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COMPLETE TITLE: RELATIONSHIP BETWEEN ABDOMINAL OBESITY, PLATELET BLOOD COUNT AND MEAN PLATELET VOLUME IN PATIENTS WITH METABOLIC SYNDROME

Abstract: There is evidence that patients with the metabolic syndrome have altered platelet indices including higher mean platelet volume. According to the 2009 International Diabetes Federation criteria of metabolic syndrome diagnosis, elevated waist circumference (≥94 cm in M, ≥80 cm in F), as a determinant of abdominal obesity, is not an obligatory component.

Purpose: The aim of this study was to evaluate the relationship between platelet indices, including mean platelet volume, and abdominal obesity in patients with metabolic syndrome.

Methods: 382 consecutive patients were enrolled in the study and divided into three groups: group A, 218 patients with metabolic syndrome and abdominal obesity (132 M, mean age 65.3 ± 10.9 yrs); group B, 35 patients with metabolic syndrome without abdominal obesity (28 M, mean age 63.3 ± 11.2 yrs); and, group C, 129 patients without metabolic syndrome and without abdominal obesity (99 M, mean age 62.2 ± 13.8 yrs).

Results: In group A, mean platelet volume was significantly higher than in group C (10.70 ± 1.01 vs. 10.35 ± 0.94 fL, p = 0.007). However, there was no difference in mean platelet volume between group A and B (10.70 ± 1,01vs. 10.63 ± 1.03 fL, p >0.05). Furthermore, in group A, mean platelet volume was correlated with waist circumference (r = 0.14, p = 0.041) and body mass index (r = 0.14, p = 0.045). In all study groups, a significant association between mean platelet volume and platelet count (r = –0.33, p <0.001) was found.

Conclusion: In individuals with metabolic syndrome and abdominal obesity mean platelet volume is positively correlated with waist circumference and significantly higher than in patients without these abnormalities.

Key words: platelets activity, mean platelet volume, abdominal obesity, metabolic syndrome, cardiovascular risk.

INTRODUCTION

The risk for developing cardiovascular disease is linked to a group of common disorders (including obesity, diabetes, dyslipidemia and hypertension) which are collectively termed the metabolic syndrome [1]. Abdominal obesity is one of a most

prevalent risk factor of cardiovascular disease. According to the current definition, the metabolic syndrome may be diagnosed in individuals who do not meet the criterion of elevated waist circumference, as a marker of abdominal obesity (e.g. for the European population waist circumference of ≥94 cm in M, ≥80 cm in F) [2]. Abdominal obesity together with the metabolic syndrome can favour the development of atherosclerosis, which is the main cause of coronary disease [3]. However, patients without abdominal obesity, but who meet other criteria of the metabolic syndrome, are still prone to development of cardiovascular disease. Such patients are often described as 'metabolically obese normal weight individuals' (MONW) [4].

The search for simple markers that allow for early identification of the patients being at highest risk from cardiovascular events is ongoing. Considering the increasing social problem of the metabolic syndrome and abdominal disease, proper recognition of the risk and early prevention of cardiovascular disease is crucial.

In the pathophysiology of ischaemic heart disease, the process of platelet activation plays an essential role [5]. Mean platelet volume (MPV) is an accessible marker of platelet activity [6, 7]. Platelets with a high volume produce a considerable amount of the vasoactive and haemostatic substances, such as thromboxane A2, serotonin or adenosine triphosphate (ATP), causing them to aggregate more quickly. Moreover, there are numerous adhesion molecules on the platelet surface, which participate in thrombus formation [8, 9]. Thus, increased MPV value is connected to the hyperaggregability and shortened time of coagulation [10].

Recent studies have assigned the process of platelet activation as vital for the development of cardiovascular disease [11]. The increased MPV is associated with increased risk of cardiac arrest, including death as its aftermath, and an elevated risk of a restenosis after coronary angioplasty [11]. Similarly, in patients with cerebral stroke, an increased MPV has been observed signaling increased platelet activity [12]. It has also been shown that patients with the metabolic syndrome have an increased MPV value and thus, have an increased risk of cardiovascular disease [13]. However, the importance of the MPV value has not been fully investigated in patients with the metabolic syndrome that do not meet the abdominal obesity criteria.

The aim of the study was to assess the correlation between the platelet markers, especially the MPV, and the incidence of abdominal obesity in patients with the metabolic syndrome. Similarly, whether MPV is determined by the degree of abdominal obesity was investigated. Moreover, we highlight the potential of MPV as a simple marker to allow for early identification of patients with an increased risk of cardiovascular disease.

MATERIALS AND METHODS

The retrospective analysis included 382 patients hospitalized in 2009–2010 in the Department of Coronary Disease of the Jagiellonian University Medical College [Klinika Choroby Wieńcowej Instytutu Kardiologii Uniwersytetu Jagiellońskiego Collegium Medicum]. The inclusion criteria were: diagnosis of metabolic syndrome according to the International Diabetes Federation definition from 2009 (Table 1), age 18–90 years old and taking acetylosalicic acid 75 mg per day. The exclusion criteria for the study were: decompensation of heart failure, thromboembolic disease and acute inflammation upon admission, taking any antiplatelet agent other than acetylosalicic acid, diagnosed cancer.

Table 1

Diagnosis of metabolic syndrome in patients included into the study was based on a co-occurrence of three out of five of the following criteria [2].

Elevated waist circumference, for the European population ≥94 cm in M and ≥80 cm in F
Elevated triglycerides ≥1.7 mmol/L (150 mg/dL) or drug treatment for elevated triglycerides (fibrates)
Reduced HDL-C <1.0 mmol/L (40 mg/dL) in M and <1.3 mmol/L (50 mg/dL) in F or drug treatment for reduced HDL-C (fibrates)
Elevated blood pressure: systolic ≥130 mmHg and/or diastolic ≥85 mmHg or antihypertensive drug treatment in a patient with a history of hypertension
Elevated fasting glucose ≥5.6 mmol/L (100 mg/dL) or drug treatment of elevated glucose

Abbreviations: HDL-C — high density lipoprotein cholesterol, M — male, F — female

The anthropometric measurements were conducted in all patients upon admission to the hospital including height, body mass and waist circumference. On the basis of metabolic syndrome and abdominal obesity diagnosis patients were divided into three study groups: group A, 218 patients with metabolic syndrome and abdominal obesity; group B, 35 patients with metabolic syndrome without abdominal obesity; and group C (control group), 129 patients without metabolic syndrome and without abdominal obesity. Selected platelet indices such as MPV and platelet blood count were measured for each patient by means of an automatic hematology analyzer SYSMEX XS-1000i in the Analytical Laboratory in the John Paul II Hospital in Krakow. Platelet blood count and MPV value were determined with use of impedance method and hydrodynamic focusing method.

The STATISTICA 10 software package was used to compare the platelet marker values (such as MPV and the platelet count), the demographic data, the incidence of ischemic heart disease and chronic heart failure between the three groups. To compare quantitative variables, the analysis of variance (ANOVA) or

its nonparametric counterpart (the Kruskal–Wallis one-way analysis of variance by ranks) were used. For qualitative variables, the chi square test (X^2) was used. The post-hoc tests included the Scheffe's method and the least significant difference test (LSD). In order to assess the correlation between MPV value and other examined variables, the Pearson correlation coefficient and the Spearman correlation coefficient were implemented.

RESULTS

The basic characteristics and drug treatment in the examined groups are presented in Table 2 and Table 3. The examined groups did not differ significantly

Table 2

Basic characteristics of the study groups.

Parameter	Group A n = 218	Group B n = 35	Group C n = 129	*P* value (between marked groups)
Male, n (%)	132 (60.6)	28 (80)	99 (76.7)	0.035[a]
Age, [years]	65.3 ± 10.9	63.3 ± 11.2	62.2 ±13.8	NS
Body mass, [kg]	84.2 ± 14.1	70.3 ± 10.1	65.1 ±9.8	<0.0001[a,c]
BMI, [kg/m^2]	29.4 ± 4.1	24.3 ± 2.1	23 ± 2.7	<0.0001[a,c]
Waist circumference, [cm]	102.9 ± 13.3	85.3 ± 7.6	82.9 ± 7.4	<0.0001[a,c]
Abdominal obesity, n (%)	218 (100)	0	0	<0.0001[a,c]
Hypertension, n (%)	205 (94)	34 (97.1)	19 (14.7)	<0.0001[a,b]
Diabetes mellitus type 2, n (%)	88 (40.4)	15 (42.9)	4 (3.1)	<0.0001[a,b]
IGT, n (%)	31 (14.2)	4 (11.4)	4 (3.1)	NS
IFG, n (%)	31 (14.2)	5 (14.3)	1 (0.8)	NS
Hypercholesterolemia, n (%)	116 (53.2)	21 (60)	81 (62.8)	NS
Hypertriglyceridemia, n (%)	18 (8.3)	1 (2.9)	3 (2.3)	NS
Mixed hyperlipidemia, n (%)	64 (29.4)	13 (37.1)	16 (12.4)	0.03[a]
Ischemic heart disease, n (%)	199 (91.3)	33 (94.3)	102 (79.1)	NS
Chronic heart failure, n (%)	54 (24.8)	9 (25.7)	28 (21.7)	NS
Diastolic dysfunction, n (%)	96 (44)	14 (40)	63 (48.8)	NS
LVEF, [%]	51.7 ± 11.7	53.4 ± 11.1	51.8 ± 13.8	NS

a gr. A vs. gr. C; b gr. B vs. gr. C; c gr. A vs. gr. B;
Data are expressed as mean ± standard deviation or number of patients (percentage).
Abbreviations: BMI — body mass index; IFG — impaired fasting glucose; IGT — impaired glucose tolerance; LVEF — left ventricle ejection fraction.

Table 3

Drug treatment in study groups.

Drug	Group A n = 218	Group B n = 35	Group C n = 129	*P* value (between marked groups)
ASA, n (%)	218 (100)	35 (100)	129 (100)	NS
Clopidogrel, n (%)	0	0	0	NS
Antidiabetic drugs, n (%)	68 (31.2)	10 (28.6)	3 (2.3)	<0.0001[a]
Insulin, n (%)	30 (13.8)	4 (11.4)	2 (1.6)	NS
Statin, n (%)	202 (92.7)	33 (94.3)	101 (78.3)	NS
Fibrate, n (%)	9 (4.1)	1 (2.9)	4 (3.1)	NS
ACEI/ARB, n (%)	205 (94)	34 (97.1)	88 (68.2)	0.0002[a] 0.0259[b]
Beta blocker, n (%)	189 (86.7)	32 (91.4)	81 (62.8)	0.0006[a] 0.0280[b]
Diuretic, n (%)	108 (49.5)	14 (40)	42 (32.6)	0.025[a]
Calcium channel blocker, n (%)	65 (29.8)	8 (22.9)	31 (24)	NS
Alpha blocker, n (%)	18 (8.3)	1 (2.9)	7 (5.4)	NS

a gr. A vs. gr. C; b gr. B vs. gr. C; c gr. A vs. gr. B;
Data are expressed as number of patients (percentage).
Abbreviations: ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; ASA — acetylsalicylic acid.

according to the incidence of ischemic heart disease. Similarly, the increase of the angina pectoris symptoms in all groups was comparable — the median angina grade was II according to Canadian Cardiovascular Society (CCS) scale. Furthermore, there were no differences in the incidence of chronic heart failure, left ventricular ejection fraction value, or the incidence of the left ventricular diastolic dysfunction, assessed on the basis of transthoracic echocardiograms.

Considering the platelet parameters, the platelet blood count did not differ significantly between the examined groups. However, there were some differences in the MPV values. The highest MPV value was observed in the metabolic syndrome and abdominal obesity group (group A) and this value was statistically significant from the patients with no metabolic syndrome (group C). This analysis has not revealed any considerable differences in the MPV value between groups with metabolic syndrome (groups A and B) (Table 4).

Moreover, only in patients with metabolic syndrome and abdominal obesity (group A), a weak but statistically significant correlation between the MPV value and waist circumference and the body mass index (BMI) was observed ($r = 0.14$, $p = 0.041$, and $r = 0.14$, $p = 0.045$, respectively) (Fig. 1, 2). In all examined groups, a negative correlation between the MPV value and platelet blood count was shown ($r = -0.33$, $p < 0.001$) (Fig. 3).

Table 4

Laboratory parameters between study groups.

Parameter	Group A n = 218	Group B n = 35	Group C n = 129	*P* value (between marked groups)
PLT, [×10^9/L]	225.8 ± 79.1	224.5 ± 57.1	226.0 ± 69.7	NS
MPV, [fL]	10.70 ± 1.01	10.63 ± 1.03	10.35 ± 0.94	0.007[a]
TC, [mmol/L]	4.68 ± 1.35	4.59 ± 1.16	4.89 ± 1.29	NS
TG, [mmol/L]	1.47 ± 0.89	1.39 ± 0.83	1.09 ± 0.72	0.0004[a]
LDL-C, [mmol/L]	2.68 ± 1.02	2.62 ± 0.97	2.86 ± 1.03	NS
HDL-C, [mmol/L]	1.17 ± 0.32	1.23 ± 0.31	1.29 ± 0.31	0.003[a]

a gr. A vs. gr. C; b gr. B vs. gr. C; c gr. A vs. gr. B;
Data are expressed as mean ± standard deviation.
Abbreviations: PLT — platelet count; MPV — mean platelet volume; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; TC — total cholesterol, TG — triglycerides

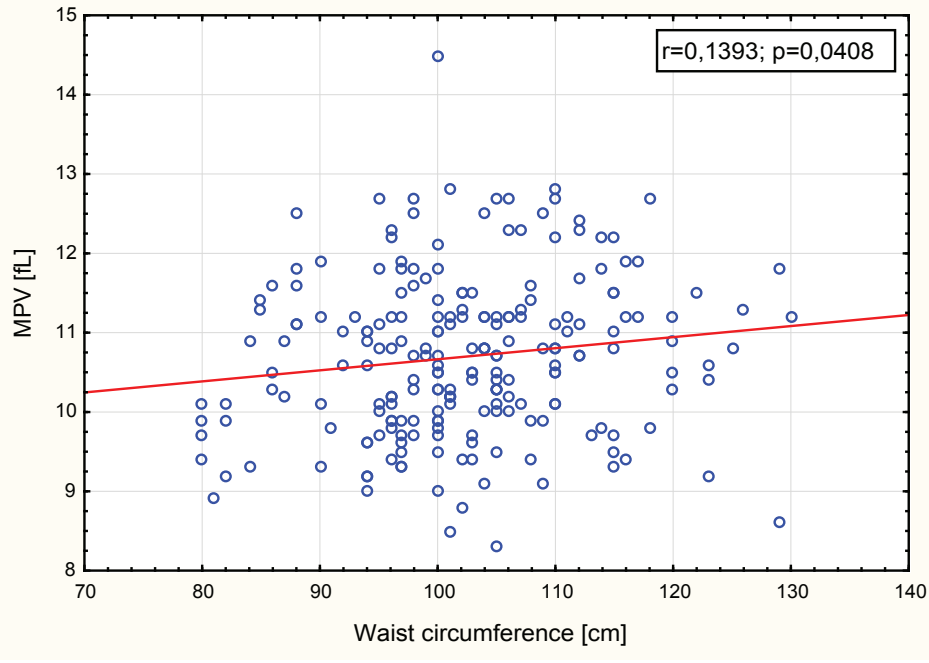

Fig. 1. Correlation between mean platelet volume (MPV) and waist circumference in patients with metabolic syndrome and abdominal obesity (group A).

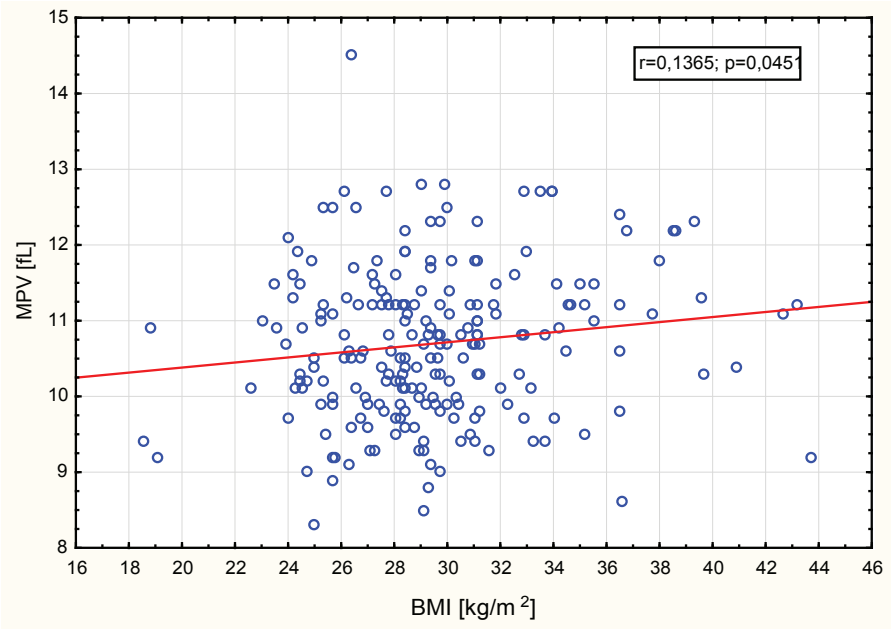

Fig. 2. Correlation between mean platelet volume (MPV) and body mass index (BMI) in patients with metabolic syndrome and abdominal obesity (group A).

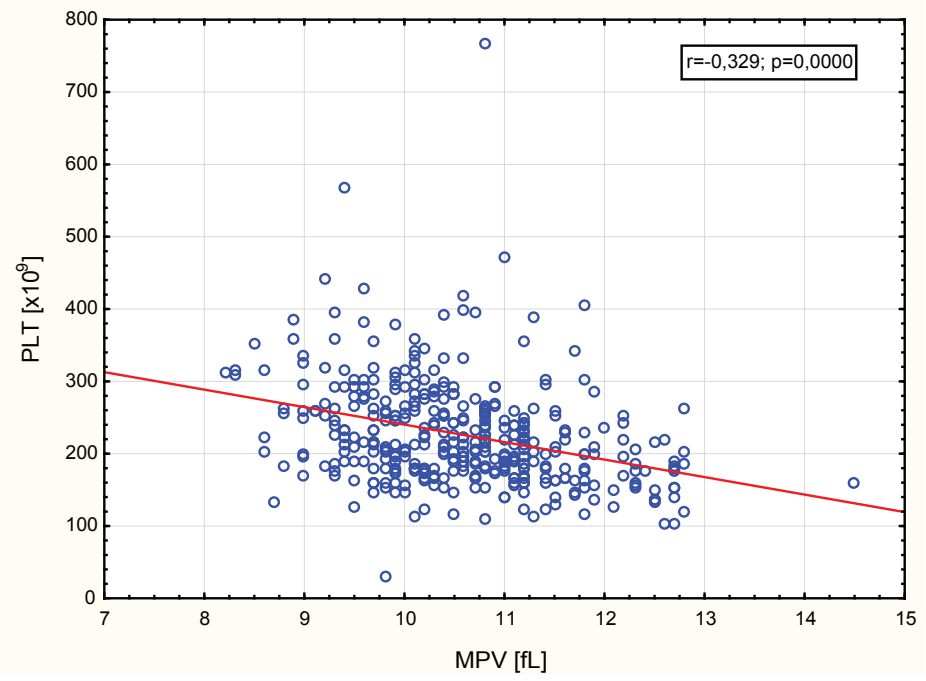

Fig. 3. Correlation between platelet count (PLT) and mean platelet volume (MPV) in study population.

DISCUSSION

Patients with the metabolic syndrome are characterized by increased platelet activity and thus, are more prone to cardiovascular disease. To date, the occurrence of abdominal obesity in patients with metabolic syndrome has not been proven to affect the platelet size considerably. However, in patients with abdominal obesity, there is a correlation between their waist circumference and the volume and activity of their platelets. Indeed, current studies have revealed that in obese individuals, the MPV value is larger compared to those of healthy weight [14]. Moreover, body mass reduction in these obese individuals is correlated with a decrease in their MPV value [15, 16].

The precise correlation mechanism between abdominal obesity and the activity of platelets has not been thoroughly explained. It is certain that in the obese patients there is a considerable amount of a metabolically active adipose tissue covering the organs in the abdominal cavity. This adipose tissue constitutes an endocrine organ secreting numerous active substances [17]. For example, the adipose tissue secretes a considerable amount of the plasminogen activator inhibitor-1 (PAI-1), which is responsible for inhibition of fibrinolysis, the physiological process of atherothrombus decomposition [18].

The adipose tissue also has an increased sensitivity to adrenergic stimulation, which increases the release of free fatty acids into the portal venous system. These free fatty acids will, in turn, influence liver metabolism, favouring the release of glucose and production of very-low-density lipoproteins (VLDL) [19]. As a result, development of lipid disorders, glucose metabolism disorders and hyperinsulinemia begin [20]. Insulin is a hormone that stimulates the creation of bigger platelets in a process termed megakaryocytopoiesis [20]. The presence of these high volume platelets in patients indicates an increased consumption of smaller volume platelets [21]. The increased platelet rotation results in a reverse correlation between the total number of platelets and MPV as the organism maintains a constant level of total platelet mass [22]. Furthermore, the increased consumption of small platelets constitutes a strong stimulus for the creation of bigger platelets from megakaryocytes in bone marrow [23].

Although no correlation between MPV value and accompanying occurrence of abdominal obesity has been found in patients with the metabolic syndrome, the probability of its existence cannot be excluded. One should bear in mind that in the study described above the group of patients with the metabolic syndrome and without abdominal obesity was rather small (35 patients). Currently, the criteria for abdominal obesity diagnosis are more strict than before. It is also worth highlighting that the occurrence of risk factors such as diabetes, hypertension or lipid disorders are considerably more frequent in patients with abdominal obesity, which often initiates the metabolic syndrome development. Hence, there are few individuals with metabolic syndrome of normal body weight. Current research

shows that in the Polish population fewer than 1% of people [24] with normal body weight meet the criteria of the metabolic syndrome, while in the European population the percentage is 7% [25]. Considering the complexity of metabolic disorders present in patients with the metabolic syndrome, further investigation of factors influencing cardiovascular risk in this group is recommended.

To conclude, MPV is a simple, low-cost and accessible marker of platelet activity that could be used in everyday clinical practice to assess cardiovascular risk. The marker is especially useful in patients with the metabolic syndrome and abdominal obesity for its value correlates positively with waist circumference. The combination of these two intertwined indices could possibly enable easy identification of patients with a high risk of cardiovascular disease for early implementation of effective prevention methods. It is worth promoting the application of these simple indices in clinical practice. As body mass reduction may ultimately lead to a reduction in platelet volume, it may be profitable to use MPV not only as a risk marker but also as a therapeutic goal.

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