in patients with STEMI.

METHODS

Study Population

This study was conducted prospectively on 100 consecutive patients diagnosed with acute STEMI who underwent PPCI in the Cardiology Department of Tanta University between February 2019 and January 2020.

Informed consent was taken from all the patients, and the study was approved by the local ethics committee.

STEMI was defined as a chest pain that lasted longer than 20 minutes and that was associated with ST-segment elevation in at least 2 contiguous leads (≥ 2.5 mm in men <40 years old, ≥ 2 mm in men ≥40 years old, or ≥1.5 mm in women in leads V_2–V_3; and/or ≥1 mm in the other leads). [13] The diagnosis was confirmed by the elevation in troponin levels. Patients with the onset of symptoms less than 12 hours before hospital admission were included in the study.

Angiographic Procedure

Coronary angiography and PPCI were done through the femoral or radial approach. All the patients received the following regimen: 1) ticagrelor (180 mg as the initial dose, followed by a maintenance dose of 90 mg twice daily) or clopidogrel (600 mg as the loading dose orally, followed by a maintenance dose of 75 mg/d) if ticagrelor was contraindicated and 2) aspirin (300 mg, followed by 75–100 mg/d). Additionally, during the procedure, the patients received unfractionated heparin (100 IU/kg), and the dose was reduced to 70 IU/kg if a glycoprotein IIb/IIIa inhibitor (eptifibatide) was administered.

The TIMI flow rate [14] was assessed before and at the end of PPCI, and MBG [15] was assessed at the end of the procedure.

The use of manual thrombus aspiration was left at the operator's discretion.

Angiographic no-reflow was defined as a TIMI flow risk score below 3 or a TIMI flow risk score of 3 with an MBG of 0 to 1 in the absence of mechanical complications such as dissection and spasm. [16, 17]

Definition of MS

The diagnosis of MS was based on the updated 2005 clinical definition by the Third

Adult Treatment Panel of the National Cholesterol Education Program. [18] This requires the presence of any 3 of 5 of the following: 1) abdominal obesity (waist circumference >102 cm in men and >88 cm in women), 2) elevated triglyceride (TG) levels (>150 mg/dL) or consumption of drugs for elevated TG, 3) reduced high-density lipoprotein HDL-cholesterol levels (<40 mg/dL in men and <50 mg/dL in women, 4) high blood pressure (systolic >130 mm Hg or diastolic >85 mm Hg, or being on antihypertensive medication), and 5) a high fasting plasma glucose concentration (>100 mg/dL) or consumption of drugs for elevated glucose.
The MS score was defined as the number of MS components present. [11]

Echocardiographic Evaluation
Echocardiography was performed according to the recommendations of the American Society of Echocardiography using a commercially available GE Vivid 7 machine (General Electric, Norway) with a 2.5 MHz transducer. The left ventricular ejection fraction was estimated via the biplane Simpson method. [19]

Statistical Analysis
All the statistical analyses were carried out using the Statistical Package for Social Sciences software (SPSS), version 18.0, for Windows (SPSS Inc, Chicago, Illinois).
Quantitative variables are expressed as the mean ± the standard deviation (SD). Qualitative data are expressed as counts and percentages. For the comparison of values, the Student *t* test and the Fisher exact test were used for the quantitative and qualitative values, respectively. Multivariable logistic regression analysis was performed to identify independent predictors of the no-reflow phenomenon. The Mann–Whitney *U* test was employed to assess the relationship between the MS score and both the TIMI flow grade and MBG post-intervention. A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

One hundred patients with STEMI who had undergone PPCI were enrolled in the study. The patients were divided into 2 groups: the normal flow group (n =74 [74%] and the no-reflow group (n =26 [26%]).

The baseline clinical characteristics of the study population are shown in Table 1. There were no significant differences between both groups regarding age, sex, hypertension, diabetes mellitus, smoking status, family history of premature coronary artery disease, prior MI, prior PCI, prior coronary artery bypass grafting, body mass index, waist circumference, total cholesterol, low-density lipoprotein (LDL), systolic blood pressure, diastolic blood pressure, serum creatinine, peak troponin, the Killip class on admission, the ejection fraction, and major medications prescribed. Patients with no-reflow had a higher prevalence of MS, a higher level of TG, a lower level of HDL, and a higher fasting blood glucose level (P=0.005, P<0.001, P<0.001, P<0.001, and P=0.011, respectively).

The angiographic characteristics of the study population are presented in Table 2. There were no significant differences between the groups regarding the number of diseased vessels, the rate of stent utilization, the use of drug-eluting stents, balloon pre-dilatation, balloon post-dilatation, infarct-related arteries, reference vessel diameter, stent length, stent diameter, time from the STEMI diagnosis to wire crossing, the rate of use of glycoprotein IIb/IIIa inhibitors, the rate of use of thrombus aspiration devices, and the TIMI flow grade before PPCI. Time from symptom onset to wire crossing was

significantly longer in the no-reflow group ($P \leq 0.001$).

A multivariable logistic regression model was built to identify the independent predictors of the no-reflow phenomenon (Table 3). The fasting blood glucose level and time from symptom onset to wire crossing were independent predictors of the no-reflow phenomenon (odds ratio [OR], 1.225; 95% confidence interval [CI], 1.105 to 2.854; $P<0.001$ and OR, 1.049; 95% CI, 1.026 to 1.073; $P<0.001$, respectively).

The Mann–Whitney *U* test was used to detect the relationship between the MS score and both the post-intervention TIMI flow grade and MBG. There were significant negative correlations between the MS score and both the post-intervention TIMI flow grade and MBG ($P \leq 0.001$ for both) (Table 4). As the MS score increased, the TIMI flow grade and MBG became worse.

Table 1. Baseline clinical characteristics of the studied patients

Variables	Normal Flow n=74 (74%)	No-Reflow n=26 (26%)	*P*-value
Age, y	54.338±5.711	56.115±3.011	0.134
Male	42(56)	17(65)	0.297
Hypertension	26(35)	10(38)	0.469
Diabetes mellitus	16(22)	6(23)	0.538
Smoking	22(29)	8(31)	0.553
Family history of premature CAD	8(11)	3(12)	0.585
Prior MI	5(7)	1(4)	0.507
Prior PCI	7(9)	3(12)	0.510
Prior CABG	2(3)	1(4)	0.599
MS	20(27)	15(58)	0.005
BMI, kg/m^2	27.473±2.696	27.962±2.807	0.433
Waist circumference, cm	93.176±6.648	92.538±5.085	0.658
Total cholesterol, mg/dL	194.365±29.274	196.577±28.629	0.740
LDL, mg/dL	124.176±21.704	128.846±21.899	0.349
HDL, mg/dL	50.027±6.754	41.308±5.214	<0.001
TG, mg/dL	128.797±25.253	189.038±44.632	<0.001
Fasting blood glucose, mg/dL	125.081±13.455	(133.231±14.594)	0.011
Systolic blood pressure, mm Hg	128.243±10.251	130.192±9.217	0.395
Diastolic blood pressure, mm Hg	81.068±8.141	84.231±9.454	0.106
Creatinine, mg/dL	1.158±0.292	1.085±0.226	0.247
Peak troponin, ng/mL	5.980±4.139	4.649 ±3.306	0.142
Killip class 3/4 at admission	5(7)	2(8)	0.587
EF%	56.595±6.666	59.731±7.743	0.074
Medications			
Clopidogrel	15(20)	5(19)	0.578
Ticagrelor	59(80)	21(81)	0.578
ACEI/ARB	52(70)	18(69)	0.553
Beta-blockers	67(91)	23(88)	0.510
statins	68(91)	24(92)	0.656

Values are expressed as mean ± SD or n (%).

CAD, Coronary artery disease; MI, Myocardial infarction; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting; MS, Metabolic syndrome; BMI, Body mass index; LDL, Low-density lipoprotein; HDL, High-density lipoprotein; TG, Triglycerides; EF, Ejection fraction; ACEI, Angiotensin-converting-enzyme inhibitor; ARB, Angiotensin receptor blockers

Table 2. Angiographic characteristics of the studied patients

Variables	Normal Flow n=74 (74%)	No-Reflow n=26 (26%)	*P*-value
Number of Diseased Vessels			
1	16(22)	7 (27)	0.816
2	33(45)	10 (38)	
3	25(34)	9 (35)	
Stent utilization	71(96)	24 (92)	0.602
Drug-eluting stent implantation	59(80)	20 (76)	0.783
Balloon pre-dilatation	53(72)	18 (69)	0.807
Balloon post-dilatation	12(17)	4 (15)	1.00
Infarct related artery			
Left anterior descending artery	34(46)	11 (42)	0.956
Left circumflex artery	23(31)	8 (35)	
Right coronary artery	17(23)	6 (23)	
RD	3.082±0.359	(3.158±0.428)	0.381
Stent length	3.095±0.345	(3.183±0.384)	0.280
Stent diameter	21.176±5.535	(23.462±5.054)	0.067
Time from symptom onset to wire crossing, min	233.581±59.717)	(382.500±47.755)	<0.001
Time from STEMI diagnosis to wire crossing	51.230±14.499)	(56.192±12.574)	0.128
G IIb/IIIa inhibitors	55(74)	20 (77)	0.782
Thrombus aspiration	14(19)	6(23)	0.782
TIMI flow before PCI			
0	52(70)	20(77)	0.616
1	22(30)	6(23)	

Values are expressed as mean ± SD or n (%).
RD, Reference diameter; STEMI, ST-segment elevation myocardial infarction; ST-segment elevation myocardial infarction; G IIb/IIIa inhibitors, Glycoprotein IIb/IIIa inhibitors; TIMI, Thrombolysis in myocardial infarction; PCI, Percutaneous coronary intervention

Table 3. Multivariable logistic regression analysis to predict no-reflow

	Odds Ratio	95% CI for Odds Ratio		*P*-value
		Lower	Upper	
Fasting blood glucose, mg/dL	1.225	1.105	2.854	<0.001
TG, mg/dL	0.844	0.687	1.587	0.752
HDL, mg/dL	0.803	0.887	1.22	0.115
Time from symptom onset to wire crossing, min	1.049	1.026	1.073	<0.001
Sex	0.620	0.106	3.625	0.596
Hypertension	0.458	0.035	6.058	0.554
BMI, kg/m^2	1.081	0.908	1.288	0.379
Waist circumference, cm	0.979	0.907	1.057	0.594
EF, %	1.500	0.795	2.828	0.211

CI, Confidence interval; MS, Metabolic syndrome; TG, Triglycerides; HDL, High-density lipoprotein; BMI, Body mass index; EF, Ejection fraction

Table 4. Mann-Whitney *U* test presenting the relationship between the MS score and post-PCI TIMI flow and post-PCI MBG

	N	MS Score		U	*P*-value
		Mean ± SD.	Median		
Post-PCI TIMI flow					
0 – 2	14	3.6 ± 1.4	4	205.0	<0.001
3	86	1.6 ± 1.4	1		
Post-PCI MBG grade					
0 – 1	26	3.5 ± 1.3	4	244.0	<0.001
2 – 3	74	1.4 ± 1.2	1		

MS, Metabolic syndrome; TIMI, Thrombolysis in myocardial infarction; PCI, Percutaneous coronary intervention; MBG, Myocardial blush grade

DISCUSSION

We aimed to assess the relationship between the MS score and myocardial perfusion in patients with STEMI who had undergone PPCI. The main findings of the present study were as follows:

(i) Patients with no-reflow had a higher prevalence of MS. (ii) As the severity of MS increased with a rise in the MS score, the TIMI flow and MBG became worse. (iii) Time to reperfusion and fasting plasma glucose were independent predictors of no-reflow.

No-reflow is a devastating complication of PPCI. It is an independent predictor of mortality at 1 year and is associated with poor short and long-term outcomes due to larger infarction size, reinfarction, and left ventricular failure. [20-22] The most important way in the management of no-reflow is to prevent its occurrence from the start as all the available management lines, including intracoronary injection of vasodilators and distal embolic protection devices, have failed to show any clinical benefits. [23] The prediction of the risk of no-reflow could lead to the application of certain techniques to decrease the risk of no-reflow such as direct stenting and avoidance of inflation at high pressure.

Previous studies have confirmed the association between the occurrence of no-reflow and clinical variables. [24, 25] Hadadi et al [26] showed that 2 simple clinical risk scores, GRS and ACEFm, predicted the occurrence of no-reflow after PPCI, while the angiographic Syntax score failed to predict such complications. In another study, the CHA2DS2-VASc score was associated with an increase in the risk of no-reflow and in-hospital mortality in patients who underwent PPCI. [27]

The relationship between MS and no-reflow came from the fact that most of the risk factors of no-reflow are the components of MS such as dyslipidemia, hypertension, diabetes, and inflammatory markers. [6] Celik et al [28] assessed patients with STEMI who underwent PPCI and reported a higher incidence of MS in patients with impaired myocardial perfusion compared with those with normal myocardial perfusion (40% vs 20%, respectively; *P*=0.002). Moreover, MS was an independent predictor of impaired myocardial perfusion after PPCI (adjusted OR, 2.54, 95% CI, 1.35 to 4.75; *P*=0.003). In a previous investigation, MS was also related to major adverse cardiac events (MACE) in STEMI patients. [29, 30] The exact mechanism by which MS is associated with impaired myocardial reperfusion after PPCI in patients with STEMI is not clearly understood. However, some potential mechanisms may help to understand this association. First, in intravascular ultrasound and multidetector computed tomography-based studies, MS was significantly associated with lipid-rich plaques. Therefore, impaired coronary microcirculation in patients with MS may be caused by distal embolization due to the increased prevalence of lipid-rich plaques. [31, 32] The second possible mechanism is the presence of prothrombotic, procoagulant, and proinflammatory alternations in patients with MS, leading to microvascular obstruction with subsequent impaired myocardial perfusion. [28] The third potential mechanism is the association between MS and microvascular endothelial dysfunction due to oxidative stress and decreased levels of nitric oxide. Pre-existing microvascular dysfunction may contribute to the development of poor myocardial perfusion after PPCI. [33]

A major criticism of the MS score is that it cannot predict the risk above and beyond its single components. [34, 35] Nevertheless, when the number of MS components is integrated into the MS score, it is more useful in the prediction of the clinical outcome than binary MS. [36]

Lee et al [37] studied the effects of the combination of MS and obesity among 14 357 STEMI patients who underwent PPCI. They divided the patients into 4 groups

(obese-/MS-, 'obese-/MS+, obese+/MS-, and obese+/MS+). They found no differences in the rate of MACE at 12 months' follow-up and concluded that among male obese STEMI patients, MS was not useful in predicting the clinical outcome. On the other hand, the MS score in recent clinical trials was found to be a more useful and effective tool in the prediction of cardiovascular risk. [38, 39] Lovic et al [40] examined 507 patients with STEMI treated with PPCI and divided them into 2 groups: 217 patients with MS and 290 subjects without MS. They detected an increase in the incidence of mortality with an increased number of MS components, but it did not reach a significant difference (*P* =0.382). In contrast, there was a high significance trend between the incidence of MACE and the number of risk factors (*P*=0.006 for trend) with the highest incidence of MACE in those patients with the 5 components of MS. Gui et al [36] found that in 1191 patients who underwent diagnostic coronary angiography, only the MS score and increased fasting blood glucose level were significantly correlated with the severity of coronary artery disease. They also showed that elevated TG levels and increased blood pressure had no correlations with the severity of coronary artery disease, meaning that different MS components made different contributions to the severity of the disease. In our study, and from all MS components, only fasting blood glucose was significantly correlated with the incidence of no-reflow. The relationship between elevated blood glucose levels and no-reflow could be explained by different mechanisms. Elevated blood glucose levels increase intracellular adhesion molecule and P selectin levels, augmenting leukocyte adhesion and plugging small capillaries. Another mechanism by which elevated blood glucose levels could lead to no-reflow is through the augmentation of thrombus formation and the prevention of ischemic preconditioning, a mechanism that could decrease reperfusion injury and no-reflow. Furthermore, elevated blood glucose could be a reflection of large infarction and more catecholamine release. [41] Another advantage of the MS score is that it can predict future CHD events beyond HbA1C in diabetic patients. Gurka et al [42] studied the data of 1419 diabetic patients and 7241 nondiabetic patients and arbitrated CHD diagnoses over 20 years. They used 2 MS scores: the standard score and another score without incorporating the blood glucose level as a component of MS. Their results demonstrated that in patients with diabetes, an elevated MS score at baseline was associated with the occurrence of CHD, using both the standard MS score (HR, 1.29; 95% CI, 1.21 to 1.39) and the no-glucose score (HR, 1.42, 95% CI, 1.24 to 1.62) (*P*<0.001 for both). For the baseline-diabetes group, this relationship remained significant when HbA1C was included in the model, both for the standard MS score (HR, 1.21, 95% CI, 1.09 to 1.34; *P*<0.001) and the no-glucose score (HR, 1.25, 95% CI, 1.04 to 1.51; *P*=0.02).

CONCLUSIONS

The present study showed that the presence of MS might play an important role in the development of no-reflow in STEMI patients treated with PPCI. Moreover, an increased MS score was associated with a worse post-intervention TIMI flow grade and MBG. Therefore, the MS score could be a useful predictor of the no-reflow phenomenon.

Conflict of Interest

The authors declare that there are no conflicts of interest.

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