Platelet indices and blood cell ratios in acute coronary syndrome and their predictive values

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Background
Platelets have a chief role in the pathogenesis of acute coronary syndrome (ACS), where plaque rupture is followed by platelet activation and thrombus formation, leading to coronary artery occlusion. When platelets are activated, they become bigger in size, which can be measured by both mean platelet volume (MPV) and platelet distribution width (PDW).

Aim
The aim of this study was to evaluate the predictive value of blood count parameters, including platelet indices such as MPV, mean platelet component, plateletcrit, PDW, and mean platelet mass and blood cell ratios such as neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, white blood cell to mean platelet volume (WMR) in ACS.

Patients and methods
This work was carried out at the Clinical Pathology and Cardiology Departments at Assiut University Hospital during the period between January 2017 and December 2017. It included two groups of participants: 250 patients with ACS (patient group) and 100 apparently healthy age-matched and sex-matched individuals (control group).

Results
Mean age of the patient group was 57.41 ± 12.15 years, with range between 31 and 90 years old. Of 250 patients with ACS, 187 (74.8%) patients were males. The patient group had significantly higher MPV, PDW, WMR, and neutrophil-to-lymphocyte ratio in comparison with the control group, but the control group had higher mean platelet component and platelet-to-lymphocyte ratio ($P < 0.05$). Both groups had insignificant differences regarding plateletcrit and mean platelet mass. Low hemoglobin and increased MPV and WMR were predictors for development of major cardiac events in patients with ACS.

Conclusion
Low hemoglobin and increased RDW, MPV, and WMR were predictors for the development of major adverse cardiac event in patients diagnosed with ACS.

Keywords:
acute coronary syndrome, percutaneous coronary intervention, platelet indices

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Introduction

Acute coronary syndromes (ACS) are a set of signs and symptoms because of rupture of a plaque and are a consequence of platelet-rich coronary thrombus formation. The thrombus leads to partial or complete coronary artery occlusion, which leads to myocardial ischemia and various clinical manifestations, ranging from unstable angina (UA) to myocardial infarction [1].

There are two main phases of inflammation during myocardial infarction: the inflammatory phase and the proliferative phase. Neutrophils are the first leukocytes to be found in the damaged area. Their activation produces large amounts of inflammatory mediators that regulate the response to tissue injury, demonstrating hypoxic damage, proteolytic enzymes, and other mediators [2].

Mean platelet volume (MPV) is determined in the progenitor cell, the bone marrow megakaryocyte. The platelet volume is found to be associated with cytokines (thrombopoietin, interleukin-6, and interleukin-3) that regulate megakaryocyte ploidy and platelet number and result in the production of larger platelets [3].

Platelet distribution width (PDW) is a quantitative measure of platelet size variation. An increased PDW shows more difference in the size (anisocytosis), which results from formation of pseudopodia and may be a predictor of platelet activation and turnover [4].

Mean platelet component (MPC) is a new platelet variable detected by modern complete blood count analyzers that denotes the mean refractive index of the platelets. MPC is linearly related to platelet density and is reduced when platelets degranulate, thus indicating that platelets have undergone activation [5].

Neutrophil-to-lymphocyte ratio (NLR) is a simple parameter to assess easily the inflammatory status of a patient. It has proven its usefulness in the stratification of mortality in most cardiac events or as a predictor and a marker of inflammatory or infectious pathologies and postoperative complications [6].

Platelet–leukocyte interactions increase the recruitment of leukocytes to the atherosclerotic lesion and stimulate neutrophils, resulting in the development of neutrophil extracellular traps, which contribute to enhanced atherogenesis and atherothrombosis by binding platelets [7].

Aim

The aim of this study was to evaluate the predictive value of blood count parameters, including platelet indices such as mean platelet volume (MPV), MPC, plateletcrit (PCT), PDW, and mean platelet mass (MPM) and blood cell ratios such as NLR, platelet-to-lymphocyte ratio (PLR), white blood cell to mean platelet volume (WMR) in ACS.

Patients and methods

This study was conducted at the Clinical Pathology and Cardiology departments at Assiut University Hospitals. It was performed in the period from January 2017 to December 2017. The study included 250 cases diagnosed with ACS and 100 apparently healthy individuals age-matched and sex-matched as a control group. Formal consent was obtained from patients and controls. The study was approved by Ethical committee of Faculty of Medicine Assuit University.

Approach to the patient

Patients' evaluation included age, sex, family history of ischemic heart disease, medical history, and detailed history about clinical presentation of chest pain.

Investigations

The following investigations were performed for all participants:

(1) Random plasma glucose for diagnosis of diabetes.
(2) Cardiac enzymes [creatine kinase, creatine kinase-MB (CK-MB), and troponin] for the diagnosis of the type of ACS.
(3) Serum creatine for the diagnosis of uremia.
(4) Prothrombin time and prothrombin concentration were done using SysmexCA1500 (SYSMEX Corporation, Made in Jappan, Germany).
(5) Assessment of platelet count and platelet indices (MPV, MPC, PDW, PCT, and MPM) and blood cell ratios (NLR, PLR, and WMR) by an autoanalyzer (ADVIA 2120i Heamatology System, SIEMENS, Ireland).

Statistical analysis

Data were collected and analyzed using statistical package for the social science, version 20 (IBM Corp., Armonk, New York, USA). Continuous data were expressed in the form of mean ± SD or median (range), whereas nominal data were expressed in the form of frequency (%).

χ^2 test was used to compare the nominal data of different groups in the study, whereas Student's *t*-test was used to compare mean of different two groups and analysis of variance test for more than two groups.

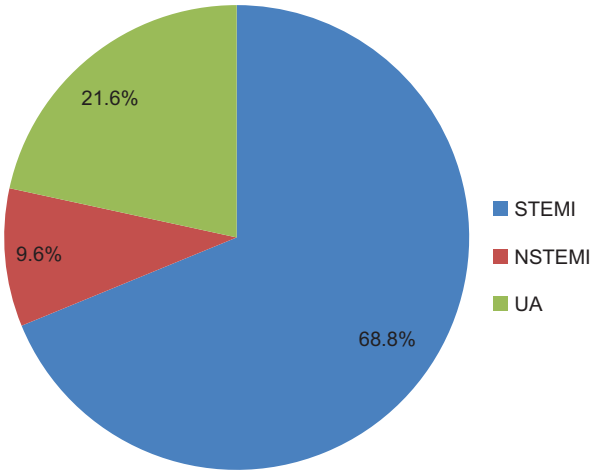
Multivariate regression analysis was used to determine the independent risk factors for prediction of ACS.

The diagnostic accuracy of different blood indices for prediction of ACS was assessed by receiver operating characteristic curve, whereas correlation of these indices with different continuous variables was done by Pearson's correlation. *P* value was considered significant if less than 0.05.

Results

The final diagnosis in the study group was ST-elevation myocardial infarction (STEMI), UA, and non-ST-elevation myocardial infarction (NSTEMI), being present in 172 (68.8%), 54 (21.6%), and 24 (9.6%) patients, respectively.

The patient group had significantly higher MPV, PDW, WMR, and NLR in comparison with the control group, but the control group had higher MPC and PLR ($P < 0.05$). Both groups had insignificant differences regarding PCT and MPM.



Final Diagnosis in the Study Group.

Table 1 Platelet indices and blood cell ratios in patient and control groups

	Patient group (*n*=250)	Control group (*n*=100)	*P*
MPV (fl)	9.47±1.82	7.94±0.62	**<0.001**
MPC (g/dl)	21.26±2.58	22.56±1.87	**<0.001**
PDW (%)	49.96±8.88	45.72±5.67	**<0.001**
PCT (%)	0.23±0.08	0.22±0.04	0.33
MPM (pg)	1.90±0.33	1.71±0.14	0.12
WMR	1.17±0.55	0.89±0.23	**<0.001**
NLR	0.66±0.14	0.57±0.08	**<0.001**
PLR	27.67±5.87	42.87±13.98	**<0.001**

Data were expressed in form of mean±SD. MPC, mean platelet components; MPM, mean platelets mass; MPV, mean platelets volume; NLR, neutrophil-to-lymphocyte ratio; PCT, plateletcrit; PDW, platelets distribution width; PLR, platelet-to-lymphocyte ratio; WMR, white blood cell to mean platelet volume. *P*<0.05, significant. Bold: *P* value >0.05 is not significant and *P* value <0.05 is significant.

Table 2 Correlations of platelet indices and blood cell ratios with creatine kinase-MB

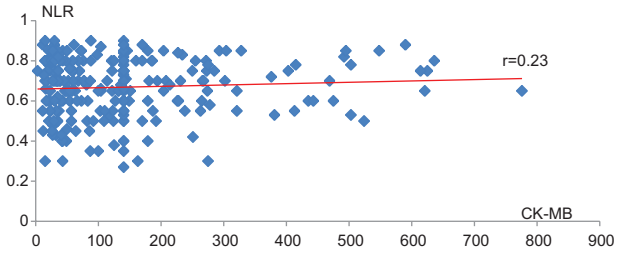
	r	*P*
MPV (fl)	−0.05	0.29
MPC (g/dl)	−0.03	0.63
PDW (%)	0.08	0.12
PCT (%)	−0.08	0.12
MPM (pg)	−0.07	0.30
WMR	**0.32**	**0.01**
NLR	**0.23**	**<0.001**
PLR	**−0.32**	**0.03**

MPC, mean platelet components; MPM, mean platelet mass; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLR; platelet-to-lymphocyte ratio; PCT, plateletcrit; PDW, platelet distribution width; *r*, strength of correlation; WMR, white blood cell to mean platelet volume. *P*<0.05, significant. Bold: *P* value >0.05 is not significant and *P* value <0.05 is significant.

WMR and NLR had significant positive correlation with CK-MB [*r* (*P*)=0.32 (<0.001) and 0.23 (0.01), respectively], whereas PLR had significant negative correlation with peak CK-MB [*r* (*P*)=−0.32 (0.03)]. Other correlations were insignificant (*P* > 0.05) (Table 1, Fig. 1).

Only one patient died in this study, whereas heart failure occurred in 7 (2.8%) patients. Overall, six (2.4%) patients needed blood transfusion, whereas 10 (4%) patients experienced bleeding (Table 2).

Figure 1



Correlation between NLR and CK-MB.

Table 3 Major adverse cardiac events in this study

Adverse effects	Frequency (%)
Mortality	1 (0.4)
Heart failure	7 (2.8)
Reinfarction[a]	5 (4)
Stent thrombosis[a]	5 (4)
Target lesion revascularization[a]	5 (4)
Bleeding	10 (4)
Need for transfusion	6 (2.4)
Stroke	1 (0.4)

Data were expressed in the form of frequency (%). [a]Those calculated among patient undergo percutaneous coronary intervention.

Table 4 Demographic data and risk factors in the study group based on development of major cardiac events

	Developed MCE (*n*=30)	Without MCE (*n*=220)	*P*
Age	58.71±13.42	57.93±10.98	0.72
Male sex	22 (71)	165 (75.3)	0.37
BMI (kg/m^2)	26.02±3.33	26.85±3.67	0.23
Risk factors			
Diabetes mellitus	14 (45.2)	62 (28.3)	**0.04**
Hypertension	14 (45.2)	81 (37)	0.24
Smoking	18 (58)	130 (59.4)	0.52
Final diagnosis			
STEMI	24 (77.4)	148 (67.6)	0.53
NSTEMI	2 (6.5)	22 (10)	
UA	5 (16.1)	49 (22.4)	

Data were expressed in the form of mean±SD and frequency (%). MCE, major cardiac events; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina. *P*<0.05, significant. Bold: *P* value >0.05 is not significant and *P* value < 0.05 is significant.

It was noticed that demographic data and risk factors had no significant differences between patients with major cardiac events (MCE) and those without (*P* > 0.05), with the exception of diabetes mellitus, which was more frequent in those patients who developed major adverse cardiac events (MACE) (Table 3).

Total leukocytic count, neutrophils, and platelets were significantly higher in those patients who developed MCE, whereas red blood cells, hemoglobin, MCV, and MCH were significantly higher in those patients who did not develop MCE (Table 4).

Table 5 Complete blood picture in the study group based on development of major cardiac events

	Developed MCE (*n*=30)	Without MCE (*n*=220)	*P*
TLC (×10³/mm³)	13±1.09	10.57±1.11	**<0.001**
Neutrophil (×10³/mm³)	9.48±1.07	6.33±2.09	**0.01**
Lymphocyte (×10³/mm³)	2.66±1.40	2.54±1.27	0.63
Monocyte (×10³/mm³)	0.76±0.50	0.65±0.30	0.07
Eosinophil (×10³/mm³)	0.08±0.01	0.06±0.01	0.44
Basophil (×10³/mm³)	0.01±0.01	0.01±0.01	0.35
RBC (×10³/mm³)	4.43±0.79	4.76±0.69	**0.01**
Hemoglobin (g/dl)	11.73±2.77	12.98±1.85	**<0.001**
HCT (%)	35.66±8.50	40.55±7.88	0.19
MCV (fl)	82.78±8.65	85.80±7.94	**0.04**
MCH (g/dl)	26.18±3.48	27.39±2.89	**0.03**
MCHC (g/dl)	31.58±1.95	31.79±2.14	0.61
Platelets (×10³/mm³)	294.03±45.89	252.78±74.09	**<0.001**

Data were expressed in the form of mean±SD. HCT, hematocrit value; MCE, major cardiac events; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; TLC, total leukocytic count. *P*<0.05, significant. Bold: *P* value >0.05 is not significant and *P* value < 0.05 is significant.

Table 6 Platelet indices and blood cell ratios in the study group based on the development of major cardiac events

	Developed MCE (*n*=30)	Without MCE (*n*=220)	*P*
MPV (fl)	10.78±1.75	8.43±1.83	**<0.001**
MPC (g/dl)	20.96±2.24	21.29±2.63	0.65
PDW (%)	33.56±5.78	34.15±7.98	0.85
PCT (%)	0.26±0.2	0.23±0.07	0.11
MPM (pg)	1.85±0.21	1.91±0.025	0.88
WMR	1.99±0.67	1.01±0.53	**0.01**
NLR	0.69±0.15	0.66±0.13	0.95
PLR	27.7±6.77	27.65±7.09	0.07

Data were expressed in form of mean±SD. MCE, major cardiac events; MPC, mean platelet components; MPM, mean platelet mass; MPV, mean platelet volume; NLR, neutrophil-to-leukocyte ratio; PCT, plateletcrit; PDW, platelet distribution width; PLR, platelet-to-lymphocyte ratio; WMR, white blood cell to mean platelet volume. *P*<0.05, significant. Bold: *P* value >0.05 is not significant and *P* value < 0.05 is significant.

Table 7 Multivariate regression analysis for prediction of major cardiac events in patients with acute coronary artery syndrome

	Odds ratio	95% confidence interval	*P*
Diabetes mellitus	0.96	1.6-3.45	0.98
Total leukocytic count (×10³/mm³)	1.45	1.89-4.78	0.32
Neutrophil (×10³/mm³)	2.98	0.99-3.45	0.52
RBCs (×10³/mm³)	1.13	0.34-2.09	0.42
Hemoglobin (g/dl)	1.90	1.05-3.09	**0.02**
MCV (fl)	1.45	0.99-1.02	0.32
MCH (g/dl)	2.03	2.09-2.98	0.45
Platelets (×10³/mm³)	1.35	1.10-2.09	0.67
RDW (%)	2.34	2.13-3.78	**0.03**
MPV (fl)	1.18	1.95-4.98	**0.04**
WMR	2.98	2.03-6.97	**<0.001**

MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; MPV, mean platelets volume; RBC, red blood cell; WMR, white blood cell to mean platelet volume. *P*<0.05, significant.

Regarding platelet indices and blood cell ratios, only MPV and WMR were significantly higher in those patients who developed MCE (Table 5).

Low hemoglobin and increased MPV and WMR were predictors for development of MCE in patient with ACS (Tables 6 and 7).

Discussion

In our study, 250 patients presented with ACS, including 172 (68.8%) cases with STEMI, 54 (21.6%) cases with UA, and 24 (9.6%) cases with NSTEMI. This agreed with many authors who reported that of 400 patients with ACS, 303 patients had myocardial infarction and 97 patients had UA [8].

Our study showed that MPV was significantly higher in the patient group in comparison with the control group. This finding was in accordance with the observations by other studies [9–11].

A recent study showed that the increased MPV at the admission time is significantly higher among patients diagnosed with AMI than in patients with stable coronary artery disease or the control group of the same age [12].

In this study, MPC was significantly lower in the patient group compared with the control group. This is a new parameter in our study, and it is difficult to find similar results in other papers to compare with it.

Several studies in human medicine have recently demonstrated that MPC values are inversely correlated with platelet membrane P-selectin expression [13].

MPC has emerged as an easily accessible measure of platelet activity and, for this reason, has been proposed by many as a possible tool for identifying 'at-risk' patients and monitoring the effects of new pharmacotherapy [14].

Our study showed that the PDW was significantly higher in the patient group compared with the control group, and this agrees with many studies who found that patients with ACS tended to have significantly larger PDW than the control group [15–17].

In this study, PCT was not significantly different in patient group compared with the control group. This agrees with the results of Assiri *et al*. [15] who found that no statistically significant difference was detected regarding the PCT among the three groups. This disagrees with a study which showed that increased PCT might be a useful predictor of coronary slow flow phenomenon [18].

In our study, MPM was not significantly different in the patient group compared with the control group, but we also found that NSTEMI was significantly higher

compared with STEMI, UA, and control group. This is a new parameter in our study, and it is difficult to find similar results in other papers to compare with it.

In this study, WMR was significantly higher in the patient group compared with the control group. This agrees with Dehghani *et al.* [19] who investigated a novel parameter called WMR as a marker for predicting long-term outcomes in patients with NSTEMI. They suggested that WMR is a better predictor of worse outcomes in patients with NSTEMI than WBC and MPV.

In this study, the NLR was significantly higher in the patient group compared with the control group. Similarly some researchers found that mean NLR and mean absolute neutrophil count were higher in patients who had STEMI compare with those with NSTEMI/UA [20,21]. They found a significant association between higher NLR and increased morbidity like congestive heart failure.

In a recent study, the average distribution of NLR in the patients was examined. NLR was found to be higher in the patients with positive troponin-I than in the patients with negative troponin-I and in the patients with positive CK-MB than in the patients with negative CK-MB [22].

In our study, PLR was significantly lower in the patient group compared with the control group, and this agrees with a previous study that demonstrated that PLR may be a useful inflammatory marker in clinical practice [23].

In this study, WMR and NLR had significant positive correlation with CK-MB whereas PLR had significant negative correlation with peak CK-MB, and this is in accordance with the study of Tahto *et al.*[24] who observed that there were significant positive correlations between the NLR and high-sensitive troponin level and between NLR and CK-MB activity.

Our study showed that low hemoglobin and increased RDW, MPV, and WMR were predictors for development of MCE in patients with ACS ($P = 0.02$, 0.03, 0.04, and < 0.001, respectively), and this agrees with other study that reported combined use of the WBC count, hemoglobin, and MPV levels may represent a biochemical-integrated assessment of inflammatory status, thrombotic risk, and the extent of myocardium at risk. Their results showed that WBC count, hemoglobin, and MPV levels were the three predictors, providing the best MACE risk discrimination, underscoring the importance of these pathophysiologic mechanisms in patients with ACS [25]. Another study reported that the combination of an elevated NLR and elevated MPV is a strong predictor of MACE in patients undergoing percutaneous coronary intervention, especially in patients presenting with ACS [26].

Conclusion

(1) PLR and MPC were significantly lower in the patient group as compared with the control group.
(2) Platelet indices mainly MPV and PDW and blood cell ratios mainly WMR, NLR, and PLR might be useful as an assisting rule-out test in conjunction with other conventional biochemical cardiac markers in the early prediction of the risk of ACS in patients admitted to the Emergency Department.
(3) A positive correlation between NLR and CK-MB was observed, suggesting the importance of NLR in assessing myocardial lesion intensity in ACS.
(4) Low hemoglobin and increased MPV and WMR were predictors for the development of MCE in patients diagnosed with ACS. So, we suggested that MPV and WMR are readily available, relatively inexpensive, and useful markers for prognosis, which we detected to be significantly increased in the patients admitted with ACS.

Recommendations

(1) Large-scale studies are recommended in a larger number of cases with long-term follow-up.
(2) More studies should be conducted to identify the role of MPM and MPC in ACS.
(3) Platelet indices and blood cell ratios can be used in risk stratification of the patients with ACS.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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