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Platelet Indices in Patients with Acute Coronary Syndrome

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Abstract

The platelet indices Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Plateletcrit (PCT) provided by automated hematology analysis are rarely used in clinical practice. Platelets play a central role in the pathogenesis of acute coronary syndromes (ACS) and high MPV has been associated to more reactive platelets and regarded as an independent risk factor for myocardial infarction. In this study, platelet indices were evaluated in 39 patients with ACS presenting two altered biochemical parameters, C reactive protein (CRP) and creatine kinase fraction MB (CK-MB). The results obtained showed significantly higher MPV and PDW values in the group with ACS in comparison to the control group. Also observed was a weak but significant positive correlation between MPV and CK-MB. In view of findings of previous studies, which have associated macroplatelets with higher thrombotic potential our results suggest that the use of the MPV and PDW indices as additional and complementary markers may contribute to the investigation and follow-up of thrombotic risk in patients with ACS.

Keywords

Platelets, Platelet Indices, Acute Coronary Syndrome, CK-MB

1. Introduction

Coronary artery thrombosis caused by rupture of an atherosclerotic plaque is the final pathogenic mechanism of most cases with ACS, as documented by angiographic and pathologic studies. Atherosclerosis, a chronic inflammatory process, occurs as a response to an injury of the vascular endothelium with alterations in vascular permeability, exposition of adhesion molecules, lipid deposition and macrophage accumulation. This may alter

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vessel haemostatic properties as well as modify or stimulate platelet function and thrombosis. Platelets play a crucial role in unstable plaque rupture where subsequent thrombus formation amplifies the inflammatory response and leads to myocardial ischemia and clinical manifestations ranging from unstable angina (UA) to acute myocardial infarction (AMI) and sudden cardiac death [1]-[3].

The progression of atherosclerotic lesions seems to concur with increased thrombopoiesis activation where the cytoplasmic maturation of megakaryocytes is faster than the nuclear maturation, originating macroplatelets that produce more thromboxane A2 and show greater reactivity in platelet aggregation curves. These observations emphasize that MPV may be considered an indicator of platelet function [4]. Large platelets have also been reported in patients with vascular risk factors and have also been associated with myocardial damage in acute coronary syndromes with an unfavorable outcome of acute myocardial infarction observed in survivors [5] [6]. In laboratory analyses, macroplatelets can be identified in a complete blood count (CBC) by observing blood extension and platelet indices, which are not frequently used in clinical practice. The difficulty in standardizing reference values for platelet indices might partially explain the lack of use of these indices in the laboratory [7].

2. Materials and Methods

2.1. Patients

Thirty-nine males with acute coronary syndrome (ACS) were selected from the Hospital Regional de Osasco, SP, Brasil. The patients median age was 69 (61 - 78) and the inclusion criteria were those of American College of Cardiology and European Society of Cardiology, including chest pain and new or presumed new ECG alterations. Patients with history of infection or inflammation during the last 15 days, or with hepatic and renal disease were excluded from the study. A control group of 44 healthy individuals matched by age was selected to set the reference values for platelet indices.

All patients were hospitalized and taking anti-platelet medication. Biochemical parameters inclusion criteria were C Reactive Protein (CRP), Creatine Kinase (CK) and Creatine Kinase fraction MB (CK-MB) altered with maximum concentration of CK-MB or CRP exceeding the 99th percentile of upper limit. The study was approved by the UNISA Research Ethics Committee (CEP-UNISA, process n˚219/09). All participants signed an informed consent form.

2.2. Methods

For each patient (ACS) and control (CG), 10 mL of blood were collected and distributed in two vacutainer® tubes; the first tube, containing no anticoagulant was centrifugated and the serum used for biochemical determination of CRP, CK and CK-MB in the analyzer XL-600, Testline, Transasia Bio-Medicals Ltd. Reference values: CRP < 5 mg/L; CK: 24 - 190 U/L; CK-MB: 1 - 25 U/L.

Platelet indices and platelet counting determination were obtained from blood samples collected in the second tube using EDTA as anticoagulant. For platelet count (PLC), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT), samples were analyzed within 30 minutes after collection with Pentra 80®, Horiba-ABX, automated cell counter. The reference values adopted for platelet indices were obtained based on the mean ± 2SD of the results from controls: Platelets: 196,500 - 260,000/mm^3; MPV: 7.6 - 9.3 fL; PDW: 12.6% - 16.2%; PCT: 0.09% - 0.29%.

2.3. Statistical Analysis

Results were presented as mean ± SD. Data was analyzed using SPSS version 15. Categorical variables were analyzed by chi-square test and the continuous variables with student “t” test. Correlation between continuous variable was determined by Pearson’s correlation test. P value < 0.05 (5%) was considered to be statistically significant.

3. Results

Mean platelet count and platelet indices are shown in **Table 1**. Comparative results showed a significantly lower value for platelet count in patients with ACS. A significant higher MPV and PDW ($P < 0.01$) were observed in these patients as can be seen in **Figure 1**. **Table 2** compares the mean values for CKMB and CRP in both groups ACS and CG.

Table 1. Mean and standard deviation (M ± SD) values of platelets count and platelet indices in the ACS and control groups.

Group	PTL (/mm^3)	MPV (fL)	PDW (%)	PCT (%)
CG (n = 44)	228 ± 31	8.1 ± 0.6	14.1 ± 1.7	0.19 ± 0.1
ACS (n = 39)	172 ± 39*	9.6 ± 0.9*	16.7 ± 2.8*	0.16 ± 0.1

*P < 0.01; PTL = platelet count; CG = control group; ACS = acute coronary syndrome.

Table 2. Mean and standard deviation (M ± DP) values of the biochemical parameters analyzed in the ACS and control groups.

Group (U/L)	CKMB	CK (U/L)	CRP (mg/L)
CG (n = 44)	13.0 ± 3.5	93 ± 41	22.3 ± 1.3
ACS (n = 39)	60.1 ± 10.6	228.5 ± 123.6	34.0 ± 27.2

CG = control group; ACS = acute coronary syndrome.

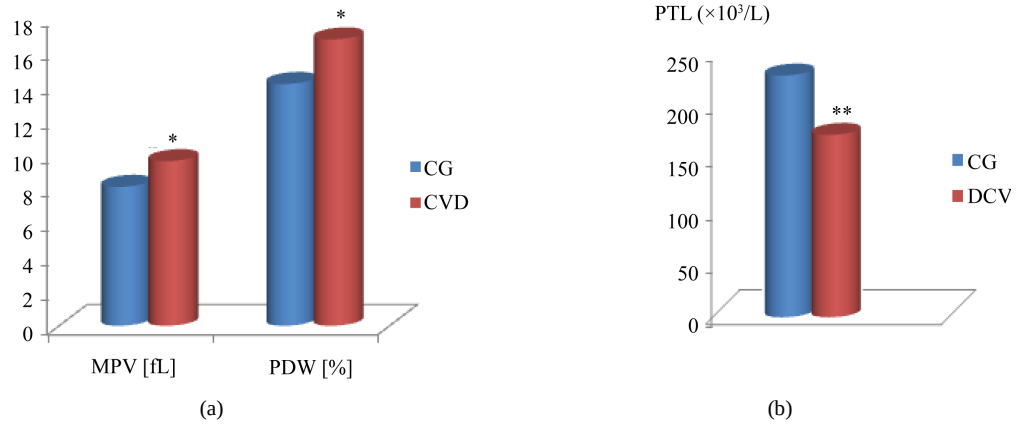

Figure 1. (a) Mean of MPV and PDW results in control (CG) and CVD patients (*P < 0.01); (b) Mean of platelet count in controls and CVD patients (**P < 0.01).

Pearson's correlation test was positive but not significant for most variables when compared to biochemical markers and platelet indices. A significant correlation (P < 0.05) was only observed between CKMB and VPM (**Figure 2**).

4. Discussion

The findings of the present study showed significantly higher PDW and MPV values in patients with ACS when compared to the control group (P < 0.01). According to previous studies, increased prothrombotic activity might be evaluated by platelet histogram indices and the presence of macroplatelets since evidence of high MPV is associated with a greater aggregation potential inducing thrombus formation, which constitute a risk factor for unstable angina, myocardial infarction, and stroke [4] [8]. In spite of the small sample of the present study, our results corroborate previous findings that emphasize the essential role of platelets in ACS, suggesting that MPV and PDW are indeed related to the presence of platelets with different sizes including macroplatelets that may contribute as independent hematological marker to cardiovascular risk [9]-[11].

All patients in this study were under anti-platelet therapy. It has been shown that MPV values vary between different ethnicities and can be altered by medication and illness [2]. Effects of anti-platelet therapy on MPV values have been investigated in other studies. Guthikonda *et al.* demonstrated that large platelets are associated with increased platelet reactivity in patients with coronary artery disease being treated with both aspirin and clopidogrel [12]. A recent study showed an increased fraction of immature platelets in patients with ST-segment myocardial infarction using aspirin which seems to have an important effect and can perhaps be associated to the development of acute coronary thrombosis [13]. Controversially, in a study of 62 patients with acute coronary

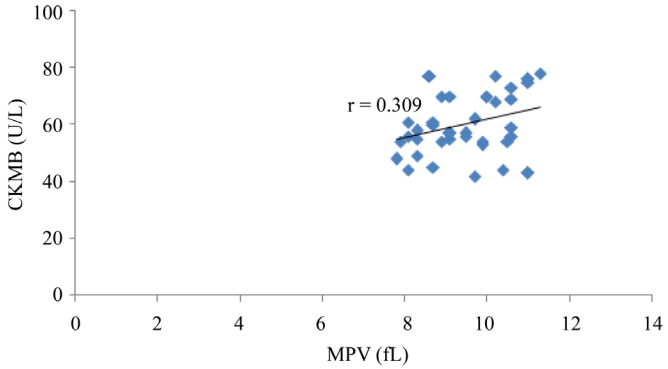

Figure 2. Pearson's correlation: positive correlation between CKMB and MPV ($P < 0.05$).

syndrome under aspirin therapy although a significant increase in MPV, with a reduction in platelet count was found, they observed that larger MPV does not necessarily imply higher platelet reactivity and may not monitor the efficacy of anti-platelet therapies [14].

Biomarkers play an important role in the diagnosis of ACS. Among these, cardiac troponin and creatine kinase MB appear to be the most sensitive and specific markers of myocardial injury. Creatinine kinase MB is one of the three CK isoenzymes present primarily in cardiac muscle. CK-MB is rapidly released after myocardial infarction (MI), rises to twice the normal levels 4 to 6 hours after symptoms and peaks within 12 to 24 hours, returning to normal in 48 - 72 hours. Its value in the early and late diagnosis of acute MI is limited. However, CK-MB is an essential component in assessing re-infarction or infarct extension in patients [15]. Also elevation of CK-MB levels is strongly related to mortality in ACS patients. When associated with pathologically demonstrable myocardial necrosis, minor CK-MB elevation maybe a marker of ongoing vascular instability resulting in recurrent platelet clumps and microscopic infarction [16]. Our results showed a significant positive correlation between MPV and absolute CK-MB levels ($r = +0.309$, $P < 0.05$), suggesting that MPV analysis could be an additional tool for diagnostic investigation of MI risk when CK-MB levels are above normal. Since there is no information about the patients outcome in this study, future research is needed to clarify this issue.

Also for risk stratification and to confer greater cardiac specificity both absolute CK-MB and the CK-MB relative index (CK-MB as a percentage of total CK) have been used in this study, although the World Health Organization international diagnostic criteria, and several others, recommend use of absolute CK-MB [17]. We found 21 patients (55%) with CK-MB relative index > 5% and confirmed the MI diagnosis; 12 patients (30%) with relative index between 3% and 4.9%; and 6 patients (15%) with CK-MB relative index between 2% and 2.9%. Statistical analysis was performed in these groups as separated for VPM, PDW and platelet count. Except for a significantly lower platelet count on group with CK-MB relative index > 5% (21 patients) when compared to the ACS group (39 patients), the other results showed the same pattern observed when using absolute CK-MB levels (data not show).

Osuna *et al.* investigated the influence of MPV on death rates, recurrent ischemia, and heart failure during the hospitalization and showed that an MPV > 9fL was related to an independent increase of combined death rate, heart failure, and ischemic events after myocardial infarction (MI). In the present study we found that 27 patients (69%) with a history of MI had a MPV > 9fL, suggesting that a risk stratification system for MPV and acute coronary syndrome is worthy of consideration [18]. Schultheiss *et al.* reported that platelets continue to circulate in an activated state after MI considering that CK-MB elevation and decrease in platelet count might possibly constitute a prognostic factor for the short-term outcome in these patients [19]. We observed a significantly lower platelet count in patients with ACS ($172 \pm 39 \times 10^3/mm^3$, $p < 0.01$) when compared to controls ($228 \pm 31 \times 10^3/mm^3$); that, in the presence of MPV and PDW alterations, might be related to greater reactivity and, consequently, to greater platelet consumption due to atheromatous and/or inflammatory lesions in these patients.

5. Conclusions

In conclusion, the results of the present study appear to confirm and substantiate that an increased MPV contri-

butes to the prothrombotic state in ACD and that larger platelets may also play a specific role in MI. Hence, the use of platelet indices in laboratory routines could be an important complement in the assessment and follow-up of cardiac patients, since these indices are easily provided by automated equipment when a complete blood count is requested by the attending physician.

Future studies including the use of MPV and platelet count as a cost effective tool in a risk stratification system to predict acute coronary events as well as the response to medical interventions are worthy of consideration.

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Declaration of Conflicting Interests

The authors declare no conflict of interest in regards to research, authorship, and/or publication of this article.

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