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Red cell distribution width to platelet ratio as a predictor of no-reflow phenomenon in patients with ST segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

O.S.Arafa,M.A.Tabl, A.S.Elnagar and M.M.Saleh
Cardiology Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-Mail:Mostafamsaleh1988@gmail.com

Abstract

Background: The new inflammatory measure, the red cell distribution ratio platelet width (RPR), is now utilised to predict inflammation in chronic illnesses. It may be linked with unfavourable effects among coronary artery disease, although its predictive value in the ST segment of myocardial elevation (STEMI) has not been well studied. There are no data concerning the relationship between RPR and major cardiovascular events in hospitals (MACEs). This research examined the relationships between preoperative RPR and no reflow and hospital results in primary PCI STEMI patients. Methods: 100 STEMI patients were included in this research (66% males; average age: 55 ± 11 years). The patients were split into two groups based on myocardial infarction thrombolysis (TIMI) in the flow rates after initial PCI. No-reflow was defined as a flow rate of 0, 1 or 2 after PCI TIMI (group 1). Angiographical success has been described as the flow grade 3 of TIMI (group 2). Results: The proportion of neutrophil and lymphocyte, red cell spread, neutrophil–lymphocyte ratio (NLR), platelet-lymphocyte-ratio (PLR) and RPR was greater in patients without reflow. With multivariate analyses, ballon pain times, TIMI thrombus gradation, tirofiban, NLR, PLR and RPR, the non-reflow predictors after initial PCI remain independent. In the non-reflow group, patients in the MACE hospital tended to have greater percentages than in patients in reflows, including non-fatal myocardial infarctions and cardiovascular mortality. Conclusions: NLR, PLR and RPR admission are independent non-reflow correlations between primary PCI STEMI patients.

Keywords: ST segment elevation myocardial infarction, in-hospital prognosis, primary percutaneous coronary intervention, red cell distribution width–platelet ratio, neutrophil–lymphocyte ratio, platelet lymphocyte ratio.

1. Introduction

The impact of inflammation on developing and destabilising atherosclerosis has been more well recognised in recent years and inflammatory biomarkers are widely utilised in the screening and prognosis of coronary artery disease (CAD) [1].

The myocardial ST segment (STEMI) is a major source of morbidity and death in ischemic heart disease. Primary percutaneous coronary intervention (PCI) is the primary technique of therapy for STEMI patients. However, restore full reflux in 2.3-29% of patients after opening occlusion cannot be accomplished. This situation is referred to as the phenomenon of no reflow [2].

There is no reflow of the main PCI heel in Achilles and studies indicate that such an event is a significant and independent predictor of poor cardiovascular outcomes, which include acute heart failure, cardiogenic shock and life threatening arrhythmias in STEMI patients [3].

The complete blood count (CBC) is one of the most used clinical laboratory procedures. Various studies have assessed the performance and risk of illness and death of various haematological CBC parameters [4].

Many clinical labs regularly have automated cell counters that may be used to measure red cell width (RDW), platelet counts, and certain ratios such as the Neutrophil-Lymphocyte Ratio (NLR) and the RDW-Tablet Rate (RPR).

NLR and PLR were recognised as independent predictors of angiographical impairment and long-term death in STEMI main patients [4].

The RPR can predict inflammation, a new regularly accessible, cheap and readily computed indicator [5].

The RPR has been recently examined as a novel predictor for significant cardiovascular adverse events. There are no data, however, on the RPR's forecasting value for STEMI patients who have primary PCI after procedural non-reflow and in-hospital major cardiovascular adverse events (MACEs).

We will therefore evaluate the association between RPR and non-reflow in patients with primary PCI for acute STEMI.

2. Patients and methods

This is observational cross sectional, two center study, conducted at Benha University hospital and Nasser institute hospital in the period from August 2019 to April 2021, it included 100 patients admitted by ST segment elevation myocardial infarction, and the patients were divided into two groups according to thrombolysis in myocardial infarction (TIMI) flow grades after primary PCI. No-reflow was defined as a post-PCI TIMI flow grade < 3 without clear evidence of dissection, stenosis or vasospasm (group 1). Angiographic success was defined as TIMI flow grade 3 group (2) [6].

Key inclusion criteria

Patients of both genders with age range (25 – 80) with first ST segment elevation acute myocardial

infarction which is defined as presence of ST-segment elevation measured at the J point and found in two contiguous leads and be ≥0.25 mV in men

below the age of 40 years, ≥0.2 mV in men over the age of 40 years, or ≥0.15 mV in women in leads V2–V3 and/or ≥0.1 mV in other leads (in the absence of left ventricular (LV) hypertrophy or left bundle branch block) and accompanied by ischemic symptoms for primary PCI [7].

Key exclusion criteria

Patients with culprit lesion in left main coronary artery, left main stenosis > 50%, Previous coronary artery bypass surgery, Cardiogenic shock, Pain to balloon time > 12 h, Treatment with fibrinolytics in previous 24 h, Active infectious or inflammatory diseases, presence of any chronic inflammatory-autoimmune disease including rheumatologic disorders, hematalogic diseases, end-stage liver and renal failures, known malignancy and Patient refusal.

All patients undergone full medical history and clinical examination, lab examination including admission blood sugar, INR, serum creatinine, serum cardiac troponin, CKMB and complete blood count with whole blood counting parameters were analyzed including red cell distribution width (RDW), platelet count, neutrophil-lymphocyte ratio (NLR),

platelet-lymphocyte ratio (PLR), RDW-platelet ratio (RPR).

All the subjects underwent a comprehensive two-dimensional and color flow Doppler echocardiographic examination and left ventricular Ejection fraction (LVEF) will be assessed by Simpson's method. All echocardiographic measurements were made using commercially available devices.

Also all participants underwent coronary angiography performed in multiple orthogonal projections using Judkins technique and PCI using standard femoral or radial route with 6-Fr or 7-Fr guiding catheters. The choice of balloon predilatation, primary stenting was at discretion of treating operator.

Upon admission all the patients received aspirin 300 mg, bolus intravenous unfractioned heparin 5,000 IU (70 U/kg), clopidogrel with a loading dose of 300 mg or Ticagrelor 180mg as loading dose.

Primary stenting was performed whenever possible although balloon predilatation was used in the remaining cases. The technical aspects of the procedure, duration and pressure of inflation were determined by individual operators.

The use of other medications, including intravenous tirofiban was left at the discretion of the attending operator (including bolus tirofiban administration.

Multivessel disease was defined as presence of at least 1 lesion with greater than 50% diameter stenosis in ≥ 1 major epicardial coronary artery or its major branches remote from infarct related artery (IRA).

To evaluate clot burden we performed TIMI thrombus grade in all patients [8].

3. Results

This study included 100 STEMI patients (66% men, mean age: 55 ± 11 years). The patients were divided into two groups according to TIMI flow grades after primary PCI. The patients with TIMI flow grades 0–2 formed no-reflow group (n = 30, 20 men, mean age: 54 ± 10 years) and reflow group 2 (n = 70, 46 men, mean age: 55 ± 12 years), respectively.

Regarding demographical and risk factors parameters, there was no statistical difference between the two groups table (1).

According to Lab and echo parameters; LVEF, Tirofiban, neutrophil, lymphocytes, NLR, PLR and RPR showed statistically significant difference between the two groups Table (2).

The comparison of angiographic characteristics of the two groups showed no statistically significant differences apart from chest pain to balloon time, TIMI thrombus grade, number of post dilatations, stent length and presence of multivessel disease Table (3).

Table (1) Baseline demographical, clinical and loading medications of the studied patients.

Variable	All patients(100)	Reflow group (70)	No reflow group(30)	P value
Mean (SD)				
Age (years)	55.12 (11.39)	55.43 (12.11)	54.4 (9.64)	0.681
Number (%)				
Sex Male	66	46 (65.7)	20 (66.7)	0.927
Female	34	24 (34.3)	10 (33.3)	
DM	28	16 (22.9)	12 (40)	0.08
HTN	38	24 (34.3)	14 (46.7)	0.242
smoker	52	36 (51.4)	16 (53.3)	0.861
Previous CAD	24	14 (20)	10 (33.3)	0.153
Family history	16	10 (14.3)	6 (20)	0.475
Clopidogrel	60	42 (60)	18 (60)	1
Ticagrelor	40	28 (40)	12 (40)	
Diuretic	16	8 (11.4)	8 (26.7)	0.75
Tirofiban	32	16 (22.9)	16 (53.3)	0.003

Table (2) Lab and echo parameters of the studied patients.

Variable	All patients	Reflow group	No reflow group	P value
		Mean (SD)		
Pain to balloon time	5.56 (2.4)	4.94 (2.4)	7 (1.7)	< 0.001
LVEF	48.76 (11.48)	51 (11.69)	43.53 (9.18)	0.002
Cr	0.97 (0.33)	1 (0.34)	0.88 (0.3)	0.09
Urea	25.28(11.47)	26.43 (12.03)	22.6 (9.7)	0.127
CKMB	91.06(74.7)	82.17 (62.99)	111.8 (94.74)	0.069
RBS	149.38(70.5)	144.29 (67.87)	161.27 (76.15)	0.272
INR	1.06(0.17)	1.05 (0.13)	1.11 (0.23)	0.07
Hemoglobin	12.8 (2.04)	12.56 (2.03)	13.33 (2)	0.093
WBC	10.39 (3.22)	10.34 (3.24)	10.5 (3.22)	0.804
Neutrophil	70.83 (13.73)	68.24 (13.48)	76.89 (12.55)	0.003
Lymphocyte	22.19 (12.21)	24.87 (12.31)	16.15 (9.72)	0.001
Eosinophil	0.9 (0.7)	1 (0.77)	0.65 (0.44)	0.02
Basophil	0.53 (0.34)	0.57 (0.32)	0.44 (0.39)	0.071
Monocyte	5.43 (2.59)	5.31 (2.16)	5.71 (3.42)	0.474
Platelet count	288.94 (89.33)	299.74 (93.34)	263.73 (74.66)	0.064
RDW	12.16 (1.3)	11.63 (0.86)	13.37 (1.33)	< 0.001
NLR	5.88 (6.94)	4.25 (3.67)	9.68 (10.53)	< 0.001
PLR	20.01 (19.38)	15.96 (10.19)	29.47 (30.04)	0.001
RDW-platelet ratio	4.67 (1.66)	4.32 (1.54)	5.49 (1.69)	0.001

Table (3) angiographic characteristics of the studied patients.

Variable		All patients(100)	Reflow group (70)	No reflow group(30)	P value
			Number (%)		
IRA	**LAD**	48	34 (48.6)	14 (46.7)	0.881
	LCX	22	16 (22.9)	6 (20)	
	RCA	30	20 (28.6)	10 (33.3)	
Single vessel		50	40 (57.1)	10 (33.3)	0.029
Multi vessel		50	30 (42.9)	20 (66.7)	
Site of occlusion					0.712
•	**Proximal**	54	36 (51.2)	18 (60)	
•	**Mid**	32	24 (34.3)	8 (26.7)	
•	**Distal**	14	10 (14.3)	4 (13.3)	
Type of occlusion					1
•	**Total**	80	24 (80)	56 (80)	
•	**Subtotal**	20	6 (20)	14 (20)	
TIMI.T grade					0.017
•	**< 4**	58	46 (65.7)	12 (40)	
•	**≥ 4**	42	24 (34.3)	18 (60)	
PCI procedure					0.634
• **Balloon and stenting**		70	48 (68.6)	22 (73.3)	
• **Primary stenting**		30	22 (31.4)	8 (26.7)	
No of pre dilatations					0.138
0		30	22 (31.4)	8 (26.7)	
1		42	32 (45.7)	10 (33.3)	
2		14	10 (14.3)	4 (13.3)	
3		14	6 (8.6)	8 (26.7)	
No of post dilatation					0.025
0		54	44 (62.9)	10 (33.3)	
1		28	16 (22.9)	12 (40)	
2		18	10 (14.3)	8 (26.7)	
Mean (SD)					
Stent length		32.2 (18.47)	28.31 (12.54)	41.27 (25.86)	0.001
Stent diameter		3.29 (0.54)	3.28 (0.57)	3.32 (0.45)	0.747

Effects of some clinically important variables on the no-reflow were analyzed by using univariate and multivariate logistic regression analyses. Data for two groups were combined and all the variables were analyzed and pain to balloon time, TIMI thrombus grade, tirofiban, NLR, PLR and RPR remained independent predictors of no reflow after primary PCI. Adjusted ORs were calculated as 1.08 for NLR (p value 0.025; CI = 1.02–1.81), 1.2 for PLR (p value 0.041; CI = 1.31–1.75), 1.8 for RPR (p < 0.001; CI = 1.53–2.24) Table (4).

In-hospital MACEs of the study patients were given in Table 4. Patients in no-reflow group tended to be higher percent in-hospital MACE, including nonfatal MI and cardiovascular mortality compared to those of reflow patients (p < 0.05) Table (5).

ROC curve analysis of NLR, PLR, and RPR showed that showed that NLR > 3.08 (sensitivity 74%, specificity 55%), PLR > 16.23 (sensitivity 67%, specificity 66%) and PRP > 4.2 (sensitivity 74%, specificity 55%) were the best cutoff values for predicting no reflow phenomenon Figure (1).

Table (4) Effects of various variables on no reflow in univariate and multivariate analysis.

	Univariate			Multivariate		
	Unadjusted OR	**95% CI**	**P value**	**Adjusted OR**	**95% CI**	**P value**
Age	1.01	0.97-1.05	0.7			
Sex	1.04	0.42-2.58	0.9			
DM	2.25	0.9-5.64	0.08			
HTN	1.68	0.7-4.01	0.2			
Pain to balloon	0.67	0.54-0.83	<0.001	0.72	0.48-1.08	0.01
Tirofiban	3.86	1.55-9.57	0.004	0.56	0.07-4.53	0.04
LVEF	1.07	1.02-1.11	0.004	1.06	0.98-1.13	0.14
TIMI thrombus	0.35	0.14-0.84	0.02	0.25	0.04-1.52	0.03
Multi vessel	0.38	0.15-0.92	0.03	1.49	0.26-8.62	0.66
IRA	0.92	0.56-1.5	0.7			
Stent length	0.96	0.94-0.99	0.006	1.01	0.96-1.07	0.62
NLR	0.89	0.82-0.96	0.004	1.25	0.68-2.32	0.045
PLR	0.96	0.93-0.99	0.009	0.85	0.63-1.16	0.031
RPR	0.65	0.49-0.86	0.002	0.75	0.26-2.16	0.01

Table (5) in hospital major adverse cardiac events of the study group.

In hospital MACEs	**All patients(100)**	**Reflow group (70) Number (%)**	**No reflow group(30)**	**P value**
In stent thrombosis	5	2 (2.9)	3 (10)	0.158
Non-fatal MI	6	2 (2.9)	4 (13.3)	0.043
Hospital mortality	7	2 (2.9)	5 (16.7)	0.024

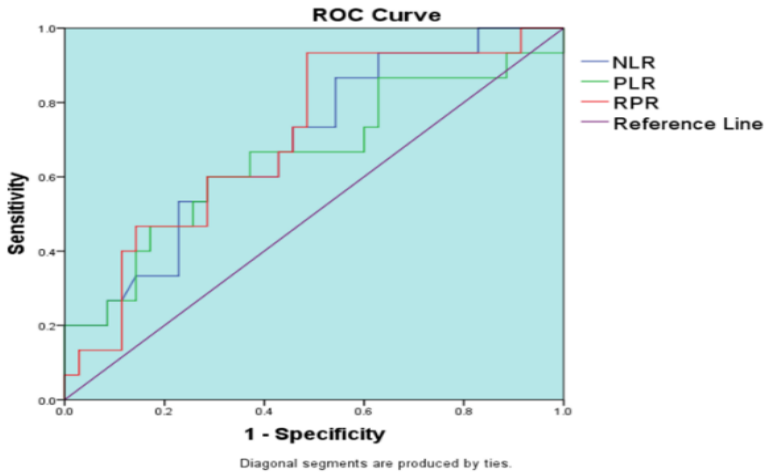

Fig. (1) ROC curve of NLR, PLR, RPR.

4. Discussion

Because of an increasing knowledge of the significance of the inflammatory state in the start and development of atherosclerosis in recent years, epidemiological studies have focused on inflammatory status indicators and their connection to adverse events for people with various CAD phänotypes [1].

Short-term mortality risk shows significant diversity in individuals with STEMI having coronary angiography. Early and individual risk assessment in every single patient enables more accurate decision-making about selection of pharmacological and interventional therapies, clinical resource allocation and triage among hospital alternatives.

In order to prepare for this kind, the risk factors for morbidity and death in STEMI patients who are having angiography must be known.

One of the early late death causes as a non-reflow phenomena may be described as an incomplete reperfusion on the microvascular level although the artery is adequately recanalized. However, this pathological process is subject to rapid coronary reperfusion, leading to tissue edoema, endothelial wound, capillary plugging by neutrophils and microthrombes, and inflammation owing to free radicals production and supplemental activation [9].

Several investigations have shown a link between no-reflow and enhanced inflammatory activity. Recent investigations have revealed that the phenomena of no reflux have a greater incidence of early and late morbidity and death [10, 11].

The CBC is one of the most commonly requested clinical laboratory tests. CBC is the most commonly accessible early in-hospital laboratory data available during the first 30 minutes.

CBC is a simple, cost-free, routine examination method that provides information on blood content, red and white cells, platelets, cell sub-group numbers and dimensions, and characteristics including distribution widths and ratios. Different research examined the performance of various haematological CBC characteristics in order to predict the severity and mortality risk of STEMI diseases.

Results from our research were comparable to those of Turgay et al. in 2016, which also primarily examined platelet RDW for predicting no reflow in 580 PCI-treatments of STEMI patients and found that neutrophil and lymphocyte percentages, red cell widths, NLR and RPR values were greater among no-reflow patients.

Multivariate analysis of their research included ballon pain, vascular disease, TIMI thrombus grade, tirofiban, aspirin, prior coronary artery disease, NLR and RPR and remained independent no-reflow predictors after initial PCI. They also observed that in the non-reflow group patients were usually higher in hospital MACE, including nonfatal myocardial infarction and cardiovascular death in patients with reflow. (12) Compared to Yang et al., 2020, which studied 1658 STEMI patients under 1ry PCI clinical information and laboratory examinations to identify independent risk factors and to establish a risk no-reflow scoring system (aged <60 years, not antagonistic angiotonase inhibitor/angiotensin receptor patients, collateral circulation >grade 2, burden of thrombosis <10 years old, target lesional diameter <3.5 mm) The difference in patients in both trials and statistical techniques should be noted [13].

They also found that LVEF, Killip classification, antiplatelet loading, NLR and PLR were similar to our results, and Oktay et al., 2021 mainly studied the utility of the pre-procedural platelet/lymphocyte ratio (PLR) for forecast of no reflow phenomena following aspiration from thrombus during percutaneous coronary intervention (PCI). The homogenous distribution of findings may have been influenced by the thrombus aspiration of various devices by different operators. (14) In addition, the NLR and PLR were noted for their function as independent CAD prognostic variables. Many studies have examined the relationship between NLR and PLR and short-term morbidity and death in patients with primary PCI STEMI. Cheap and readily detectable laboratory variables NLR and PLR are independently related with the development of non-reflow and hospital-based MACEs in STEMI patients with Primary PCI [14, 15]. In this research, we reported the same findings.

Elevated RDW has been documented for death and other serious adverse events in STEMI patients undergoing primary angioplastic treatment [16].

RDW is an inflammatory marker that is widely accessible, readily generated and repeatable. The increased RDW was shown to be linked with poor clinical results for patients with cardiac failure, preceding MI, stable CAD, strokes, infections and peripheral artery disease, regardless of haemoglobin levels [16, 17 and 18].

RPR, a new marker, is a more strong predictive fibrosis index [19]. The RPR indicates the degree of inflammation.

It may be a helpful and significant marker for the prediction of death of patients with certain chronic illnesses in the accompanying clinical practise [20].

A inexpensive, accessible and readily computed indicator, RPR may predict inflammation in no-reflow patients in patients who are subject to primary PCI pathophysiology.

4. Conclusion

Red cell distortion width at the level of the platelet, which is an easily acquired inflammatory measure, may play a significant part in patients who are treated with primary PCI, as an independent predictor of no reflow event.

5. Limitations

A very small number of patients were included in this research, which resulted in some statistically insignificant findings thus it should be verified in other investigations.

The beginning of the covid 19 pandemic period was in our research, but only non-covid patients were investigated, and 100 percent exclusion was not guaranteed particularly at the beginning of the pandemic.

We did not examine the reasons of high RDW levels, such as iron, folic acid, or lack in vitamin B12. Although we have eliminated some illnesses that may affect RPR levels, certain diseases in our research group may not be identified.

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