CLINICAL STUDY

The Relationship Between TIMI Flow and MAPH Score in Patients Undergoing Primary Percutaneous Coronary Intervention for STEMI

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Summary

The MAPH (mean platelet volume, age, total protein and hematocrit) score is a newly developed simple scoring system for patients with STEMI that has been associated with satisfactory predictive values to determine thrombus burden in STEMI patients. Therefore, the aim of our study was to determine the relationship between the MAPH risk score and TIMI flow in patients with STEMI.

The study included 260 patients who underwent primary percutaneous coronary intervention between December 2019 to July 2022, and had TIMI 0 flow in the responsible coronary artery due to STEMI. According to the TIMI flow score after stent implantation, the patients were classified into either the no-reflow group (n = 59) or the normal flow group (n = 201). In order to calculate the MAPH score, ROC analysis was performed to find the cutoff point for each component of the MAPH score. MAPH scores were calculated (MPV + Age + Protein + Hematocrit) for both groups. Our study was a retrospective, observational study.

In the multivariable regression analysis, the MAPH score (OR: 0.567; 95%CI: 0.330-0.973, P = 0.04) and glycoprotein IIb/IIIa inhibitors (OR: 0.249; 95%CI: 0.129-0.483, P < 0.001) were parameters found to be independent predictors of TIMI flow. An MAPH score value > 2.5 predicted the presence of low TIMI coronary flow in patients with STEMI, with 78% specificity and 45% sensitivity (ROC area under curve: 0.691, 95% CI: 0.617-0.766, P < 0.001).

The MAPH risk score is simple, inexpensive, and quick to calculate. A high MAPH score may be an indicator of coronary no-reflow in patients with STEMI.

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Key words: Myocardial infarction, TIMI flow grade, Predictors, No-reflow

ST-segment elevation myocardial infarction (STEMI) is an acute coronary syndrome (ACS) condition resulting from total occlusion of epicardial coronary arteries.[1)] Therefore, there is a need for urgent percutaneous coronary intervention (PCI) as this situation arises from a thrombotic process faced with total occlusion in the coronary artery.[2)] Although various mechanisms have been considered in the formation of this thrombotic process, the most likely pathophysiological condition associated with it is the increased blood viscosity.[3,4)] In addition, some studies have indicated that blood components such as proteins, platelets and hematocrit are responsible for the increase in blood viscosity, and a few studies have shown that it slows down blood flow in the coronary arteries.[5-7)]

Early revascularization of the coronary artery that is responsible for STEMI is of critical importance. Sometimes, despite being revascularized, the blood flow in the responsible coronary artery may be slow or even disappear completely.[8)] This situation, which is described as a no-reflow phenomenon, refers to TIMI (Thrombolysis in Myocardial Infarction) flow scores < 3.[9)] PCI can become complex in more than half of STEMI patients.[8,10)]

Intracoronary thrombus burden and its components are important predictors of prognosis in STEMI as well-known risk factors for long-term adverse cardiovascular (CV) events, distal embolism and stent thrombosis. Recent studies have shown a positive correlation between an increase in mean platelet volume (MPV) and a tendency to thrombosis.[11-14)] Çetin, *et al.* in their PALSE study emphasized the importance of parameters such as age and total protein in demonstrating thromboembolism in patients with atrial fibrillation ablation procedure plan.[15)] The MAPH (mean platelet volume, age, total protein and hematocrit) score is a newly developed simple scoring system for patients with STEMI that is calculated with basic data.[16-19)] The MAPH score has been associated with satisfactory predictive values as a new score that can be used to determine thrombus burden in STEMI patients.

The aim of our study was to determine the relation-

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ship between the MAPH risk score and TIMI flow in patients who visited our cardiology department for STEMI consultation.

Methods

Study population and definitions: We retrospectively examined 260 patients who underwent primary percutaneous coronary intervention in our hospital between December 2019 and July 2022 and who had TIMI 0 flow in the responsible coronary artery due to STEMI. Patients between the ages of 18-90 who underwent PCI for STEMI were eligible for inclusion in the study. Patients who were pregnant, had an active malignancy, had severe hepatic and/or renal dysfunction, or for whom optimal angiographic images could not be obtained were excluded. According to the TIMI flow score after stent implantation, the patients were classified into either a no-reflow group (n = 59) or a normal flow group (n = 201).

Demographic and angiographic data were obtained from the registry system of our hospital. The drugs used by the patients before STEMI and the treatments used in the PCI were recorded. The blood samples taken when the patients were first diagnosed with STEMI (before PCI) were analyzed from the hospital information recording system with respect to routine hemogram, renal function tests, fasting blood glucose, albumin, total protein, and lipid panel.

Hypertension was defined as blood pressure above 140/90 mmHg or ongoing antihypertensive treatment. A diagnosis of diabetes mellitus was defined as a fasting blood glucose level above 126 mg/dL or ongoing antidiabetic treatment (oral medication or insulin). Hyperlipidemia was defined as total cholesterol > 200 mg/dL, low density lipoprotein cholesterol (LDL-C) > 130 mg/dL, or triglycerides > 150 mg/dL. Chronic renal failure (CRF) was defined as GFR (glomerular filtration rate) < 60 mL/minute/1.73 m^2 according to the MDRD (Modification of Renal Disease) formula. Smoking status was classified as active user or non-smoker.

The MAPH score of all patients was calculated according to the following formula: MAPH score = MPV + Age + Total protein + Hematocrit.[19] While calculating the MAPH score, according to the predictive cut-off values for each component; each parameter above the cut-off value was given 1 point, and the parameters below the cut-off value were given 0 points.[19]

Coronary angiography and procedural approach: PCI was performed in all patients in the same session following angiographic imaging via the radial or femoral artery in accordance with current guidelines. In addition to the antiaggregant loading dose (acetylsalicylic acid 300 mg + clopidogrel 600 mg, prasugrel 60 mg, ticagrelor 180 mg) that they received in the emergency room, standard heparin (70-100 IU/kg) was administered at a dose appropriate for weight during PCI. In cases lasting more than 1 hour, an additional dose of heparin was administered to maintain the ACT (activated clotting time) above 200. Despite standard ACS treatment, patients with high thrombus burden underwent manual thromboaspiration and after an intracoronary bolus dose of glycoprotein IIb/IIIa inhibitor agent (tirofiban) was adjusted according to weight, the percutaneous transluminal coronary angioplasty (PTCA) dose was continued as a 24-hour maintenance infusion.

Due to health insurance reimbursement conditions, BMS (Ephesos™ II, Alvimedica) was used in cases with a reference vessel diameter > 4 mm, and for those ≤ 4 mm, DES was used (Everolimus-eluting stents [Xience Pro, Abbott Vascular Devices and Promus Premier, Boston Scientific]). Following stent placement, at the physician's discretion, postdilatation was performed at 12-18 atmospheres of pressure with an NC balloon (NC QuantumApex, Boston Scientific) of a size appropriate to the reference vessel for stent optimization. Due to health insurance reimbursement conditions, clear stent imaging was used instead of intravascular ultrasound (IVUS) to assess stent expansion. Clear stent imaging is an enhancement of the radiological edge of the stent by digital management of regular X-ray images. The procedure was carried out on a Siemens Artis zee floor-mounted angiography system integrated with CLEARstent software.

Cineangiogram images during PCI were viewed retrospectively as 30 frames/second, and the coronary artery originating from the culprit lesion was noted. The degree of TIMI flow grade[20,21] after stent implantation in the coronary artery responsible for STEMI was evaluated by 2 experienced cardiologists and recorded.

TIMI coronary flow classification system: TIMI 0: Absence of contrast material passage distal to the stenosis; TIMI 1: At least 1 contrast agent passing distal to the stenosis and staining of the entire coronary artery; TIMI 2: Compared to the proximal segment of the lesion, the contrast medium passes through the stenotic area and fills the most distal segment of the coronary artery with weaker and slower clearance of the contrast medium; TIMI 3: Antegrade flow in the distal stenosis is the same as in the proximal stenosis up to the distal part of the coronary artery, and the contrast medium is cleared as quickly as the proximal segment from the distal segment.

Those with a TIMI flow grade of 0, 1, or 2 were considered no-reflow (Group 1), while those with a TIMI flow grade of 3 were considered normal flow (Group 2).

Statistical analysis: Statistical analysis was performed using SPSS Windows version 24.0. First, the normality of the distribution of continuous variables was checked using the Kolmogoro Smirnov test. Next, the mean ± standard deviation (SD) was performed for continuous variables, and the number and frequency for categorical variables. Student's t-test was used to compare continuous variables. Comparison analysis of categorical variables was performed using Pearson's chi-square test and Fisher's exact test. For each parameter of the MAPH score, a cut-off value was determined by ROC curve analysis using the Youden index. Logistic regression analysis was then performed to evaluate whether the MAPH score was an independent predictor of no-reflow in STEMI patients, and finally, ROC curve analysis was performed again for sensitivity and specificity, and the statistics were completed. A P value < 0.05 was considered significant.

Written informed consent was obtained from all patients individually. Furthermore, approval for our study was obtained from the ethics committee of Izmir Bakırcay

Table I. Baseline Clinical Features and Demographic Data

Variables	Group 1 (n = 59)	Group 2 (n = 201)	P value
Age, years (mean ± SD)	62.27 ± 12.32	58.57 ± 12.16	0.04
Male gender, n (%)	41 (69)	153 (76)	0.31
Hypertension, n (%)	24 (39)	61 (30)	0.15
Diabetes mellitus, n (%)	19 (32)	60 (29)	0.74
Smoking, n (%)	26 (44)	108 (53)	0.23
Heart failure, n (%)	3 (5)	7 (3)	0.69
CAD history, n (%)	10 (16)	33 (16)	1
Hyperlipidemia, n (%)	18 (30)	39 (19)	0.07
CRF, n (%)	9 (15)	21 (10)	0.35
CVD history, n (%)	0 (0)	6 (2)	0.34
Angiographic procedural data			
MI type, n (%)			
Anterior	26 (44)	77 (38)	0.23
Inferior	12 (20)	91 (45)	
Others	21 (35)	33 (16)	
Culprit vessel, n (%)			
LAD	33 (55)	72 (35)	0.05
Cx	13 (22)	39 (19)	
RCA	13 (22)	90 (44)	
Balloon predilatation, n (%)	45 (76)	144 (72)	0.51
Stent, mm (mean ± SD)			
Diameter	2.96 ± 0.32	3.03 ± 0.34	0.15
Length	22.56 ± 6.58	23.60 ± 9.36	0.43
Postdilatation, mm (mean ± SD)			
Balloon diameter	2.98 ± 0.31	3.04 ± 0.36	0.27
Balloon length	13.56 ± 3.61	14.06 ± 3.56	0.34
Thromboaspiration during PCI, n (%)	9 (47)	19 (9)	0.23
Gp IIb/IIIa inhibitors using, n (%)	36 (61)	65 (32)	< 0.001

SD indicates standard deviation; CAD, coronary artery disease; CRF, chronic renal failure; CVD, cerebrovascular disease; MI, myocardial infarction; LAD, left anterior descending artery; Cx, circumflex artery; RCA, right coronary artery; PCI, percutaneous coronary intervention; Gp, glycoprotein; Group 1, no-reflow; and Group 2, normal flow.

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Results

The patients included in the study were divided into 2 groups; group 1 (TIMI flow 0-2) (no-reflow) (59 patients) and group 2 (TIMI flow 3) (normal coronary flow) (201 patients). The mean age of group 1 (62.27 (± 12.32) was higher than group 2 (58.57 (± 12.16), P = 0.04). The male sex ratio was the same between groups 1 and 2 (respectively, 69% versus 76%, P = 0.31). Active smokers constituted 51.5% of all patients. No statistically significant difference was found between the 2 groups in demographic data, except for age (Table I).

The rates of hypertension (39% versus 30%, P = 0.15), diabetes mellitus (32% versus 29%, P = 0.74), history of coronary artery disease (16% versus 16%, P = 1.00), and chronic renal failure (15% versus 10%, P = 0.35) were found to be same in group 2 and group 1. There was no significant difference between the no-reflow group and normal flow group in terms of myocardial infarction type (P = 0.23) and rate of culprit vessel types (P = 0.05). The rate of use of glycoprotein IIb/IIIa inhibitors was higher in the low TIMI flow group than the good TIMI flow group (61% versus 32%, P < 0.001) (Table II). There was no significant difference between the groups in terms of oral antiplatelet and anticoagulant drugs used by the patients before STEMI.

Among hematological and biochemical parameters, hematocrit (43.71 (± 5.25) versus 42.02 (± 5.25), P = 0.003), mean platelet volume (8.35 (± 1.08) versus 7.98 (± 0.84), P < 0.001), and total protein (6.71 (± 1.22) versus 6.34 (± 1.25), P = 0.004) were higher in group 1 than group 2. A total protein value > 6.48 was a predictor of poor TIMI flow presence in patients with STEMI, with 61% sensitivity and 58% specificity (ROC area under curve: 0.616, 95% CI: 0.535-0.698, P = 0.007). MPV > 8.05 was a predictor of poor TIMI flow presence in patients with STEMI, with 56% sensitivity and 55% specificity (ROC area under curve: 0.585, 95% CI: 0.500-0.670, P = 0.047). Age > 59.5 was a predictor of poor TIMI flow presence in patients with STEMI, with 58% sensitivity and 55% specificity (ROC area under curve: 0.595, 95% CI: 0.511-0.680, P = 0.026). A hematocrit value > 43.05 was a predictor of poor TIMI flow presence in patients with STEMI, with 51% sensitivity and 52% specificity (ROC area under curve: 0.586, 95% CI: 0.502-0.670, P = 0.044) (Figure 1).

After performing the above-mentioned ROC analysis of the MAPH score components, each parameter above the cut-off value was given 1 point, and the parameters below the cut-off value were given 0 points. Thus, the MAPH score was calculated for the groups. Next, univari-

Table II. Hematological and Biochemical Parameters

Laboratory	Group 1 (n = 59)	Group 2 (n = 201)	P value
WBC, x10^3/L	11.94 ± 2.94	12.61 ± 3.89	0.22
Neutrophils, x10^3/L	8.36 ± 2.63	8.86 ± 4.07	0.37
Lymphocytes, x10^3/L	2.31 ± 1.71	2.63 ± 1.77	0.22
Hemoglobin, mg/dL	13.35 ± 0.91	12.92 ± 1.74	0.74
Htc	43.71 ± 5.25	42.02 ± 5.25	0.03
Platelets, x10^3/L	255.94 ± 81.65	255.45 ± 70.58	0.96
MPV, fL	8.35 ± 1.08	7.98 ± 0.84	< 0.01
Glucose, mg/dL	187.1 ± 102.3	175.8 ± 97.79	0.44
Urea, mg/dL	40.79 ± 21.9	36.48 ± 17.03	0.11
Creatinine, mg/dL	1.1 ± 0.56	1.03 ± 0.72	0.48
Total protein, mg/dL	6.71 ± 1.22	6.34 ± 1.25	0.04
Albumin, mg/dL	3.53 ± 0.93	3.78 ± 1.08	0.1
Total cholesterol, mg/dL	186 ± 44.2	188 ± 44.9	0.78
Triglycerides, mg/dL	164 ± 136	169 ± 137	0.81
HDL, mg/dL	43 ± 13	40 ± 12	0.12
LDL, mg/dL	110 ± 37	120 ± 62	0.27
MAPH score	2.36 ± 0.88	1.68 ± 0.92	< 0.01

WBC indicates white blood cells; Htc, hematocrit; MPV, mean platelet volume; HDL, high density lipoprotein; LDL, low density lipoprotein; MAPH, mean plalelet volume-age-protein-hematocrit; Group 1, no-reflow; and Group 2, normal flow.

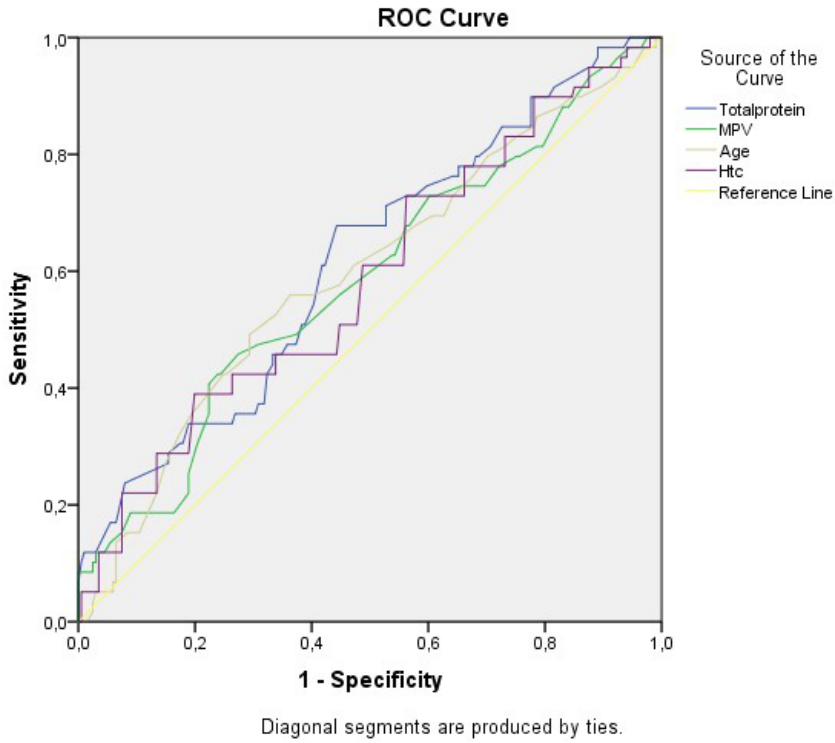


Figure 1. The sensitivity and specificity of MAPH score components associated with TIMI flow in the ROC curve.

able and multivariable regression analyses were performed to identify parameters that were significantly related to low TIMI flow. ROC analysis was used for the MAPH score and glycoprotein IIb/IIIa.

In the univariable regression analysis of the factors affecting the TIMI flow in a coronary artery; MPV (OR: 0.653; 95%CI: 0.476-0.896, P < 0.001), age (OR:0.976; 95%CI: 0.953-0.999, P = 0.004), total protein (OR: 0.733; 95%CI: 0.573-0.937, P = 0.01), hematocrit (OR: 0.938; 95%CI: 0.884-0.995, P = 0.03), MAPH score (OR:0.442; 95%CI: 0.311-0.627, P < 0.001), and glycoprotein IIb/IIIa inhibitors (OR: 0.305; 95%CI: 0.167-0.557, P < 0.001) were predictors. In the multivariable regression analysis; MAPH score (OR: 0.567; 95%CI: 0.330-0.973, P = 0.04) and glycoprotein IIb/IIIa inhibitors (OR: 0.249; 95%CI: 0.129-0.483, P < 0.001) were found to be independent

Table III. Univariate and Multivariate Logistic Regression Analyzes in Predicting No-Reflow in Patients with STEMI

	Univariate Logistic Regression			Multivariate Logistic Regression		
Variables	OR	95% CI	*P* value	OR	95% CI	*P* value
MPV	0.653	0.476-0.896	0.008	0.839	0.571-1.231	0.36
Age	0.976	0.953-0.999	0.04	0.977	0.949-1.007	0.13
Total protein	0.733	0.573-0.937	0.01	0.787	0.571-1.085	0.14
Hematocrit	0.938	0.884-0.995	0.03	0.980	0.911-1.055	0.58
MAPH score	0.442	0.311-0.627	< 0.01	0.567	0.330-0.973	0.04
Gp2B/3A inhibitor	0.305	0.167-0.557	< 0.01	0.249	0.129-0.483	< 0.01

MPV indicates mean platelet volume; MAPH, mean platelet volume-age-protein-hematocrit; and Gp, glycoprotein.

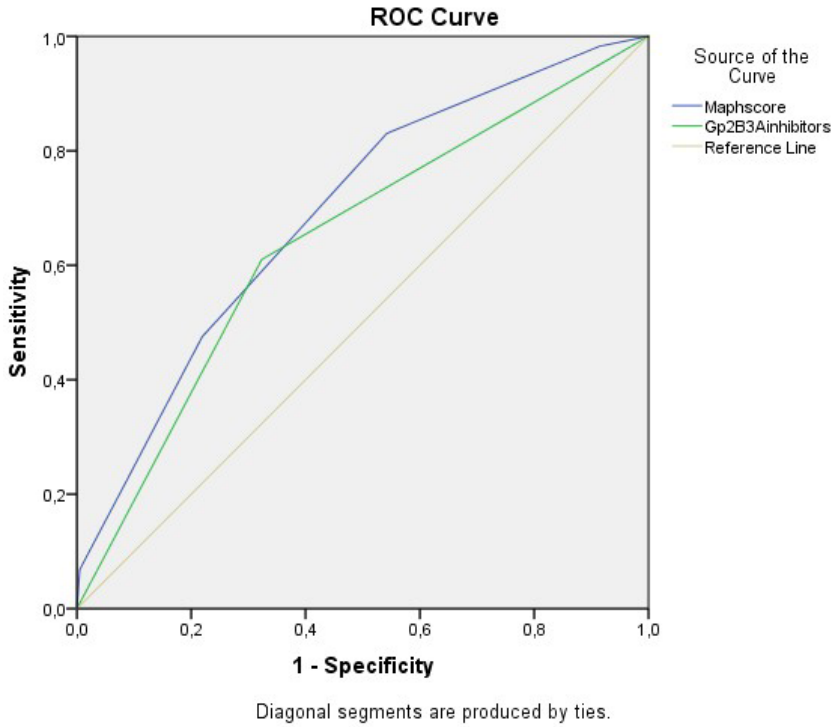


Figure 2. The sensitivity and specificity of MAPH score and glycoprotein 2B/3A inhibitor for TIMI flow in the ROC curve.

predictors (Table III).

The MAPH score was statistically significantly higher in group 1 (2.36 ± 0.88) than in group 2 (1.68 ± 0.92) ($P < 0.001$). An MAPH score value > 2.5 was a predictor of the presence of low TIMI coronary flow in patients with STEMI, with 78% specificity and 45% sensitivity (ROC area under curve: 0.691, 95% CI: 0.617-0.766, $P < 0.001$) (Figure 2).

Discussion

The main finding in our study was that there was a negative correlation between TIMI flow grade and MAPH score in patients who underwent percutaneous coronary intervention for STEMI.

STEMI is still one of the leading causes of death in the world. The atherothrombosis process responsible for the pathogenesis of STEMI progresses with platelet aggregation that occurs after plaque rupture. With the increase in platelet volume (more adhesion receptors), activation increases and more prothrombotic molecules (such as thromboxane A2 and thromboglobulin) are released, thereby deteriorating hemostasis.[22,23]

The MAPH score consists of 4 parameters; MPV, age, total protein, and hematocrit. The MAPH score has been developed to predict thrombus burden,[19] and coronary flow reserve is affected due to increased intravascular coagulation. There are studies showing that a low TIMI flow grade after PCI is associated with in-hospital mortality and both short- and long-term poor prognosis.[24]

Several studies have shown that an elevated MPV is associated with increased vascular ischemic events, as well as increased mortality and morbidity and recurrent MI.[25] In a study by Reddy, *et al.*, consisting of 364 pa-

tients, the patients were divided into 2 groups and MPV was found to be significantly higher in the STEMI group compared to the control group.[26] In addition, in the study of Zenon, *et al.* on acute MI patients, the no-reflow phenomenon was significantly higher in the group with high MPV.[27] Elevated MPV, a marker of platelet function, is associated with an increased risk of CV diseases such as myocardial infarction, stroke, and transient ischemic attack. Han, *et al.* showed that stroke and coronary artery disease incidences were higher in the group with MPV > 8 fL.[28] Vizioli, *et al.* predicted that the MPV value should not be considered insignificant because it affects the prognosis in MI and stroke.[29] In the present study, the MPV value was found to be significantly higher in the no-reflow group, with a cut-off value of 8.05 fL by ROC curve analysis [AUC: 0.585 (0.500-0.670), $P = 0.04$)].

Total serum protein consists of albumin, globulin and fibrinogen. Considering the positive contribution of albumin increase in antioxidant activity, formation of negative acute phase reactants and binding to drugs in plasma (such as oral antiplatelet drugs), the adverse effect of an increase in total protein suggests that non-albumin proteins are primarily associated with vascular disease.[30,31] In particular, considering the relationship between fibrinogen and coagulation, the high rate of vascular events can be explained.[32,33] In the study of total protein mortality estimation in STEMI patients who underwent primary PCI by Yılmaz, *et al.*, total serum protein level was found to be high in the group with high no-reflow.[34]

In a study by Elakabawi, *et al.*, the effects on predictors of suboptimal coronary blood flow and short-term outcomes after primary PCI in 1104 anterior STEMI patients were investigated; age was significantly higher in the suboptimal flow group than in the optimal group.[35] In our study, the mean age was higher in the group with no-reflow.

Studies have been conducted showing an increased risk of thrombosis with elevated hematocrit. At the same time, a relationship has been established between coronary artery disease and mortality with an increase in hematocrit levels.[36,37] Gabriel, *et al.* showed hematocrit levels as a predictor of mortality in 1402 nonanemic patients with STEMI.[38] Based on the view that erythrocytosis creates a prothrombotic state, it is thought that hyperviscosity creates a more thrombogenic vascular bed and contributes negatively to the no-reflow phenomenon.

Gp IIb/IIIa receptor antagonists act by inhibiting the binding of fibrinogen to activated platelets and thrombus formation in the coagulation cascade. All GPIs (glycoprotein inhibitors) improve blood flow in the coronary arteries by reducing the clot burden in the microvascular bed, reducing no reflow and infarct size, and thus providing benefits.[39,40] Although bleeding complications are avoided in patients undergoing primary PCI, GPIs (most commonly Abciximab) are used together with heparin.[41,42] In the ESC 2018 myocardial revascularization guideline, it is recommended as bail-out class 2a in patients with ACS with a high thrombus burden and slow coronary blood flow, although it does not benefit mortality.[43] In the present study, Gp 2b/3a inhibitors were used to a statistically significant higher degree in the no-reflow group in accordance with the literature.

Limitations: There are some limitations to our study. It was a retrospective study and the number of patients is relatively small. TIMI flow grades were evaluated only angiographically. Intracoronary imaging modalities such as IVUS (intravascular ultrasound), OCT (optical coherence tomography), or FFR were not used for the optimization of procedure. Since the components that make up the MAPH score in STEMI patients do not have a universal cut-off value, the calculation of these cut-off values was made over the patient population included in the study.

Conclusion

The MAPH risk score is simple, inexpensive, and quick to calculate. The MAPH risk score, which consists of mean platelet volume, age, total protein, and hematocrit, is associated with low TIMI flow in STEMI patients. A high MAPH score may be an indicator of coronary no-reflow.

Disclosure

Conflicts of interest: None.

References

1. Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, *et al*. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012; 33: 2569-619.
2. Vecchio S, Varani E, Chechi T, *et al*. Coronary thrombus in patients undergoing primary PCI for STEMI: prognostic significance and management. World J Cardiol 2014; 6: 381-92.
3. Previtali E, Bucciarelli P, Passamonti SM, Martinelli I. Risk factors for venous and arterial thrombosis. Blood Transfus 2011; 9: 120-38.
4. Koupenova M, Kehrel BE, Corkrey HA, Freedman JE. Thrombosis and platelets: an update. Eur Heart J 2017; 38: 785-91.
5. Hathcock JJ. Flow effects on coagulation and thrombosis. Arterioscler Thromb Vasc Biol 2006; 26: 1729-37.
6. Casa LDC, David H, Deaton DH, Ku DN. Role of high shear rate in thrombosis. J Vasc Surg 2015; 61: 1068-80.
7. Weisel JW, Litvinov RI. Red blood cells: the forgotten player in hemostasis and thrombosis. J Thromb Haemostasis 2019; 17: 271-82.
8. Ibanez B, James S, Agewall S, *et al*. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2018; 39: 119-77.
9. TIMI Study Group. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. N Engl J Med 1985; 312: 932-6.
10. Niccoli G, Kharbanda RK, Crea F, Banning AP. No-reflow: Again prevention is better than treatment. Eur Heart J 2010; 31: 2449-55.
11. Bath P, Algert C, Chapman N, Neal B. Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease. Stroke 2004; 35: 622-6.
12. Thompson CB, Jakubowski JA, Quinn PG, Deykin D, Valeri CR. Platelet size and age determine platelet function independently. Blood 1984; 63: 1372-5.

13. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Bentham science publishers Ltd. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 2011; 17: 47-58.
14. Korniluk A, Koper-Lenkiewicz OM, Joanna Kamiń ska J, Halina Kemona H, Dymicka-Piekarsk VD. Mean platelet volume (MPV): new perspectives for an Old marker in the course and prognosis of inflammatory conditions. Mediators Inflamm 2019; 2019: 9213074.
15. Cetin EHO, Ozbay MB, Cetin MS, *et al*. A new risk model for the evaluation of the thromboembolic milieu in patients with atrial fibrillation: the PALSE score. Kardiol Pol 2020; 78: 732-40.
16. Sianos G, Papafaklis MI, Daemen J, *et al*. Angiographic stent thrombosis after routine use of drug-eluting stents in ST-segment elevation myocardial infarction: the importance of thrombus burden. J Am Coll Cardiol 2007; 50: 573-83.
17. Napodano M, Ramondo A, Tarantini G, *et al*. Predictors and time-related impact of distal embolization during primary angioplasty. Eur Heart J 2009; 30: 305-13.
18. Fokkema ML, Vlaar PJ, Svilaas T, *et al*. Incidence and clinical consequences of distal embolization on the coronary angiogram after percutaneous coronary intervention for STelevation myocardial infarction. Eur Heart J 2009; 30: 908-15.
19. Abacioglu OO, Yildirim A, Karadeniz M, *et al*. A New Score for Determining Thrombus Burden in STEMI Patients: The MAPH Score. Clin Appl Thromb Hemost 2022; 28: 1-7.
20. Gibson CM, Cannon CP, Daley WL, *et al*. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation 1996; 93: 879-88.
21. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. TIMI Study Group. N Engl J Med 1985; 312: 932-6.
22. Chu SG, Becker RC, Berger PB, *et al*. Mean platelet volume as predictor of cardiovascular risk: a systemic review and meta-analysis. J Thromb Haemostat 2010; 8: 148-56.
23. Ihara A, Kawamoto T, Matsumoto K, *et al*. Relationship between platelet indexes and coronary angiographic findings in patients with ischemic heart disease. Pathophysiology of Haemostasis and Thrombosis 2007; 35: 376-9.
24. Ndrepepa G, Mehilli J, Tiroch K, *et al*. Myocardial perfusion grade, myocardial salvage indices and long-term mortality in patients with acute myocardial infarction and full restoration of epicardial blood flow after primary percutaneous coronary intervention. Rev Esp Cardiol 2010; 63: 770-8.
25. Chu SG, Becker RC, Berger PB, *et al*. Mean platelet volume as predictor of cardiovascular risk: a systemic review and meta-analysis. J Thromb Haemostat 2010; 8: 148-56.
26. Reddy SK, Shetty R, Marupuru S, Yedavalli N, Shetty K. Significance of platelet volume indices in STEMI patients: a case-control study. J Clin Diagn Res 2017; 11: LC05-7.
27. Huczek Z, Kochman J, Filipiak KJ, *et al*. Mean platelet volume on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. J Am Coll Cardiol 2005; 46: 284-90.
28. Han JY, Choi H, Choi SW, *et al*. Stroke or coronary artery disease prediction from mean platelet volume in patients with type 2 diabetes mellitus. Platelets 2013; 24: 401-6.
29. Vizioli L, Muscari S, Muscari A. The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. Int J Clin Pract 2009; 63: 1509-15.
30. Berg K, Jynge P, Bjerve K, Skarra S, Bass S, Wiseth R. Oxidative stress and inflammatory response during and following coronary interventions for acute myocardial infarction. Free Radic Res 2005; 39: 629-36.
31. Taverna M, Marie AL, Mira JP, Guidet B. Specific antioxidant properties of human serum albumin. Ann Intensive Care 2013; 3: 1-7.
32. Kwaan HC. Role of plasma proteins in whole blood viscosity: a brief clinical review. Clin Hemorheol Microcirc 2010; 44: 167-76.
33. Hutchinson RM, Eastham RD. A comparison of the erythrocyte sedimentation rate and plasma viscosity in detecting changes in plasma proteins. J Clin Path 1977; 30: 345-9.
34. Yılmaz AS, Özyıldız AG, Kahraman F, Çetin M. Total Serum Protein Predicted Mortality in Patients with St-elevation Myocardial Infarction Who Underwent Primary Percutaneous Coronary Intervention: Results of 8-Year Follow-up. E J Cardiovasc Med 2021; 9: 122-9.
35. Elakabawi K, Huang X, Shah SA, *et al*. "Predictors of suboptimal coronary blood flow after primary angioplasty and its implications on short-term outcomes in patients with acute anterior STEMI". BMC Cardiovascular Disorders 2020; 20: 1-12.
36. Schreijer AJM, Reitsma PH, Cannegieter SC. High hematocrit as a risk factor for venous thrombosis. Cause or innocent bystander? Haematologica 2010; 95: 182-4.
37. Brækkan SK, Mathiesen EB, Njølstad I, Wilsgaard T, Hansen JB. Hematocrit and risk of venous thromboembolism in a general population. The Tromso study. Haematologica 2010; 95: 270-5.
38. Greenberg G, Assali A, Assa HV, *et al*. "Hematocrit level as a marker of outcome in ST-segment elevation myocardial infarction". Am J Cardiol 2010; 105: 435-40.
39. de Lemos JA, Antman EM, Gibson CM, *et al*. Abciximab improves both epicardial flow and myocardial reperfusion in ST-elevation myocardial infarction. Observations from the TIMI 14 trial. Circulation 2000; 101: 239-43.
40. Neumann FJ, Blasini R, Schmitt C, *et al*. Effect of glycoprotein IIb/IIIa receptor blockade on recovery of coronary flow and left ventricular function after the placement of coronary-artery stents in acute myocardial infarction. Circulation 1998; 98: 2695-701.
41. Montalescot G, Antoniucci D, Kastrati A, *et al*. Abciximab in primary coronary stenting of ST-elevation myocardial infarction: a European meta-analysis on individual patients' data with long-term follow-up. Eur Heart J 2007; 28: 443-9.
42. De Luca G, Suryapranata H, Stone GW, *et al*. Abciximab as adjunctive therapy to reperfusion in acute ST segment elevation myocardial infarction: a meta-analysis of randomized trials. JAMA 2005; 293: 1759-65.
43. Uva MS, Neumann FJ, Ahlsson A, *et al*. 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur J Cardiothorac Surg 2019; 55: 4-90.