Folia Cardiologica 2015
tom 10, nr 6, strony 418–422
DOI: 10.5603/FC.2015.0079

ISSN 2353–7752

Mean platelet volume and platelet-large cell ratio as prognostic factors for coronary artery disease and myocardial infarction

Średnia objętość płytek krwi i wskaźnik dużych komórek jako czynniki prognostyczne choroby wieńcowej i zawału serca

Marcin Gawlita, Jarosław Wasilewski, Tadeusz Osadnik, Rafał Reguła, Kamil Bujak, Małgorzata Gonera

3rd Department of Cardiology, Silesian Centre for Heart Diseases, School of Medicine with the Division of Dentistry, Medical University of Silesia, Zabrze, Poland

Abstract

Platelets represent an important link between inflammation and thrombosis and play an important role in all stages of atherosclerotic lesion formation. Increased platelet activity and their tendency to clot formation favour the incidence of thrombotic complications, such as unstable angina pectoris (UA), myocardial infarction (MI) and sudden cardiac death, in the course of coronary artery disease (CAD). Mean platelet volume (MPV) reflects the average size of platelets and, under normal circumstances, ranges between 7.5 fL to 10.5 fL. Platelet-large cell ratio (P-LCR) is defined as the percentage of platelets that exceed the normal value of platelet volume of 12 fL in the total platelet count. Platelet size has been shown to reflect platelet activity; therefore MPV and P-LCR are a simple and easy method of indirect assessment of platelet stimulation. In general population, higher MPV values are associated with increased risk of CAD. Higher MPV and P-LCR values are observed in CAD patients compared to patients without coronary atherosclerosis. In acute coronary syndromes (ACS) the MPV value is higher in patients with myocardial infarction than in patients with unstable CAD. In cases of stable CAD, elevated MPV correlates with the severity of coronary artery involvement and is a predictive factor of ACS. In patients with acute MI high MPV value has been reported to have impact on the no-reperfusion phenomenon following a percutaneous coronary intervention (PCI). Therefore, MPV and P-LCR indices, combined with other prognostic parameters, may be an important element of various scoring systems used in long-term prognosis in both stable CAD and ACS.

Key words: MPV, P-LCR, coronary artery disease, myocardial infarct

(Folia Cardiologica 2015; 10, 6: 418–422)

Introduction

Thrombotic complications of atherosclerosis are, inter alia, connected with platelet function, including their activation and the ability to aggregate [1–2]. Mean platelet volume (MPV) reflects the average size of platelets (ranges from 7.5 fL to 10.5 fL), while the platelet-large cell ratio (P-LCR) reflects the proportion of platelets greater than 12 fL (the norm for P-LCR is < 30% in the total platelet count).

Larger platelets are usually relatively young and contain more intracellular granules. They have, therefore, greater thrombogenic potential [3–4]. Platelets size is determined by

Address for correspondence: Marcin Gawlita, III Katedra i Oddział Kliniczny Kardiologii, Śląskie Centrum Chorób Serca, Wydział Lekarski z Oddziałem Lekarsko-Dentystycznym w Zabrzu, Śląski Uniwersytet Medyczny w Katowicach, ul. Marii Skłodowskiej-Curie 9, 41–800 Zabrze, e-mail: marcin.gawlita@wp.pl

the rate of platelet turnover [5]. At the developmental stage of precursor cells (megakaryocytes) the activity of cytokines (especially interleukin 3 and interleukin 6) plays a significant role in the regulation of platelet pool and leads to the production of larger platelets that are more reactive [6–8].

Increased MPV value is associated, among others, with hypertension [9], diabetes mellitus [10–11], renal failure [12] and atrial fibrillation [13]. Higher MPV values were also observed in the elderly [14], obese patients [15] and smokers [4, 16–17]. P-LCR is not routinely reported in a complete blood count. However, there exist some data suggesting its prognostic value similar to that of MPV.

Because platelets form an important link between inflammation and thrombotic complications in atherosclerosis [18], this paper attempts to review an up-to-date outlook for the assessment of platelet indices in patients with coronary artery disease (CAD).

The role of MPV and P-LCR in stable coronary artery disease and acute coronary syndromes

In patients with stable CAD, higher MPV and P-LCR values are observed in comparison with healthy persons [1], whereas in ACS the indices are higher in cases of myocardial infarction than in unstable CAD [4]. For example, Khode et al. have proven that MPV is significantly higher in patients with myocardial infarction (9.65 ± 0.96 fL) than in stable CAD patients (9.37 ± 0.88 fL) and lowest in the control group (9.21 ± 0.58 fL) [19]. Additionally, Pol et al. have demonstrated greater MPV values in acute coronary syndrome (ACS) patients compared with non-ACS patients (11.44 ± 1.23 fL versus 9.91 ± 1.27 fL) [20]. Thus, the rise in MPV and P-LCR values may be considered a hallmark of plaque thrombosis.

MPV and the complexity of coronary artery disease

Sani Namik Murat et al., in order to assess the CAD severity and complexity, have used the Gensini and SYNTAX scores [21]. Patients were divided into two groups according to the MPV value — one with low MPV (8.3 ± 0.9 fL) and second with high MPV (10.8 ± 0.4 fL). Both angiographic Gensini and SYNTAX scores were higher in patients with high MPV value compared to patients in the low MPV group (9.5 ± ± 4.4 versus 7.9 ± 4.0 on the Gensini score and 16.1 ± 8.4 versus 13.9 ± 9.0 on the SYNTAX score, respectively). In multifactorial analysis MPV was found to be an independent factor correlating with the degree of coronary artery atherosclerosis. Another study also confirmed the relationship between MPV and atherosclerosis' complexity according to the Gensini and SYNTAX scores [22]. Using the Gensini score, patients have been divided into three subgroups: patients with no coronary lesions (Gensini score 0), with minimal coronary lesions (Gensini score 1–9) and with significant coronary atherosclerosis (Gensini score ≥ 20). Additionally, the SYNTAX score has been used to divide patients into four subgroups: control group (SYNTAX score = 0), low SYNTAX group (SYNTAX score 1–22), medium SYNTAX group (SYNTAX score 23–32) and high SYNTAX group (SYNTAX score > 33). Using both the Gensini and SYNTAX scores evaluations, statistically significant differences in MPV values were found in all analysed subgroups. Spearman analysis revealed a positive correlation between MPV and the Gensini score ($p < 0.001$, $r = 0.290$).

Coronary artery calcification can be quantified using the coronary calcium score from multi-detected row computed tomography. It is believed that coronary calcification detected by using computed tomography scanning is a pathognomonic feature of atherosclerosis [23]. In this case, the Calcium Score (CS) indicates the amount of coronary artery calcification and is a surrogate marker that reflects the coronary atherosclerotic plaque burden [24]. Lesions that remain undetected during contrast angiography (because of plaque positive remodelling in the arterial wall) can be visualized through computed tomography before they protrude into the lumen of the vessel. For that reason, quantitative assessment of calcification reflects the advancement of the atherosclerotic process better than contrast angiography, which cannot detect the early stages of plaque formation [25]. Therefore, it is important to discuss the relation between MPV and the Calcium Score. In the Dong Hyuk et al. analysis, which encompassed over 2000 general population patients, it has been proven that the MPV was significantly higher in patients with a positive CS than in the control group (CS = 0) [26]. Multivariate analyses showed that MPV was positively associated with coronary calcification (odds ratio [OR], 1.61; 95% confidence interval [CI] 1.02–2.55).

To conclude, MPV correlates with the complexity and severity of CAD according to the Gensini and SYNTAX scores, as well as with the total plaque burden assessed by the Calcium Score.

The prognostic value of MPV in patients with CAD

Recently, MPV emerged as a cardiovascular risk factor in general population as well as in patients with CAD and ACS. For instance, in an Austrian population of 200,000 people, it has been shown that MPV over 11.01 fL was an independent risk factor for cardiovascular mortality [2]. In long-term observation, all-causes mortality risk was 1.5-times higher and coronary disease-related mortality was 1.8-times higher in individuals in the highest quintile of MPV value. [27].

In a multivariate analysis performed by Ozkan et al., MPV has been documented to be an independent myocardial infarction risk factor in men under the age of 44 and in women under the age of 55 [28]. Also, some other publications underline the prognostic significance of MPV in CAD patients [29–31].

For example, Alon Eisen et al. have demonstrated that in the analysed population of over 7500 CAD patients undergoing PCI, MPV was higher in individuals over the age of 75, in women, in cases of diabetes mellitus and in patients with ACS than it was in stable CAD patients [29]. In multivariate analysis, MPV remained a significant risk factor for mortality and the incidence of composite endpoints (death, myocardial infarct or the necessity for revascularization). In addition, MPV value at admission was a significant prognostic factor in cases of both planned PCI and emergency PCI.

MPV is also a substantial prognostic factor in patients with ST-elevation myocardial infarction. Akgul et al. have divided the analysed cohort into 2 groups depending on MPV: Group 1 with MPV ≤ 8.9 and group 2 with MPV > 8.9 [30]. The group with higher MPV showed greater in-hospital mortality than group 1. In 6-month observation, the percentage of deaths in group 2 was greater compared to the group with lower MPV value. Age, MPV over 8.9 fL, anaemia at admission, low left ventricle ejection fraction and unsuccessful revascularization proved to be independent mortality risk factors in 6-month observation. MPV value of over 8.9 fL predicted all-causes death in 6-month observation with high sensitivity (73.2%) and specificity (74%).

Also Rechciński et al. have demonstrated that MPV and P-LCR remain related to greater long-term mortality in patients with STEMI undergoing PCI [31]. In individuals with MPV ≥ 11.7 fL long-term mortality was nearly three times higher in comparison with patients with MPV < 11.7 fL. In cases of P-LCR values equal or over 38.1% mortality was also significantly higher compared to individuals with lower values.

Mean platelet volume and tissue reperfusion

In a large number of patients with acute myocardial infarction, despite restoring the patency of the infarct-related artery, there is no myocardial reperfusion [32–36]. The occurrence of such phenomenon is associated with worse long-term prognosis and higher risk of recurrent myocardial infarction.

The term 'no-reflow' was introduced by Kloneli et al. in 1974 [37]. Although primarily it was used to describe lack of reperfusion in animal models consisting of a temporary ligation of a coronary artery, further observations of this phenomenon in the aspect of PCI procedures resulted in the distinction between the 'no-reflow' and 'no-reperfusion' [38].

Among numerous factors responsible for the lack of tissue reperfusion after reperfusion therapy in patients with acute myocardial infarction, the following can be listed: leucocytosis, C-reactive protein (CRP) concentration, endothelin, von Willebrand factor (vWF) and fibrinogen concentration, MPV and in general, blood flow properties (blood fluidity) [39–41].

Maden et al. have reported reperfusion disturbances in about 40% of acute myocardial infarction patients treated with percutaneous coronary intervention (PCI) [42]. Individuals with impaired tissue blood flow were characterized by higher MPV values compared to patients with effective myocardial reperfusion (9.8 ± 1.3 versus 8.6 ± 1.0 fL, $p < 0.001$). Using regression analysis, MPV was shown to be independently related to impaired myocardial blood flow. The MPV cut-off value that best predicted compromised reperfusion has been established at 9.05 fL with sensitivity of 74% and specificity of 73%.

Also some other observations point out the relationship between tissue reperfusion and MPV value at admission [43–46]. In the analysis performed by Estévez-Loureiro et al., it has been shown that MPV independently predicts infarct-related artery patency before reperfusion as well as 30-day mortality in patients with STEMI undergoing PCI [47].

Conclusion

In general population, high value of MPV has negative prognostic impact. In stable CAD patients, compared with non-CAD individuals, MPV correlates with the severity of coronary artery disease. In myocardial infarction, high MPV value is linked with the no-reperfusion phenomenon and is related to the increase of in-hospital and long-term mortality. Thus, platelet indices such as MPV and P-LCR in association with other predictive parameters may be utilized as important elements of various risk scores to assess outcome in both coronary artery disease and acute coronary syndromes.

Conflict interest(s)

None declared.

Streszczenie

Płytki krwi są ważnym ogniwem łączącym zapalenie i zakrzepicę oraz odgrywają istotną rolę na wszystkich etapach powstawania zmian miażdżycowych. Zwiększona aktywność płytek krwi powodująca nasiloną krzepliwość krwi przyczynia się do większej liczby powikłań zakrzepowych, takich jak niestabilna dławica piersiowa (UA), zawał serca (MI) i nagły zgon sercowy w przebiegi choroby wieńcowej (CAD). Średnia objętość płytki krwi (MPV) odpowiada przeciętnej wielkości płytek i w normalnych warunkach mieści się w zakresie od 7,5 fl do 10,5 fl. Wskaźnik płytkowy dużych komórek (P-LCR) jest definiowany jako odsetek płytek krwi przekraczających zakres prawidłowej objętości płytek wynoszący powyżej 12 fl. Wykazano, że wielkość płytek odzwierciedla ich aktywność, dlatego oznaczenie MPV i P-LCR to proste i łatwe metody pośredniej oceny stopnia stymulacji płytek krwi. W populacji ogólnej wyższe wartości MPV wiążą się ze zwiększonym ryzykiem CAD. U chorych z CAD obserwuje się wyższe wartości MPV i P-LCR niż u osób bez zmian miażdżycowych tętnic wieńcowych. W grupie chorych z ostrymi zespołami wieńcowymi (ACS) wartość MPV jest wyższa u osób z rozpoznaniem zawału serca niż u osób z niestabilną CAD. W przypadku stabilnej CAD wielkość MPV koreluje z ciężkością zmian w tętnicach wieńcowych i jest czynnikiem predykcyjnym ACS. Opisywano wpływ wysokich wartości MPV u chorych z ostrym MI na występowanie zjawiska braku reperfuzji po przezskórnej interwencji wieńcowej (PCI). Dlatego wskaźniki MPV i P-LCR w połączeniu z innymi prognostycznymi parametrami mogą być ważnym elementem różnych systemów oceny ryzyka w perspektywie długookresowej zarówno w stabilnej CAD, jak i ACS.

Słowa kluczowe: MPV, P-LCR, choroba wieńcowa, zawał serca

(Folia Cardiologica 2015; 10, 6: 418–422)

References

1. Khandekar M.M., Khurana A.S., Deshmukh S.D. et al. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. J. Clin. Pathol. 2006; 59: 146–149.
2. Slavka G., Perkmann T., Haslacher H. et al. Mean platelet volume may represent a predictive parameter for overall vascular mortality and ischemic heart disease. Arterioscler. Thromb. Vasc. Biol. 2011: 31: 1215–1218.
3. Kanbay A., Tutar N., Kaya E. et al. Mean platelet volume in patients with obstructive sleep apnea syndrome and its relationship with cardiovascular diseases. Blood Coagul. Fibrinolysis 2013; 24: 532–536.
4. Desai K.N., Patel K, Shah M. et al. A study of platelet volume indices (PVI) in patients of coronary artery disease and acute myocardial infarction in tertiary care hospital. Int. J. Adv. Res. 2013. [Online]. Available at: http:/journaldatabase.info/articles/study_platelet_volume_indices_pvi.html. Accessed: 08-Mar-2015.
5. Martin J.F., Trowbridge E.A., Salmon G. et al. The biological significance of platelet volume: its relationship to bleeding time, platelet thromboxane B2 production and megakaryocyte nuclear DNA concentration. Thromb. Res. 1983; 32: 443–60.
6. Tschoepe D., Roesen P., Esser J. et al. Large platelets circulate in an activated state in diabetes mellitus. Semin. Thromb. Hemost. 1991; 17: 433–438.
7. Burstein S.A., Downs T., Friese P. et al. Thrombocytopoiesis in normal and sublethally irradiated dogs: response to human interleukin-6. Blood 1992; 80: 420–428.
8. Debili N., Massé J.M., Katz A. et al. Effects of the recombinant hematopoietic growth factors interleukin-3, interleukin-6, stem cell factor, and leukemia inhibitory factor on the megakaryocytic differentiation of CD34+ cells. Blood 1993; 82: 84–95.
9. Karabacak M., Dogan A., Turkdogan A.K. Mean platelet volume is increased in patients with hypertensive crises. Platelets 2014; 25: 423–426.
10. Lippi G., Salvagno G.L., Nouvenne A. et al. The mean platelet volume is significantly associated with higher glycated hemoglobin in a large population of unselected outpatients. Prim. Care Diabetes 2015; 9: 226–230.
11. Ulutas K.T., Dokuyucu R., Sefil F. et al. Evaluation of mean platelet volume in patients with type 2 diabetes mellitus and blood glucose regulation: a marker for atherosclerosis? Int. J. Clin. Exp. Med. 2014; 7: 955–961.
12. Uçar H., Gür M., Koyunsever N.Y. et al. Mean platelet volume is independently associated with renal dysfunction in stable coronary artery disease. Platelets 2014; 25: 274–278.
13. Tekin G., Tekin Y.K., Sivri N. et al. Mean platelet volume in patients with nonvalvular atrial fibrillation. Blood Coagul. Fibrinolysis 2013; 24: 537–539.
14. De Luca G., Secco G.G., Verdoia M. et al. Combination between mean platelet volume and platelet distribution width to predict the prevalence and extent of coronary artery disease: results from a large cohort study. Blood Coagul. Fibrinolysis 2014; 25: 86–91.
15. Kalay N., Dogdu O., Koc F. et al. Hematologic parameters and angiographic progression of coronary atherosclerosis. Angiology 2012; 63: 213–217.
16. Cho S.Y., You E., Lee H. J. et al. Smoking cession decreases mean platelet volume in healthy Korean populations. Clin. Lab. 2014; 60: 1413–1416.
17. Varol E., Icli A., Kocyigit S. et al. Effect of smoking cessation on mean platelet volume. Clin. Appl. Thromb. Hemost. 2013; 19: 315–319.
18. Gawaz M., Langer H., May A.E. Platelets in inflammation and atherogenesis. J. Clin. Invest. 2005; 115: 3378–3384.
19. Khode V., Nallulwar S., Ruikar K. et al. 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. 2012; 3: 272–275.

20. Pal R., Bagarhatta R., Gulati S. et al. Mean platelet volume in patients with acute coronary syndromes: a supportive diagnostic predictor. J. Clin. Diagnostic Res. 2014; 8: MC01–MC04.
21. Murat S.N., Duran M., Kalay N. et al. Relation between mean platelet volume and severity of atherosclerosis in patients with acute coronary syndromes. Angiology 2013; 64: 131–136.
22. Ekici B., Erkan A.F., Alhan A. et al. Is mean platelet volume associated with the angiographic severity of coronary artery disease? Kardiol. Pol. 2013; 71: 832–838.
23. Ultrafast CT for coronary calcification. Lancet 1991; 337: 1449–1450.
24. Sangiorgi G., Rumberger J.A., Severson A. et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using nondecalcifying methodology. J. Am. Coll. Cardiol. 1998; 31: 126–133.
25. Wasilewski J., Miszalski-Jamka K., Hudzik B. et al. Ocena uwapnienia tętnic wieńcowych za pomocą tomografii komputerowej — rokowanie i korelacja z zaawansowaniem zmian miażdżycowych. Kardiochir. Torakochir. Pol. 2011; 8: 544–549.
26. Jung D.H., Lee H.R., Lee Y.J. et al. The association between coronary artery calcification and mean platelet volume in the general population. Platelets 2011; 22: 567–571.
27. Padwal R., Straus S.E., McAlister F.A. et al. Evidence based management of hypertension. Cardiovascular risk factors and their effects on the decision to treat hypertension: evidence based review. Br. Med. J. 2001; 322: 977–980.
28. Ozkan B., Uysal O.K., Duran M. et al. Relationship between mean platelet volume and atherosclerosis in young patientswith ST elevation myocardial infarction. Angiology 2012; 64: 371–374.
29. Eisen A., Bental T., Assali A. et al. Mean platelet volume as a predictor for long-term outcome after percutaneous coronary intervention. J. Thromb. Thrombolysis 2013; 36: 469–474.
30. Akgul O., Uyarel H., Pusuroglu H. et al. Prognostic value of elevated mean platelet volume in patients undergoing primary angioplasty for ST-elevation myocardial infarction. Acta Cardiol. 2013; 68: 307–314.
31. Rechciński T., Jasińska A., Foryś J. et al. Prognostic value of platelet indices after acute myocardial infarction treated with primary percutaneous coronary intervention. Cardiol. J. 2013; 20: 491–498.
32. Keeley E.C., Boura J.A., Grines C.L. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003; 361: 13–20.
33. Jacobs A.K., Antman E.M., Ellrodt G. et al. Recommendation to develop strategies to increase the number of ST-segment-elevation myocardial infarction patients with timely access to primary percutaneous coronary intervention. Circulation 2006; 113: 2152–2163.
34. Piana R.N., Paik G.Y., Moscucci M. et al. Incidence and treatment of 'no-reflow' after percutaneous coronary intervention. Circulation 1994; 89: 2514–2518.
35. Resnic F.S., Wainstein M., Lee M.K.Y. et al. No-reflow is an independent predictor of death and myocardial infarction after percutaneous coronary intervention. Am. Heart J. 2003; 145: 42–46.
36. Abbo K.M., Dooris M., Glazier S. et al. Features and outcome of no-reflow after percutaneous coronary intervention. Am. J. Cardiol. 1995; 75: 778–782.
37. Kloner R.A., Ganote C.E., Jennings R.B. The 'no-reflow' phenomenon after temporary coronary occlusion in the dog. J. Clin. Invest. 1974; 54: 1496–1508.
38. Wasilewski J., Szyguła B., Głowacki J. No-reflow i no-reperfusion — dwie przyczyny braku reperfuzji mięśniowej po przezskórnej interwencji wieńcowej No-reflow and no-reperfusion — two reasons for impaired myocardial reperfusion after percutaneous coronary intervention. Perfusion 2006; 4: 290–293.
39. Galiuto L., Paraggio L., Liuzzo G. et al. Predicting the no-reflow phenomenon following successful percutaneous coronary intervention. Biomark. Med. 2010; 4: 403–420.
40. Wasilewski J., Turczyński B., Słowińska L. et al. Haemorheological factors and myocardial reperfusion in patients with ST-elevation myocardial infarction undergoing primary coronary intervention. Kardiol. Pol. 2007; 65: 778–785.
41. Wasilewski J., Osadnik T., Poloński L. High baseline fibrinogen concentration as a risk factor of no tissue reperfusion in ST-segment elevation acute myocardial infarction treated with successful primary percutaneous coronary intervention. Kardiol. Pol. 2006; 64: 967–972 (discussion 973–974).
42. Maden O., Kacmaz F., Selcuk H. et al. Relationship of admission hematological indexes with myocardial reperfusion abnormalities in acute ST segment elevation myocardial infarction patients treated with primary percutaneous coronary interventions. Can. J. Cardiol. 2009; 25: e164–e168.
43. Kırbaş Ö., Kurmuş Ö., Köseoğlu C. et al. Association between admission mean platelet volume and ST segment resolution after thrombolytic therapy for acute myocardial infarction. Anadolu Kardiyol. Derg. 2014; 14: 728–732.
44. Celik T., Kaya M.G., Akpek M. et al. Predictive value of admission platelet volume indices for in-hospital major adverse cardiovascular events in acute ST-segment elevation myocardial infarction. Angiology 2015; 66: 155–162.
45. Sarli B., Baktir A.O., Saglam H. Mean platelet volume is associated with poor postinterventional myocardial blush grade in patients with ST-segment elevation myocardial infarction. Coron. Artery Dis. 2013; 24: 285–289.
46. Sezer M., Okcular I., Goren T. et al. Association of haematological indices with the degree of microvascular injury in patients with acute anterior wall myocardial infarction treated with primary percutaneous coronary intervention. Heart 2007; 93: 313–318.
47. Estévez-Loureiro R., Salgado-Fernández J., Marzoa-Rivas R. et al. Mean platelet volume predicts patency of the infarct-related artery before mechanical reperfusion and short-term mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Thromb. Res. 2009; 124: 536–540.