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ORIGINAL ARTICLE

Platelet-to-White Blood Cell Ratio (PWR): A Novel Prognostic Biomarker for Spontaneous Reperfusion after Primary Percutaneous Coronary Intervention

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Abstract

Background: **Spontaneous reperfusion (SR) occurring before primary percutaneous coronary intervention (PPCI) can offer additional clinical benefits to patients with ST-segment elevation myocardial infarction (STEMI). The Platelet-to-White Blood Cell Ratio (PWR) has been recognized as a prognostic indicator in various diseases. We aimed to explore the relationship between PWR and SR in patients with STEMI undergoing PPCI.**

Methods: **We conducted a retrospective analysis involving 995 patients diagnosed with STEMI who underwent PPCI in a single-center setting. Demographic, clinical, laboratory, and angiographic data were extracted from the hospital database, and PWR was calculated by dividing serum platelet levels by white blood cell levels.**

Results: **Angiographic SR was observed in 203 patients (20.4%). The SR group displayed elevated PWR values (24.4 ± 8.9 vs. 21.6 ± 7.6, $p < 0.001$) and a lower incidence of the no-reflow phenomenon (NRF) (13.3% vs. 22.9%, $p = 0.003$), along with a reduced SYNTAX (SX) score (12.7 ± 6.4 vs. 17.8 ± 7.9, $p < 0.001$). Furthermore, the group with a high PWR was associated with a higher rate of SR, a lower NRF rate, decreased in-hospital mortality, and reduced SX scores. Multivariable logistic regression analyses revealed that female gender, hemoglobin levels, the presence of SR, Culprit lesion, and the SX score were identified as risk factors for high PWR. High PWR, SX score, and Initial CK-MB levels were the factors associated with SR.**

Conclusions: **Patients with high PWR at presentation may experience higher rates of SR, fewer complications, and a more favorable prognosis in the context of STEMI.**

Keywords: In-hospital mortality, No-reflow phenomenon, Platelet-to-white blood cell ratio, Spontaneous reperfusion, ST-segment elevation myocardial infarction

1. Introduction

Rapid and efficient reperfusion of the infarct-related arteries is the most effective strategy for improving mortality and morbidity outcomes in ST-elevation myocardial infarction (STEMI) [1]. Spontaneous reperfusion (SR) has been linked to improved clinical outcomes and a more favorable prognosis in patients diagnosed with STEMI [2,3]. It also appears to be safe to delay immediate percutaneous coronary intervention in cases of SR [4]. The induction and prediction of SR may offer alternative approaches for risk assessment, and therefore, the relevant factors may yield crucial prognostic insights to customize additional treatments during the procedure. Nevertheless, limited knowledge exists concerning the clinical predictors of SR.

Complete blood count (CBC) is a commonly employed, straightforward laboratory parameter.

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The literature contains a broad spectrum of studies on CBC for predicting SR among STEMI patients [5–8]. However, platelet-to-white blood cell ratio (PWR) is a newly recognized prognostic marker in postoperative renal malignancy surgery [9].

The primary objective of our study was to investigate the correlation between PWR and SR among STEMI patients treated with PPCI. Additionally, we aimed to assess the connection between PWR and in-hospital mortality, lesion complexity, and the no-reflow phenomenon (NRF), all of which represent potential outcomes associated with SR.

Abbreviations

CBC	Complete blood count
CK-MB	creatine kinase-myocardial band
ECG	electrocardiographic
Hgb	hemoglobin
hs-cTnI	high-sensitive cardiac troponin I
IRA	infarct-related artery
IQR	interquartile range
NRF	no-reflow phenomenon
OC	optical coherence tomography
OR	odds ratios
PPCI	primary percutaneous coronary intervention
PWR	Platelet-to-White Blood Cell Ratio
ROC	the receiver operating characteristic
SR	Spontaneous reperfusion
STEMI	ST-segment elevation myocardial infarction
SX	SYNTAX
TIMI	Thrombolysis in Myocardial Infarction
WBC	white blood cells

2. Methods

2.1. Study population

We retrospectively studied a cohort of 995 consecutive patients diagnosed with STEMI (732 males and 263 females) who underwent PPCI from January 2021 to January 2022 at a single center. Demographic, clinical, electrocardiographic (ECG), and angiographic data were extracted from the hospital database applications and the national chronic disease and drug use information system. The diagnosis of STEMI was established upon the presence of characteristic chest pain, confirmation of ST-segment elevation in at least two consecutive leads on a 12-lead surface ECG upon presentation, and further verification of an occluded epicardial coronary artery through coronary angiography. Eighty-six patients were excluded due to at least one of the following conditions; missing data, Late admission to the hospital by 12 h or more, death before PPCI, malignancy, and coronary artery bypass graft (Fig. 1).

Data regarding in-hospital mortality was ascertained by reviewing patient files and consulting the national death notification system. Following the PPCI procedure, discharge decisions were made by attending physicians based on clinical, ECG, and biochemical criteria in by the prevailing medical knowledge. We didn't use artificial intelligence-assisted technologies in the study.

2.2. Data collection

The patient cohort was initially stratified into two groups based on the Thrombolysis in Myocardial Infarction (TIMI) flow grade of the infarct-related artery (IRA) observed during coronary angiography: the SR group (TIMI flow grade 3) and the Non-SR group (TIMI flow grade 0-1-2). Subsequently, patients were further categorized into two groups by their PWR values, with a cut-off set at 22.1 as determined in the receiver operating characteristic (ROC) curve analysis using the Youden Index (which is also equivalent to the mean value within the population).

Venous peripheral blood samples were collected from all patients upon admission. These samples were acquired either in the emergency room or the coronary care unit before PCI and were processed using an automated biochemical analyzer system (Roche Diagnostic Modular Systems, Tokyo, Japan) within 10 min of collection. Subsequently, the results of all laboratory parameters were accessed through the hospital information system. The Platelet-to-White Blood Cell Ratio (PWR) was calculated by dividing the serum platelet levels by the levels of white blood cells (WBC).

2.3. Percutaneous intervention and medications

Coronary angiography was promptly conducted by two highly experienced invasive cardiologists using the Judkins method with 6-FR or 7-FR guiding catheters, with a thorough evaluation of the lesion characteristics. The treatment protocols for all patients were executed in by the 2017 STEMI guidelines provided by the European Society of Cardiology [1]. PPCI was performed on all culprit lesions, involving guidewire passage, balloon pre-dilatation, stent implantation, and subsequent balloon post-dilatation if deemed necessary. The successful post-PPCI revascularization was defined as achieving a TIMI score greater than 2 in the IRA. SR was characterized by the presence of TIMI 3 flow in the IRA before PPCI, whereas Non-SR was defined as the presence of TIMI grade 0, 1, and 2 flows [2].

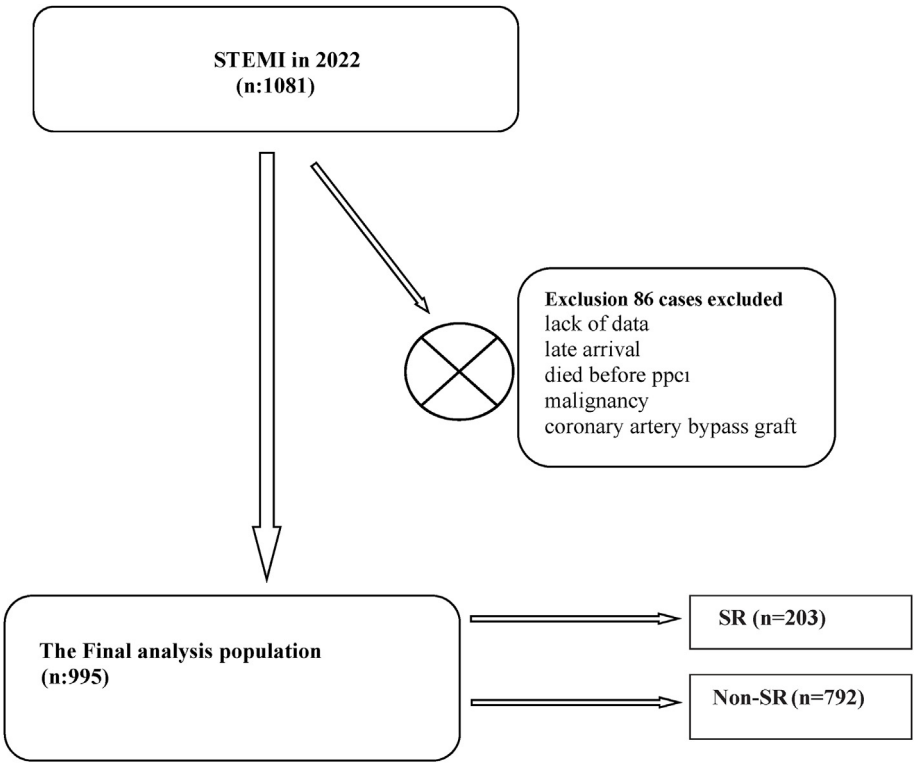

Fig. 1. Flowchart of inclusion in the study.

NRF was identified using angiographic criteria, indicating a final TIMI flow grade ≤2 in the IRA following the PPCI procedure. Additionally, the SYNTAX (SX) score was independently and blindly computed by two invasive cardiologists using the official online score calculation site (www.syntaxscore.org).

All patients received aspirin loading, P2Y12 inhibitors (clopidogrel, ticagrelor, or prasugrel) loading, and a single subcutaneous dose of low molecular weight heparin either in the ambulance or upon arrival at the emergency department. Additionally, intracoronary administration of unfractionated heparin at a dose of 100 U/kg was administered during the procedure. The intracoronary bolus of Glycoprotein IIb/IIIa (GP IIb/IIIa) inhibitors, followed by continuous infusion, was administered based on the operators' clinical judgment. Complying with the STEMI guidelines, maintenance therapies included standard 100 mg aspirin, one of the P2Y12 inhibitors, beta-blockers, angiotensin-converting enzyme inhibitors, and statins, which were arranged during the coronary intensive care follow-ups.

2.4. Statistical analysis

The data analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 software (SPSS Inc., Chicago, IL, USA). Kolmogorov−Smirnov test and visual inspection methods have used to determine normal distributions. Variables displaying homogenous distribution were reported as mean ± standard deviation and compared using independent samples t-test. Variables non-normally distributed were expressed as the median and interquartile range (IQR) and analyzed with the Mann−Whitney U test. Categorical variables were presented as counts and percentages, and comparisons were made using the chi-square test or Fisher's exact test. Multivariate binary logistic regression models were employed to identify independent determinants of SR and high PWR within the entire study population. Variables that were significant in univariate analysis were assessed in multivariate analysis. Within the independent variables in the regression analyses, any missing values were addressed through multiple imputations, employing the chain-equation method with 10 data sets and 10 iterations. Internal correlation analysis (multicollinearity) was conducted to ensure that variance inflation factor <3, condition index <15, and variance proportions <0.6 were met for all parameters. The results of both univariable and multivariable regression analyses were reported as odds ratios (OR) with corresponding 95% confidence intervals (CI). The significance of individual

variables in the multivariable models was evaluated using the permutation-based variable importance method, which ranked variables according to the Root Mean Squared Error metric. ROC analysis established the PWR cut-off values for predicting SR based on the Youden Index. Statistical significance was defined as $p < 0.05$.

3. Results

Angiographic SR was observed in 203 out of the 995 STEMI patients, constituting 20.40% of the total cohort. Age, gender, smoking status, hypertension, and diabetes characteristics were not distributed differently. In the SR group, initial high-sensitive cardiac troponin I (hs-cTnI), creatine kinase-myocardial band (CK-MB), and white blood cell (WBC) levels were significantly lower, while triglyceride levels and PWR were significantly higher. No significant difference was seen in the analysis of other tests. Additionally, reduced usage of glycoprotein IIb/IIIa inhibitors and shorter implanted stent lengths were observed in the SR group. No significant disparities were found between the two groups in terms of myocardial infarction localization, the culprit lesion, implanted stent type, implanted stent diameter, acute stent thrombosis, or the initiation of antithrombotic medications. A comprehensive comparison of clinical and laboratory parameters between the groups is presented in Table 1.

When the participants were stratified into two groups based on a PWR value of 22.1, which closely approximated the mean value of the entire population, as determined by the Youden Index, further analysis revealed that in the group with a high PWR value, higher levels of hemoglobin (Hgb) and triglycerides were observed. Conversely, lower levels of uric acid, initial hs-cTnI, and initial CK-MB were noted. Additionally, the high PWR group displayed a greater prevalence of female patients, cases of inferior STEMI location, and a lower frequency of treatment with Glycoprotein IIb/IIIa inhibitors (Table 2).

The SR group exhibited elevated PWR values (24.4 ± 8.8 *vs.* 21.6 ± 7.5, $p < 0.001$) and a lower rate of NRF (13.3% *vs.* 22.9%, $p = 0.003$), along with a reduced SX score (12.7 ± 6.4 *vs.* 17.8 ± 7.9, $p < 0.001$) when compared to the Non-SR group. On the other hand, although in-hospital mortality appeared to be lower in individuals with SR, this difference did not achieve statistical significance ($p = 0.117$). Furthermore, the High PWR group was correlated with a high rate of SR ($p < 0.001$), a low rate of NRF ($p = 0.031$), lower in-hospital mortality ($p = 0.003$), and reduced SX scores ($p < 0.001$) (Table 3).

We performed regression analyses to reveal factors associated with a high PWR. The results showed that female gender (OR = 0.615, 95% CI: 0.446–0.848; $p = 0.003$), hemoglobin levels (OR = 0.854, 95% CI: 0.790–0.924; $p < 0.001$), the presence of SR (OR = 1.908, 95% CI: 1.365–2.665; $p < 0.001$), The culprit lesion (Left anterior descending versus Circumflex: OR = 1.475, 95% CI: 1.1092–1.992; $p = 0.011$, Left anterior descending versus Right: OR = 1.507, 95% CI: 1.1039–2.186; $p = 0.031$), and SX score (OR = 0.981, 95% CI: 0.963–0.999; $p = 0.035$) were identified as risk factors for high PWR (Table 4). Similarly, in the multivariable logistic regression analysis aimed at identifying the presence of SR, high PWR (OR = 1.801, 95% CI: 1.294–2.506; $p < 0.001$), Initial CK-MB levels (OR = 0.992, 95% CI: 0.989–0.996; $p < 0.001$) and SX score (OR = 0.918, 95% CI: 0.815–0.941; $p < 0.001$) were established as factors associated with SR (Table 5). Permutation-based variable importance analyses revealed that, following hemoglobin, SR emerged as the most influential parameter in determining high PWR. On the other hand, for the presence of SR, PWR stood out as the most influential determinant after the SX score (Fig. 2).

ROC analysis revealed that PWR exhibited a significant discriminative performance in determining NRF [Area Under the Curve (AUC) = 0.564, 95% CI:0.521–0.608, $p = 0.004$], high SX score [AUC = 0.565, 95% CI:0.522–0.608, $p = 0.003$], in-hospital mortality [AUC = 0.635, 95% CI:0.548–0.721, $p = 0.001$], and the presence of SR [AUC = 0.614, 95% CI:0.570–0.657, $p < 0.001$] (Fig. 3). PWR, with a cut-off value of $\geq$22.1, was independently associated with the presence of SR with a sensitivity of 57.1% and a specificity of 61.1%.

4. Discussion

Our study's key findings can be summarized as follows: (*i*) In the overall population, we observed angiographic SR in 203 patients (20.40%), in-hospital mortality in 57 patients (5.7%), and NRF in 208 patients (20.9%). (*ii*) High PWR and SX scores were found to be associated with SR. (*iii*) Additionally, female gender, hemoglobin levels, the presence of SR, the culprit lesion, and SX scores were independently linked to higher PWR. To the best of our knowledge, this study represents the first investigation into the relationship between PWR and the presence of SR, as well as its connection with adverse outcomes, such as in-hospital mortality, lesion complexity, and NRF.

Prior research has indicated that patients with STEMI who experience SR tend to have a more

Table 1. Baseline clinical, laboratory, and angiographic data of the study population.

Variable	Total (n = 995)	Non-SR (n = 792)	SR (n = 203)	*p*-value*
Baseline characteristics and laboratory findings				
Age (Year), mean ± SD	60.6 ± 12.5	59.6 ± 12.3	61.5 ± 13.0	0.053
Male gender, n (%)	732 (73.6)	593 (74.9)	139 (68.5)	0.065
Hypertension, n (%)	704 (70.8)	564 (71.2)	140 (69.0)	0.530
Diabetes mellitus, n (%)	229 (23.0)	187 (23.6)	42 (20.7)	0.378
Smoking, n (%)	526 (52.9)	411 (51.9)	115 (56.7)	0.226
Glucose (mg/dl), median (IQR)	139 (112–193)	140 (112–193)	134 (110–192)	0.284
C-reactive protein (mg/dl), median (IQR)	0.4 (0.2–1.2)	0.4 (0.2–1.2)	0.5 (0.2–1.1)	0.514
Hemoglobin (g/dl), mean ± SD	13.5 ± 1.8	13.5 ± 1.8	13.5 ± 1.8	0.935
Urea (mg/dl), median (IQR)	29 (24–39)	30 (24–39)	29 (24–36)	0.844
eGFR (ml/min/1.73 m2), mean ± SD	111.9 ± 50.9	105.8 ± 39.6	113.4 ± 53.3	0.061
Creatinine (mg/dl), mean ± SD	0.97 ± 0.69	0.98 ± 0.62	0.97 ± 0.71	0.900
Uric acid (mg/dl), mean ± SD	5.5 ± 1.7	5.5 ± 1.6	5.7 ± 2.0	0.143
Sodium (mEq/l), mean ± SD	134.7 ± 6.2	134.5 ± 6.7	135.2 ± 3.2	0.204
Potassium (mEq/l), mean ± SD	4.2 ± 0.64	4.1 ± 0.64	4.2 ± 0.62	0.217
Initial hs-cTnI (ng/ml), median (IQR)	9.1 (1.2–50.0)	12.0 (1.8–50.0)	3.8 (0.4–14.9)	**<0.001**
Initial CK-MB (ng/ml), median (IQR)	20 (6–83)	38 (7–121)	13 (4–49)	**<0.001**
Initial NT-proBNP (ng/ml), median (IQR)	94 (32–282)	99 (33–309)	72 (20–224)	0.244
Cholesterol(mg/dl), mean ± SD				
Total	189.7 ± 47.2	190.1 ± 47.7	188.1 ± 45.2	0.633
Low-density lipoprotein	129.2 ± 41.8	130.0 ± 41.2	126.1 ± 44.4	0.316
High-density lipoprotein	38.5 ± 11.3	38.6 ± 11.4	38.2 ± 11.0	0.720
Triglycerides(mg/dl), median (IQR)	121 (76–193)	114 (73–181)	148 (89–214)	**0.001**
PLT (10^3/μl), mean ± SD	262.0 ± 84.0	260.3 ± 84.7	269.1 ± 81.0	0.207
WBC (10^3/μl), mean ± SD	12.6 ± 4.3	12.9 ± 4.5	11.7 ± 3.6	**0.001**
PWR, mean ± SD	22.2 ± 7.9	21.6 ± 7.6	24.4 ± 8.9	**<0.001**
Angiographic and procedural features				
Culprit lesion, n(%)				0.548
Left anterior descending	464 (46.6)	375 (47.7)	89 (43.8)	
Circumflex	178 (17.9)	137 (17.3)	41 (20.2)	
Right	353 (35.5)	280 (35.4)	73 (36.0)	
Type of stent, n (%)				0.523
Drug-eluting stent	627 (63.0)	503 (63.5)	124 (61.1)	
Bare-metal stent	368 (37.0)	83 (36.5)	292 (38.9)	
GP IIb/IIIa inhibitors, n (%)	226 (22.7)	194 (24.5)	32 (15.8)	**0.008**
Total stent length (mm), mean ± SD	30.3 ± 16.2	31.0 ± 16.5	27.8 ± 14.6	**0.013**
Stent diameter (mm), mean ± SD	2.9 ± 0.43	2.9 ± 0.42	3.0 ± 0.45	0.076
Acute stent thrombosis, n (%)	32 (3.2)	27 (3.4)	5 (2.5)	0.495

CK-MB, creatine kinase-myocardial band; eGFR, estimated glomerular filtration rate; hs-cTnI, high-sensitive cardiac troponin I; NT-pro BNP, N-terminal pro brain natriuretic peptid; PLT, Platelet Count; PWR, platelet-to-white blood cell ratio; SR, spontaneous reperfusion; WBC, white blood cells. Values are given as n (%), median (interquartile range (IQR), or mean ± standard deviation. P value was calculated using an independent samples t-test or the Mann–Whitney U-test for continuous variables and a chi-squared test or the Fisher's exact test for categorical variables, as appropriate. *p value < 0.05 was considered significant.

favorable ejection fraction, resulting in a lower incidence of heart failure and, notably, a reduced rate of in-hospital mortality [10–12]. Therefore, the identification of easily applicable parameters associated with SR holds significant importance for both short- and long-term prognosis. PWR has previously been associated with infection and bleeding outcomes in patients undergoing radical nephrectomy [9]. Furthermore, it serves as an independent prognostic marker for mortality in cases of acute exacerbation of chronic liver disease, pyogenic liver abscess, and various chronic liver conditions [13–16]. PWR has also been associated with in-hospital and long-term mortality in patients with infective endocarditis, acute myeloid leukemia, and pancreatic cancer [17–19], and its relationship with stroke has been explored [20]. Additionally, PWR has been identified as a related to mortality in patients with COVID-19 [21]. However, our study stands as the only analysis, to the best of our knowledge, that investigates the relationship between PWR and in-hospital adverse outcomes, as well as the presence of SR, in STEMI patients undergoing PPCI.

The Platelet-to-White Blood Cell Ratio is recognized as a contemporary hematological indication reflecting the systemic inflammation cascade. Within this context, it is worth noting that high levels of

Table 2. Clinical data of the overall population according to PWR.

Variable	PWR<22.1 (n = 527)	PWR ≥22.1 (n = 468)	*p*-value*
Baseline and laboratory findings characteristics			
Age (Year), mean ± SD	59.4 ± 12.4	60.7 ± 12.6	0.101
Male gender, n (%)	417 (79.1)	315 (67.3)	**<0.001**
Hypertension, n (%)	378 (71.7)	326 (69.7)	0.474
Diabetes mellitus, n (%)	132 (25.0)	97 (20.7)	0.106
Smoking, n (%)	294 (55.8)	232 (49.6)	**0.050**
Glucose (mg/dl), median (IQR)	140 (116–194)	137 (107–186)	0.051
C-reactive protein (mg/dl), median (IQR)	0.4 (0.2–1.2)	0.5 (0.2–1.0)	0.580
Hemoglobin (g/dl), mean ± SD	13.1 ± 1.7	13.8 ± 1.8	**<0.001**
Urea (mg/dl), median (IQR)	30 (24–39)	29 (23–38)	0.155
eGFR (ml/min/1.73 m^2), mean ± SD	111.7 ± 57.0	112.1 ± 42.8	0.901
Creatinine (mg/dl), mean ± SD	0.99 ± 0.70	0.94 ± 0.67	0.238
Uric acid (mg/dl), mean ± SD	5.7 ± 1.8	5.3 ± 1.6	**0.026**
Sodium (mEq/l), mean ± SD	134.5 ± 5.3	134.9 ± 7.1	0.365
Potassium (mEq/l), mean ± SD	4.1 ± 0.61	4.2 ± 0.67	0.238
Initial hs-cTnI (ng/ml), median (IQR)	15.0 (2.4–50.0)	4.5 (0.6–26.1)	**<0.001**
Initial CK-MB (ng/ml), median (IQR)	27 (8–94)	17 (4–69)	**<0.001**
Initial NT-proBNP (ng/ml), median (IQR)	94 (27–305)	98 (41–252)	0.553
Cholesterol (mg/dl), mean ± SD			
Total	188.7 ± 48.9	190.8 ± 45.2	0.543
Low-density lipoprotein	129.3 ± 41.9	129.1 ± 41.8	0.931
High-density lipoprotein	38.7 ± 10.8	38.3 ± 11.9	0.653
Triglycerides(mg/dl), median (IQR)	113 (71–178)	127 (86–215)	**0.002**
PLT (10^3/μl), mean ± SD	240.5 ± 66.6	290.1 ± 95.3	**<0.001**
WBC (10^3/μl), mean ± SD	14.5 ± 4.4	10.2 ± 2.8	**<0.001**
Angiographic and procedural features			
Culprit lesion, n(%)			**<0.001**
Left anterior descending	275 (52.2)	189 (40.4)	
Circumflex	86 (16.3)	92 (19.7)	
Right	166 (31.5)	187 (40.0)	
Type of stent, n (%)			0.783
Drug-eluting stent	330 (62.6)	297 (63.5)	
Bare-metal stent	197 (37.4)	191 (36.5)	
GP IIb/IIIa inhibitors, n (%)	134 (25.4)	92 (19.7)	**0.030**
Total stent length (mm), mean ± SD	30.39 ± 15.7	30.32 ± 16.8	0.948
Stent diameter (mm), mean ± SD	2.98 ± 0.43	2.93 ± 0.43	0.081
Acute stent thrombosis, n (%)	15 (2.8)	17 (3.6)	0.483

CK-MB, creatine kinase-myocardial band; eGFR, estimated glomerular filtration rate; hs-cTnI, high-sensitive cardiac troponin I; NT-pro BNP, N-terminal-pro brain natriuretic peptid; PLT, Platelet Count; PWR, platelet-to-white blood cell ratio; SR, spontaneous reperfusion; WBC, white blood cells Values are given as n (%), median (interquartile range (IQR)), or mean ± standard deviation. P value was calculated using an independent samples t-test or the Mann–Whitney U-test for continuous variables and a chi-squared test or the Fisher's exact test for categorical variables, as appropriate. *p value < 0.05 was considered significant.

Table 3. Complications and coronary complexity according to PWR and SR.

Variable	**Total (n = 995)**	**PWR<22.1 (n = 527)**	**PWR ≥22.1 (n = 468)**	*p*-value*
SR, n (%)	203 (20.4)	79 (15.0)	124 (26.5)	**<0.001**
NRF, n (%)	206 (20.9)	124 (23.5)	84 (17.9)	**0.031**
SX score, mean ± SD	16.7 ± 7.9	17.7 ± 8.1	15.6 ± 7.5	**<0.001**
In-hospital mortality, n (%)	57 (5.7)	41 (7.8)	16 (3.4)	**0.003**
	Total (n = 995)	**Non-SR (n = 792)**	**SR (n = 203)**	*p*-value*
PWR, mean ± SD	22.1 ± 7.9	21.6 ± 7.5	24.4 ± 8.8	**<0.001**
High PWR (≥22.1), n (%)	468 (47.0)	344 (43.4)	124 (61.1)	**<0.001**
NRF, n (%)	206 (20.9)	181 (22.9)	27 (13.3)	**0.003**
SX score, mean ± SD	16.7 ± 7.9	17.8 ± 7.9	12.7 ± 6.4	**<0.001**
In-hospital mortality, n (%)	57 (5.7)	50 (6.3)	7 (3.4)	0.117

NRF, no-reflow phenomenon; PWR, platelet-to-white blood cell ratio; SR, spontaneous reperfusion, SX, SYNTAX. Values are given as n (%), mean ± standard deviation. P value was calculated using an independent samples t-test, for continuous variables and a chi-squared test or the Fisher's exact test for categorical variables, as appropriate. *p value < 0.05 was considered significant.

Table 4. Univariable and multivariable regression analyses of factors related to high PWR (≥22.1).

Variable	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*p*-value*	OR (95% CI)	*p*-value*
Age (Year)	1.010 (1.000−1.020)	0.052		
Female gender	0.543 (0.408−0.722)	**<0.001**	0.615 (0.446−0.848)	**0.003**
Smoking	0.779 (0.607−1.000)	**0.050**	1.029 (0.790−1.340)	0.833
Hemoglobin (g/dl)	0.815 (0.758−0.877)	**<0.001**	0.854 (0.790−0.924)	**<0.001**
Uric acid (mg/dl)	1.036 (0.932−1.152)	0.511		
Initial hs-cTnI (ng/ml)	1.001 (1.000−1.003)	0.970		
Initial CK-MB (ng/ml)	1.002 (1.000−1.003)	0.051		
Triglycerides (mg/dl)	1.001 (1.000−1.002)	0.086		
Culprit lesion		**0.001**		**0.018**
Left anterior descending	1 (ref)			
Circumflex	1.639 (1.237−2.170)	**0.001**	1.475 (1.092−1.992)	**0.011**
Right	1.630 (1.150−2.310)	**0.013**	1.507 (1.039−2.186)	**0.031**
SR	2.004 (1.492−2.802)	**<0.001**	1.908 (1.365−2.665)	**<0.001**
NRF	0.711 (0.521−0.970)	**0.031**	0.786 (0.565−1.092)	0.151
SX score	0.966 (0.951−0.982)	**<0.001**	0.981 (0.963−0.999)	**0.035**

CK-MB, creatine kinase-myocardial band; CI, Confidence interval; OR, Odds ratio; hs-TnI, high-sensitive troponin I; NRF, no-reflow phenomenon; PWR, platelet-to-white blood cell ratio; SX, SYNTAX. Values are given as n (%), median (interquartile range (IQR)), or mean ± standard deviation. P value was calculated using an independent samples t-test or the Mann−Whitney U-test for continuous variables and a chi-squared test or the Fisher's exact test for categorical variables, as appropriate. *p value < 0.05 was considered significant.

Table 5. Univariable and multivariable logistic regression analyses of factors related to Spontaneous Reperfusion.

Variable	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*p*-value*	OR (95% CI)	*p*-value*
Age (Year)	1.012 (1.000−1.025)	0.054		
Female gender	0.729 (0.520−1.021)	0.066		
Initial hs-cTnI (ng/ml)	1.000 (0.999−1.001)	0.683		
Initial CK-MB (ng/ml)	0.991 (0.988−0.994)	**<0.001**	0.992 (0.989−0.996)	**<0.001**
Triglycerides (mg/dl)	1.001 (1.000−1.0002)	0.124		
High PWR (≥22.1)	2.166 (1.583−2.965)	**<0.001**	1.801 (1.294−2.506)	**<0.001**
NRF	1.931 (1.246−2.992)	**0.003**	0.672 (0.424−1.067)	0.092
SX score	0.907 (0.885−0.929)	**<0.001**	0.918 (0.815−0.941)	**<0.001**

CK-MB, creatine kinase-myocardial band; CI, Confidence interval; OR, Odds ratio; hs-TnI, high-sensitive troponin I; NRF, no-reflow phenomenon; PWR, platelet-to-white blood cell ratio; SX, SYNTAX. Values are given as n (%), median (interquartile range (IQR)), or mean ± standard deviation. P value was calculated using an independent samples t-test or the Mann−Whitney U-test for continuous variables and a chi-squared test or the Fisher's exact test for categorical variables, as appropriate. *p value < 0.05 was considered significant.

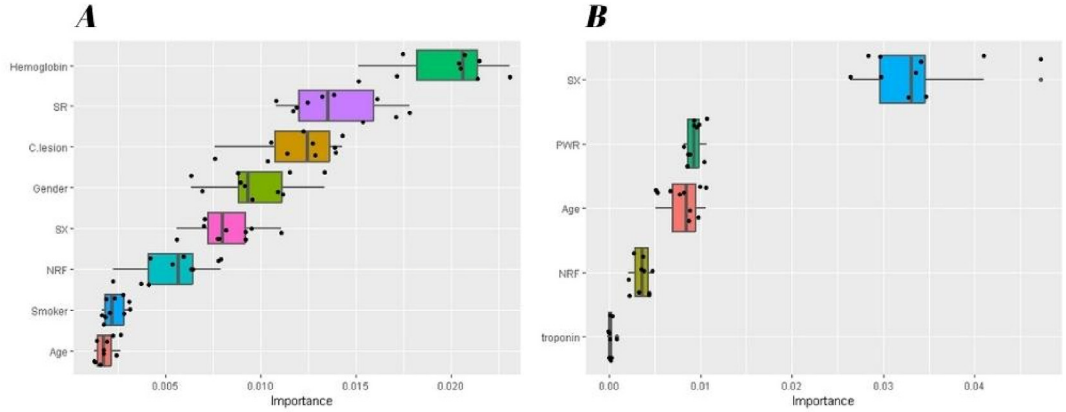

Fig. 2. Variable importance plot of multivariable logistic regression analyses. A. The individual significance of variables potentially linked to high PWR (≥22.1). B. Importance of parameters which is related to SR.

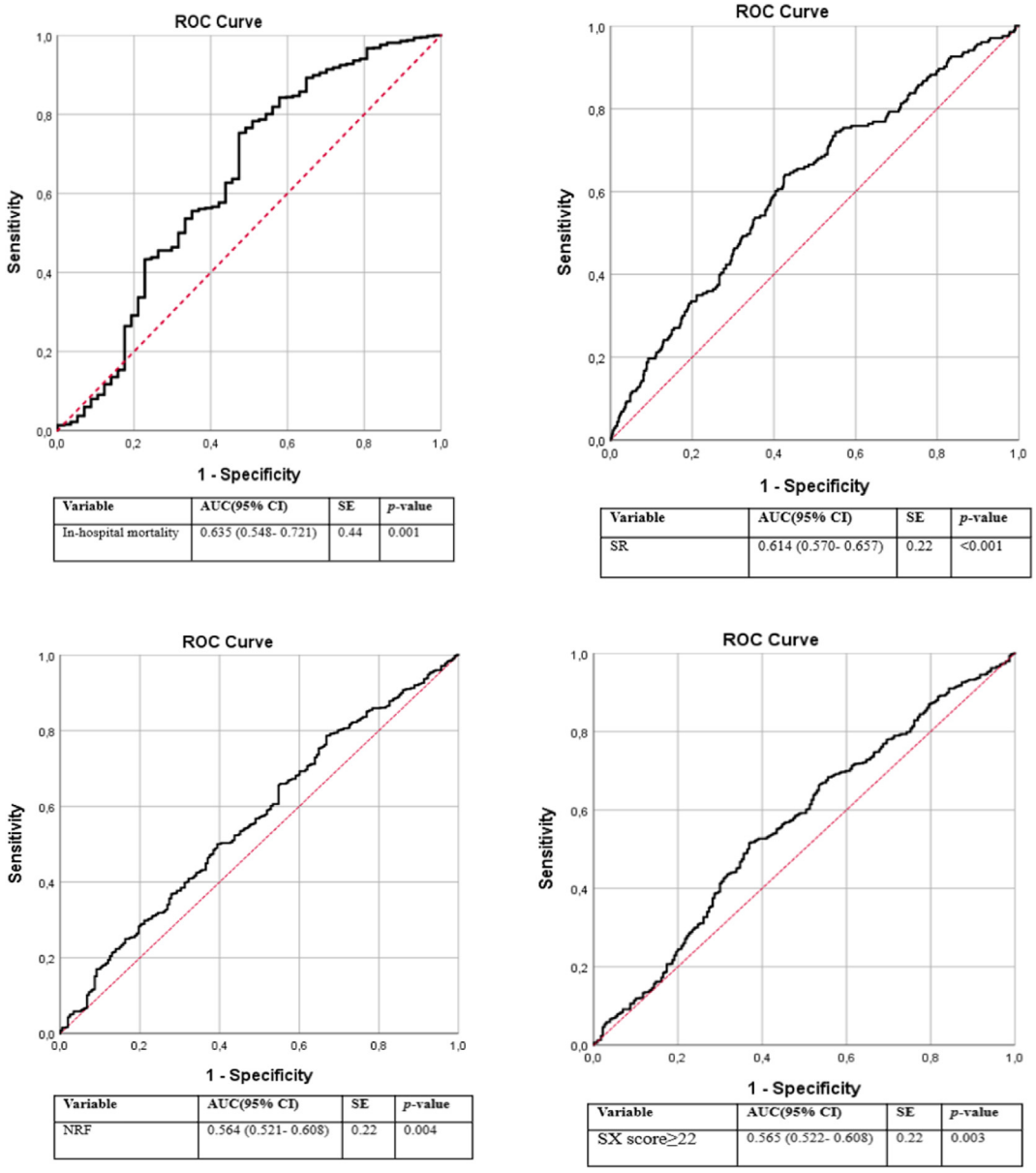

Fig. 3. ROC curves of the PWR for detecting the in-hospital mortality.

WBC have been linked to unfavorable cardiovascular events in STEMI [22,23]. It has previously been posited that elevated WBC counts may be associated with hypercoagulopathy and the development of thrombi resistant to treatment [24] Conversely, several prior studies have revealed an association between low WBC counts and SR, a finding that aligns with our data [5,8]. The other parameter within PWR, high platelet levels, has also been linked to adverse cardiovascular events in STEMI [25,26]. Elevated platelet levels in the SR group have been demonstrated in various studies [27,28], as observed in our own study. The presence of this paradox underscores the need for further exploration in the scientific literature. Consequently, it is evident that the relationship between PWR and SR, which is inclined to increase with the combination of low WBC and high platelet counts, may exert a more substantial influence compared to the independent predictors of these individual parameters. It is widely recognized that SR is related with significantly positive short-term outcomes, and our study has uncovered a significant association between high PWR and SR. Furthermore, this relationship between high PWR and SR is connected to lower in-hospital mortality, a reduced incidence of NRF, and lower SX scores, all of which are critical indicators of adverse outcomes in STEMI.

The underlying mechanism behind SR's impact on coronary morphology remains a subject of uncertainty with limited studies available. In a study involving 241 consecutive STEMI patients who underwent optical coherence tomography (OCT), the characteristics of the IRA plaque were notably distinct between the SR and non-SR groups. The SR group primarily exhibited non-ruptured plaques, and fewer red thrombi were observed [29]. In another OCT study involving 107 STEMI patients, the SR group displayed fewer red thrombi compared to the Non-SR group, while white thrombi were more prevalent [30]. The findings from these OCT studies on SR plaque morphology suggest that one of the primary mechanisms underlying SR in STEMI might involve the regression of coronary occlusion induced by an intact plaque and platelet-rich thrombus. Therefore, it is plausible that the distribution of platelet and WBC levels, which are important parameters in CBC and can impact plaque morphology, may influence SR through this mechanism. However, our hypothesis requires further investigation through OCT and other in vivo studies of lesion morphologies. Additionally, the multivariate analysis revealed that the SX score, in addition to PWR, emerged as an independent determinant of SR. Apart from our study, previous research has also revealed that the SX score is related to SR [31−33].

Another striking finding in our data was that the group of patients with a PWR value above the 22.1 cut-off exhibited a higher occurrence of SR and a lower incidence of NRF, in-hospital mortality, and had lower SX scores. It is worth noting that high PWR may have a favorable impact on adverse outcomes. We conducted two distinct regression analyses to explore the connection between SR and high PWR, and the results indicated a reciprocal association: SR was linked to high PWR, and high PWR was also related to the presence of SR. Furthermore, in our regression analysis aimed at identifying high PWR, we identified that female gender, hgb levels, and SX scores were also connected with high PWR. Although patients with high PWR exhibited lower NRF rates, the relationship between NRF and PWR did not demonstrate statistical significance in the regression analysis.

It is not uncommon in the scientific literature to encounter parameters exhibiting a positive relationship with favorable clinical outcomes but a negative relationship with adverse events, mirroring the findings in our study. For instance, in one study, low endothelin-1 levels were identified as a predictor of SR, while in another study, low endothelin-1 levels were associated with a reduced incidence of 30-day composite major adverse clinical outcomes, and they were correlated with lower SX scores in yet another study [34−36]. Similarly, another study pinpointed serum apelin levels as a determinant of SR [27], while a different investigation linked serum apelin levels to a lower rate of in-hospital mortality, lower SX scores, and fewer cases of NRF [37].

4.1. Limitations

Foremost, the study's retrospective nature restricted the inclusion of detailed angiographic and laboratory parameters, as well as pathophysiological findings potentially related to SR in the culprit vessel. These parameters, which are not typically part of routine medical practice, could not be incorporated into our study. Prospective studies utilizing OCT-IVUS and in-vivo pathological investigations of lesion morphology are warranted to offer more robust prognostic insights. While the observed weak relationship between PWR, SX score, and NRF in the statistical analysis may be considered a limitation, it is worth noting that PWR demonstrates a broader association with morbidity and complications in this patient population when viewed holistically.

5. Conclusion

The early identification of SR in patients upon admission holds the potential to provide valuable supplementary information for the recognition of high-risk patient cohorts. Consequently, the calculation of the cost-effective, rapid, and easily obtainable PWR using the standard CBC test may enhance the precision of prognostic stratification.

Author contributions

Conception and design of Study: GA, TE. Literature review: GA, CY, ÖDU. Acquisition of data: GA, AY, ÖÖA. Analysis and interpretation of data: GA, TE, ÖG, ÖDU. Research investigation and analysis: GA, TE, ÖG. Data collection: GA, TE, AY, ÖG, CY, AY. Drafting of manuscript: GA, TE, ŞD. Revising and editing the manuscript critically for important intellectual contents: GA, ÖG, ŞD. Data preparation and presentation: GA, TE, ŞD. Supervision of the research: GA, ŞD. Research coordination and management: GA, ÖÖA, CY, ÖDU.

Ethics committee approval

The study received approval from the local Clinical Research Ethics Committee of our hospital (No: 2712, Date: 20.07.2023). The study protocol adheres

to the ethical principles described in the 1975 Declaration of Helsinki and was granted prior approval by the institution's human research committee.

Informed consent

Consent forms was waived due to retrospective design of the study.

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Conflict of interest

The author(s) declared no potential conflicts of interest.

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