

Zhehestovska D. V., Hrebenyk M. V. Diagnostic and prognostic utility of the platelet parameters in patients with acute myocardial infarction. *Journal of Education, Health and Sport*. 2021;11(03): 67-76. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2021.11.03.008> <https://apcz.umk.pl/czasopisma/index.php/JEHS/article/view/JEHS.2021.11.03.008> <https://zenodo.org/record/4632272>

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8.2) and § 12.1.2) 22.02.2019.
© The Authors 2021;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland
Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.
The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 15.02.2021. Revised: 26.02.2021. Accepted: 23.03.2021.

DIAGNOSTIC AND PROGNOSTIC UTILITY OF THE PLATELET PARAMETERS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

D. V. Zhehestovska, M. V. Hrebenyk

I. Horbachevsky Ternopil National Medical University,

Faculty of Postgraduate Education, Department of Surgery, Ternopil, Ukraine

Diana V. Zhehestovska – PhD student, **I. Horbachevsky Ternopil National Medical University,** Ternopil, Ukraine

ORCID 0000-0001-6305-4143, e-mail: zhehestovska_dv@tdmu.edu.ua

Maryan V. Hrebenyk – Professor, Head of the Department of **Therapeutics and Family Medicine,** **I. Horbachevsky Ternopil National Medical University,** Ternopil, Ukraine

ORCID 0000-0002-8118-5742, e-mail: hrebenyk@tdmu.edu.ua

Abstract

Background. Complete blood count (CBC) is a simple and affordable diagnostic tool that is routinely used in therapeutic practice. At the same time, its diagnostic and prognostic potentials in terms of management of acute myocardial infarction (AMI) are currently limited. Based on a number of previous studies, we suggest that the analysis of platelet count and indices among AMI patients may have significant diagnostic and prognostic value, as well as dynamic changes in these parameters during the treatment course.

Objectives. To evaluate the value of platelet indices and ratios in terms of their diagnostic and prognostic potential among patients with AMI at the time of hospitalization and on the 7th day of treatment.

Materials and methods. The study involved 152 patients diagnosed with AMI (Group 1), 30 patients diagnosed with the chronic coronary syndrome (Group 2) and 24

healthy volunteers (Group 3). CBC was performed for all participants to determine all platelet indices. Also, anamnestic and clinical data were evaluated, as well as results of the coronary angiography. GRACE score was calculated.

Results. The highest diagnostic value was shown by the WBC/MPV ratio (AUC 0,798; sensitivity 83,1 %; specificity 65,1 %) and PLT/L ratio (AUC 0,644; sensitivity 62,7 %; specificity 53,5 %), as opposed to traditionally used MPV (AUC 0,426; sensitivity 47,5 %; specificity 48,8 %) and PLT (AUC 0,484; sensitivity 60,8 %; specificity 58,1 %). We were unable to establish a relationship between CBC platelet counts at the time of hospitalization and the risk of complications according to the GRACE score. However, those changes according to CBC were obtained on the 7th day of treatment. In particular, the number of platelets was associated with the risk of hospital (r = 0,287; p = 0,016) and 6-month mortality (r = 0,260; p = 0,30), the duration of ischemia (r = 0,238; p = 0,016) and the number of affected vessels according to the results of angiography (r = 0,395; p = 0,002). Similarly, P-LCC correlated with the risk of hospital (r = 0,483; p = <0,001) and 6-month mortality (r = 0,462; p = <0,001), the number of affected coronary vessels (r = 0,456; p = 0,001) and the duration of angina pectoris (0,392; p = 0,001), respectively.

Conclusion. We found that combined ratios such as WBC/MPV and PLT/L had a higher diagnostic value compared to MPV, PLT and P-LCR. The prognostic potential of platelet indices was significantly higher on the 7th day of hospital stay. In particular, elevated levels of platelets, platelets, and P-LCR were correlated with a higher risk of hospital and 6-month mortality.

Key words: inflammation; acute myocardial infarction; complete blood count; platelet; thrombocytes

Background

Coronary heart disease and its complications remain one of the most common causes of death among adults worldwide [1]. The pathogenetic basis for the development of coronary heart disease is the development of atherosclerotic lesions in the coronary arteries. Destabilization of the atherosclerotic plaque causes the activation of the blood coagulation system with the subsequent formation of a thrombus that blocks the lumen of the infarct-related artery (IRA) leading to the development of acute myocardial infarction (AMI) [2]. Platelet activation plays a key role in this pathological process. To date, a number of studies indicate the diagnostic and prognostic value of platelet indices of the complete blood count (CBC), in the management of patients with AMI [3, 4]. Most of these works focus on the

assessment of CBC indicators only at the time of hospitalization. We suggest that dynamic changes in platelet parameters during the course of treatment for patients with AMI may be valuable, in particular, to assess the prognosis of the further development of the disease, and therefore require further study.

Aim of the study

To evaluate the diagnostic and prognostic potential of CBC platelet parameters, including platelet counts (PLT), their volume indices (MPV, P-LCC, P-LCR) and ratios (WBC/MPV, PLT/L) in patients with AMI at the time of hospitalization and on the 7th day of the hospital stay.

Materials and methods

The study involved 152 patients with a diagnosis of AMI who were hospitalized – Group 1. In addition, two other study groups were formed: a comparison group, which included patients with the chronic coronary syndrome (n = 30) – Group 2, and also a control group of healthy volunteers without any manifestations of coronary heart disease (n = 24) – Group 3. The diagnosis of AMI was verified in accordance with the requirements of clinical guidelines [5, 6]. Exclusion criteria were: acute infectious, cancer, chronic diseases in the acute phase.

Anamnestic data were evaluated, in particular the presence of comorbid pathology, duration of pain syndrome, time from the moment of the development of symptoms to percutaneous coronary intervention (PCI), clinical symptoms of AMI. Such CBC parameters as PLT, PCT, MPV, P-LCC, P-LCR, WBC, LYM were obtained using an automated hematology analyzer. Blood sampling was performed during the first hour after hospitalization and on the 7th day after the development of AMI.

In addition, the GRACE and Gensini scores were calculated with subsequent assessment of the risk of hospital and 6-month mortality and the severity of coronary artery disease was assessed according to the results of angiography [7].

Statistical data processing was performed using the application package SPSS v25.0. Data are presented in the format "mean ± standard error of the mean". For normal data distribution Student's t-test was used, in other cases, a non-parametric Mann-Whitney test was chosen. To compare three or more independent samples we used a one-factor analysis of variances (ANOVA) and the Kruskal-Wallis ranking criterion. ROC analysis was used to identify the diagnostic value of CBC parameters. Pearson's correlation analysis was used to assess the relationships between the studied indicators, with a normal distribution of data, and Spearman's correlation in all other cases. The null hypothesis was denied at $P < 0,05$.

Results

The mean age of patients with AMI included in the study was (62.91 ± 10.90) years. Men n=116 (76,3 %) were predominated. Most patients had comorbid pathology such as diabetes mellitus – n =29 and arterial hypertension – n = 134 (88,16 %).

Table 1 - Comparison of CBC parameters between patients with AMI, CCS and healthy volunteers

	Group 1 (n=152)	Group 2 (n=30)	Group 3 (n=24)	p-value (ANOVA)	p-value between 2 groups
Age, years	63,11±0,89	56,13±1,66	45,75±3,30	<0,001	0,01 ^{a,b,c}
Men, n (%)	116 (76,3)	24 (77,4)	17 (70,8)	NS	NS
PLT, 10 ⁹ /l	230,97±0,08	224,53±12,76	251,13±11,81	NS	NS
MPV, fl	9,20±0,16	9,00±0,19	8,17±0,21	<0,001	<0,001 ^{b, c}
MPV/PLT ratio	0,43±0,02	0,44±0,03	0,34±0,02	0,014	0,001 ^b 0,003 ^c
PLT/MPV ratio	25,80±1,14	25,13±1,49	30,89±1,55	0,026	0,016 ^b 0,01 ^c
Plt/L ratio	161,59±11,86	113,99±9,07	114,36±7,83	0,004	0,02 ^a 0,001 ^b
PDW	39,80±0,52	39,79±0,48	40,12±0,35	NS	NS
P-LCC	79,39±3,10	39,50±4,67	81,35±5,52	NS	NS
P-LCR	35,09±1,04	31,15±1,50	30,54±1,60	0,024	<0,05 ^{a,b}
WBC/MPV ratio	1,03±0,05	0,76±0,03	0,78±0,04	<0,001	<0,001 ^a 0,002 ^b
MPV/L ratio	7,00±0,66	4,63±0,36	5,13±0,31	0,001	0,002 ^a <0,001 ^b
ESR, mm/year	11,20±0,75	8,26±0,81	7,71±0,92	0,048	<0,05 ^{a,b}
a – comparing groups 1 and 2, b – comparing groups 1 and 3, c – comparing groups 2 and 3					
NS – not significant					
PLT – platelet count, MPV – mean platelet volume, MPV/PLT ratio – mean platelet volume to platelet count ratio, PLT/L ratio – platelet to lymphocyte ratio, PDW – platelet distribution width, P-LCC – platelet large cell count, P-LCR – platelet large cell ratio, WBC/MPV ratio – white blood cells to mean platelet volume ratio, MPV/L ratio – mean platelet volume to lymphocyte ratio, ESR – erythrocyte sedimentation rate.					

When comparing CBC parameters between the three groups (Table 1), it was found that the mean platelet volume (MPV) did not differ between patients with AMI and CCS, but was significantly lower in the control group. A similar situation was observed with MPV/PLT ratio. If the MPV shows the average size of all platelets, then P-LCR indicates a proportional platelet count greater than 12 fL, and this parameter was higher in group 1 compared to other groups.

Plt/L, WBC/MPV, MPV/L ratios, as indicators that simultaneously reflect the processes of inflammation and platelet activation, were significantly higher among patients with AMI, compared with CCS and the comparison group.

Based on the obtained data, it was decided to evaluate the diagnostic value, as well as the sensitivity and specificity of platelet indices CBC in patients with AMI, which are presented in Table 2.

Table 2 - Diagnostic sensitivity and specificity of CBC parameters in AMI patients

	AUC	Sensitivity, %	Specificity, %	Cut-off point
PLT	0,484	60,8	58,1	225,50
MPV	0,426	47,5	48,8	9,25
MPV/PLT ratio	0,465	66,1	41,9	0,39
P-LCC	0,557	59,3	55,8	73,50
P-LCR	0,603	62,7	51,2	32,33
Plt/L ratio	0,644	62,7	53,5	117,15
WBC/MPV ratio	0,798	83,1	65,1	0,79
MPV/L ratio	0,652	67,8	55,8	4,44

AUC – area under the curve.

As can be seen in Figure 1, the best diagnostic value had WBC/MPV ratio, while other platelet parameters had a fairly low diagnostic potential.

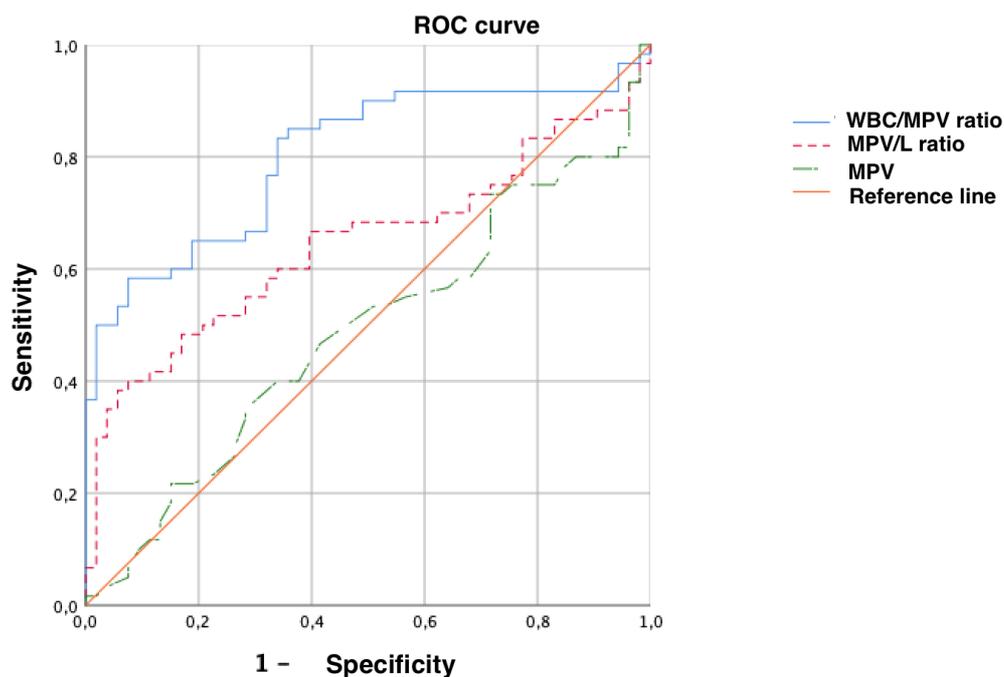


Figure 1. Receiver operating characteristics analysis of platelet parameters in AMI patients

According to the correlation analysis, a positive correlation was found between the time from the development of symptoms to the PCI and PLT/L ($r = 0,380$; $p = 0,06$), MPV/L ratios ($r = 0,351$; $p = 0,011$), as well as with P-LCR ($r = 0,313$; $p = 0,024$). The same relationships were found between the duration of the pain syndrome (ie the duration of ischemia), and the PLT/L ratio ($r = 0,260$; $p = 0,045$).

Significant relationships between CBC parameters and prognostic markers of AMI, including GRACE score, were not established at this stage.

The changes of the general blood analysis in patients with AMI were further analyzed.

Table 3 - Comparison of CBC parameters in AMI patients at the time of hospitalization and on the 7th day after MI

	Day 1	Day 7	p value
PLT, $10^{12}/\mu$	240,21±11,09	272,18±18,61	NS
PCT	0,21±0,01	0,24±0,02	NS
MPV, fl	9,00±0,19	8,92±0,20	NS
MPV/PLT ratio	0,40±0,02	0,36±0,02	0,045
Plt/L ratio	141,45±14,50	145,31±12,05	NS
PDWs	13,28±0,43	13,08±0,40	NS
PDWc	39,90±0,26	39,99±0,24	NS
P-LCC	80,04±4,18	89,68±4,70	NS
P-LCR	34,26±1,61	35,01±1,51	NS

We see a significant decrease in the MPV/PLT ratio ($p = 0,045$) (Table 3).

When performing a correlation analysis with the parameters of CBC on the 7th day, it was found that the duration of chest pain was associated with a higher risk of hospital ($r = 0,246$; $p = 0,002$) and 6-month ($r = 0,231$; $p = 0,005$).) mortality, and also higher GRACE score ($r = 0,229$; $p = 0,005$). In addition, a positive correlation was found with the severity of coronary artery disease according to the Gensini score ($r = 0,210$; $p = 0,021$) and the level of CPK MB ($r = 0,323$; $p = 0,001$).

It was found that PLT was associated with the risk of hospital ($r = 0,287$; $p = 0,016$) and 6-month mortality ($r = 0,260$; $p = 0,30$), GRACE score ($r = 0,250$; $p = 0,037$), the duration of the angina pectoris ($r = 0,238$; $p = 0,016$) and the number of affected vessels according to the angiography ($r = 0,395$; $p = 0,002$).

At the same time, P-LCC was characterized by stronger correlations with the risk of hospital ($r = 0,483$; $p = <0,001$) and 6-month mortality ($r = 0,462$; $p = <0,001$), GRACE score

(0,435; $p = <0,001$), the number of affected vessels ($r = 0,456$; $p = 0,001$) and the ischemic time (0,392; $p = 0,001$).

Discussion

Platelet activation is the main pathogenetic link in the development of AMI. CBC test performed by automated hematology analyzer not only allows to estimate quantitative indicators of platelet parameters, but also certain volume indicators of thrombocytes. To date, a number of studies confirm the fact that the functional activity of a platelet directly correlates with its size [8, 9]. The larger the platelet is the more granules it contains. That leads to the higher expression of adhesion molecules, and, accordingly, to the higher the prothrombotic potential [10, 11]. Thus, the parameters that reflect platelet size are affordable and informative markers of the development and course of AMI.

Our study identified differences in platelet volume parameters, including MPV and P-LCR, between patients with AMI and healthy volunteers. At the same time, we didn't manage to detect differences in MPV levels between patients with AMI and CCS. This can be explained by the fact that MPV level is usually elevated compared to the healthy population, and at the same time, the pronounced inflammatory process that accompanies AMI can reduce the level of MPV [4, 12, 13]. There are data showing MPV decrease 3 hours after hospitalization, and a further increase of its level on the 3rd and 7th day [14].

The potential of MPV for the diagnosis of AMI in patients with angina pectoris still remains the subject of research. The results of our work resonate with a number of other works and demonstrate that the indicators of specificity and sensitivity of MPV are insufficient to use as a stand-alone diagnostic tool [15] [17]. At the same time, the use of MPV in combination with existing markers can significantly improve their diagnostic capabilities. In particular, X.Wang shows that MPV and troponin I used together had better sensitivity and specificity [18]. We were able to find that combined indicators, such as WBC/MPV and PLT/L ratios have a significantly higher diagnostic value than single platelet parameters.

Another important aspect is the prognostic value of platelet parameters. A number of studies illustrate the association between elevated MPV levels and a higher risk of mortality, as well as restenosis after PCI [19]. Similar patterns were also observed with platelet count [20]. At the same time, the decrease of those parameters is associated with the potential negative consequences of AMI. If an increase in MPV levels reflects platelet activation, then a decrease is associated with a high-grade inflammation [21]. In the case of platelets, this relationship is inverse: a high number of platelets indicates a more active inflammatory

process, and low – indicates the activation of platelets. That is why nowadays some scientists state that assessing ratios MPV/PLT ratio can provide us more valuable information [12, 22]. The dynamics of MPV/PLT on the 7th day of the disease are shown in our study, while the difference between individual levels of platelets and MPV was not statistically significant.

We didn't manage to establish reliable correlations between the CBC parameters and at the time of hospitalization, as well as angiographic and prognostic characteristics of AMI. The fact that platelet count and size correlated with the prognosis of AMI only on the 7th day, may be related to the treatment effectiveness. Antiplatelet therapy is one of the key elements in the management of AMI patients [5, 6]. However, the effectiveness of such treatment depends on a number of factors and can vary significantly. Thus, we suggest that indicators such as total platelet count (PLT) as well as large platelet concentration (P-LCC) may be secondary indicators of platelet functional activity and indicate insufficient effectiveness of antiplatelet therapy, which could potentially be associated with the worst prognosis of AMI [16].

Conclusion

Platelet parameters and their ratios, such as P-LCR, MPV, WBC/MPV are affordable and informative markers that provide additional information about inflammation and thrombosis during the acute phase of myocardial infarction.

We were unable to establish a link between complete blood count parameters at the time of hospitalization and prognostic factors for AMI. Instead, parameters obtained on day 7th of treatment, such as P-LCC and PLT were associated with the higher risk of hospital and 6-month mortality. Thus, we emphasize the importance of assessing the complete blood count test within AMI patients, as an inexpensive and informative method of stratification of the risks of AMI, not only at the time of admission but also in the dynamics.

References

1. Khan MA, Hashim MJ, Mustafa H, et al (2020) Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. *Cureus* 12:e9349–e9349
2. Hansson GK, Libby P, Tabas I (2015) Inflammation and plaque vulnerability. *J Intern Med* 278:483–493
3. Lassale C, Curtis A, Abete I, van der Schouw YT, Verschuren WMM, Lu Y, Bueno-de-Mesquita HB (2018) Elements of the complete blood count associated with cardiovascular disease incidence: Findings from the EPIC-NL cohort study. *Sci Rep* 8:3290

4. Khode V, Sindhur J, Kanbur D, Ruikar K, Nallulwar S (2012) Mean platelet volume and other platelet volume indices in patients with stable coronary artery disease and acute myocardial infarction: A case control study. *J Cardiovasc Dis Res* 3:272–275
5. Collet J-P, Thiele H, Barbato E, et al (2020) 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. <https://doi.org/10.1093/eurheartj/ehaa575>
6. Ibanez B, James S, Agewall S, et al (2018) 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Socie. *Eur Heart J* 39:119–177
7. Granger CB, Goldberg RJ, Dabbous O, et al (2003) Predictors of Hospital Mortality in the Global Registry of Acute Coronary Events. *Arch Intern Med* 163:2345–2353
8. Pereg D, Berlin T, Mosseri M (2010) Mean platelet volume on admission correlates with impaired response to thrombolysis in patients with ST-elevation myocardial infarction. *Platelets* 21:117–121
9. Vizioli L, Muscari S, Muscari A (2009) The relationship of mean platelet volume with the risk and prognosis of cardiovascular diseases. *Int J Clin Pract* 63:1509–1515
10. Italiano JE, Hartwig JH (2013) Chapter 2 - Megakaryocyte Development and Platelet Formation. In: Michelson ADBT-P (Third E (ed). Academic Press, pp 27–49
11. Korniluk A, Koper-Lenkiewicz OM, Kamińska J, Kemonia H, Dymicka-Piekarska V (2019) Mean platelet volume (MPV): New perspectives for an old marker in the course and prognosis of inflammatory conditions. *Mediators Inflamm*. <https://doi.org/10.1155/2019/9213074>
12. Bolat I, Akgul O, Cakmak HA, Pusuroglu H, Somuncu U, Ozbey S, Ornek V, Erturk M, Gul M (2016) The prognostic value of admission mean platelet volume to platelet count ratio in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Kardiol Pol* 74:346–355
13. Sansanayudh N, Anothaisintawee T, Muntham D, McEvoy M, Attia J, Thakkinstian A (2014) Mean platelet volume and coronary artery disease: A systematic review and meta-analysis. *Int J Cardiol* 175:433–440
14. Sušilović Grabovac Z, Baković D, Lozo M, Pintarić I, Dujčić Ž (2017) Early Changes in Platelet Size and Number in Patients with Acute Coronary Syndrome. *Int J Angiol*

15. Acapulco K, Morales SJ, Verame TF (2020) Diagnostic Performance of Mean Platelet Volume in the Diagnosis of Acute Myocardial Infarction: A Meta-Analysis. *Philipp J Pathol* 5:34–46
16. Dorn O.Yu., Tsikalenko E.A., Stepanova E.G., Palamarchuk M.V. VLV (2015) The plcc indicator as a laboratory marker of platelet hemostasis activation in patients with ischemic heart disease. *J Sib Med Sci* 8:22–25
17. Ding L, Sun L, Wang F, Zhu L, Zhang T, Hua F (2019) Clinical Significance of Platelet Volume and Other Platelet Parameters in Acute Myocardial Infarction and Stable Coronary Artery Disease. *Arq Bras Cardiol* 112:715–719
18. Wang X, Xu X-L, Li X-M, Zhao R, Yang X, Cong H-L (2016) Diagnostic Value of Mean Platelet Volume Combined With Troponin I for Acute Coronary Syndrome. *Am J Med Sci* 352:159–165
19. Zenon H, Janusz K, J. FK, J. HG, Marcin G, Radoslaw P, Joanna W, Andrzej Z, Bernhard M, Grzegorz O (2005) 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* 46:284–290
20. Nikolsky E, Grines CL, Cox DA, Garcia E, Tchong JE, Sadeghi M, Mehran R, Lansky AJ, Na Y, Stone GW (2007) Impact of baseline platelet count in patients undergoing primary percutaneous coronary intervention in acute myocardial infarction (from the CADILLAC trial). *Am J Cardiol* 99:1055–1061
21. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitis GD (2011) Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des* 17:47–58
22. Azab B, Shah N, Akerman M, McGinn JTJ (2012) Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction. *J Thromb Thrombolysis* 34:326–334
23. Azab B, Shah N, Akerman M, McGinn JT (2012) Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction. *J Thromb Thrombolysis* 34:326–334

Conflicts of Interest

Authors declare no conflict of interest.