

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

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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

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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

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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-detector 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 $MPV \leq 8.9$ 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 $MPV \geq 11.7$ 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 przebiegu 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 reperuzji 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

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