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Original research article

Association between mean platelet volume and adiponectin in patients with metabolic syndrome

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Abstract
Background: Metabolic syndrome is a significant pro-inflammatory and pro-coagulant condition. The clinical association of adiponectin, a mainly antidiabetogenic molecule, and its interaction with platelets and platelet indices remains insufficiently investigated.
Objective: The aim of our study was to investigate the association of adiponectin with platelets and platelet indices in patients with metabolic syndrome.
Methods: The investigation was conducted as a cross-sectional study involving 113 subjects: 63 patients with the diagnosis of metabolic syndrome, and 50 healthy controls – with clear inclusion and exclusion criteria. The group of patients with metabolic syndrome was divided into two subgroups according to the platelet/high-density lipoprotein (HDL) ratio.
Results: The subgroup with a higher platelet/HDL ratio was prediabetic. In the same subgroup of patients, a positive correlation between the adiponectin and mean platelet volume (MPV) was seen, while linear regression (95% CI) confirmed the association.
Conclusion: Considering that MPV is the index that indicates average platelet volume and activity, we believe this association with adiponectin can represent a protective compensatory response in patients with metabolic syndrome and prediabetes. Our results provide a basis for a more precise selection of patients in whom the future therapeutic application of recombinant adiponectin would be most effective.

Keywords: Adiponectin; Mean platelet volume; Metabolic syndrome; Platelets

Highlights:
- We showed a positive association between MPV and adiponectin.
- MPV and adiponectin could be early markers for the evaluation of thrombogenic risk.
- Our results are important for the future therapeutic use of recombinant adiponectin.

Introduction

Metabolic syndrome is a pathological condition with a continuously increasing incidence globally (Saklayen, 2018). Some of the main characteristics of metabolic syndrome are the development of a low-grade inflammatory state and increased thrombogenic potential (Devaraj et al., 2004). Both of these conditions, which develop simultaneously, have a significant pathophysiological connection, which is predominantly reflected through the function of platelets and their interaction with leukocytes and monocytes (Hottz et al., 2022; Schrottmaier et al., 2020). Modern lifestyle, bad eating habits, insufficient physical activity, and lack of sleep are considered to be some of the most important factors that contribute to the increase in the incidence of this condition (Cornier et al., 2008). As one of the obesity-related diseases, metabolic syndrome is considered a condition that precedes type 2 diabetes.

Adipose tissue, an endocrine organ, produces a significant number of bioactive molecules that play an important role in maintaining metabolism and immune responses (Scheja and Heeren, 2019). Adiponectin, a 30 kDa collagen-like protein product is mainly secreted by adipocytes in white adipose tissue and has been proven to have strong antidiabetic prop-

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erties. There are three different forms of this molecule in the body: low molecular weight, middle molecular weight, and high molecular weight (HMW) (Khoramipour et al., 2021). The adiponectins HMW isoform is more biologically active than the others and plays a key role in antidiabetic properties.

Although the function of adiponectin has been investigated in numerous conditions, in the literature there is no causal association between adiponectin and some widely available routine platelet-related assays, such as platelet indices. The main objective of our study was to determine whether there is any relationship between HMW adiponectin, platelets, and platelet indices in patients with metabolic syndrome.

Materials and methods

Patients and study design

The research was conducted within the department of the daily hospital of the Clinic for Endocrinology, Diabetes and Metabolic Diseases of the University Clinical Centre Kragujevac. The investigation was conducted as a retrospective cross-sectional study involving 113 ambulatory subjects: 63 patients with the diagnosis of metabolic syndrome, and 50 healthy controls – with clear inclusion and exclusion criteria. Participants were included in the study on a non-consecutive basis. Each subject had to meet the clearly defined inclusion criteria for their respective group while simultaneously not meeting any exclusion criteria.

The control group was formed from patients who were without known previous glycoregulation disorders and who had been referred for screening to the Clinic for Endocrinology, Diabetes and Metabolic Diseases, in order to assess the potential presence of glycoregulation disorders (Diabetes Prevention Program of the Ministry of Health of the Republic of Serbia). From the pool of subjects formed in this way, only those who met the inclusion criteria without the presence of exclusion criteria were included in the study. The criteria for inclusion in the control group were: aged over 18 years and signed informed consent form. Exclusion criteria for the control group were: presence of at least one of the components of the metabolic syndrome (according to the International Diabetes Federation definition – hypertension, hyperlipidemia, dysglycemia), use of corticosteroids, antipsychotics or antidepressants, acute infection in the last 2 weeks, malignant diseases within the last 5 years, liver and kidney failure.

The diagnosis of metabolic syndrome was confirmed according to the International Diabetes Federation consensus definition (Alberti et al., 2006). The criteria for inclusion in the experimental group were: aged over 18 years, signed an informed consent form, and met the criteria for diagnosis of metabolic syndrome. Exclusion criteria from the experimental group were: previously known diabetes, subjects taking oral antidiabetics, obesity drugs, corticosteroids, antipsychotics, antidepressants, subjects who have had an acute infection in the last 2 weeks, malignant diseases within the past 5 years, or who have liver or kidney failure.

Informed consent was obtained from all subjects involved in the study. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University Clinical Centre Kragujevac, Serbia (number 01/22-432).

Clinical evaluation and sampling

During the clinical examination, anthropological parameters such as waist circumference (WC), hip circumference (HC), body mass, and height were determined. Venous blood samples were collected after a 12 h fasting period for blood count, leukocyte formula, and biochemical analysis – such as clinical parameters of inflammation (CRP, fibrinogen), lipid profile (total cholesterol, HDL, LDL, triglycerides, nonHDL cholesterol, and remnant cholesterol), and glycosylated hemoglobin A1C (HbA1c). All analysis was conducted at the laboratory of the University Clinical Center Kragujevac.

Insulin sensitivity was determined by calculating the Matsuda index. The homeostatic model assessment for insulin resistance index (HOMA-IR Index) was determined to calculate the level of relative insulin resistance. Homa beta was calculated to estimate the relative beta-cell burden. All listed indices are free and the calculation method for all mentioned indices is provided on the website: http://mmatsuda.diabetes-smc.jp/MIndex.html.

After sampling, the plasma samples were stored at a temperature of –80 °C until analysis. Adiponectin HMW level was determined by the ELISA method (Elabscience, Houston, TX, USA catalog number E-EL-H5621) following the manufacturer's instructions.

After the analysis of demographic and basic clinical parameters, we divided the group of subjects with metabolic syndrome according to platelets and HDL cholesterol ratio (platelet/HDL). The platelet/HDL ratio value of 220 was obtained by calculating the median ratio in the group of patients with metabolic syndrome, using the capabilities of the statistical analysis program SPSS version 22.

The power of the study

The study power was calculated using the G Power program, with adiponectin data from a paper by Kowalska et al., with a study power of 85% and error type α 0.05. The calculation showed the minimum sample size of 52 subjects with at least 26 subjects per group (Kowalska et al., 2008).

Statistics

Statistical analyses were conducted using the SPSS 22. Results were presented as mean ± standard deviation. The variables distribution was assessed using the Shapiro–Wilk test. *T*-test or non-parametric Mann–Whitney *U*-test were used to analyse the differences between the two groups. In those parts of the results, p was considered significant when lower than 0.05. In the results section where the three groups were compared, we used tests like ANOVA, Kruskal–Wallis, and Mann–Whitney test. To reduce the error of the first α type during the comparison of two or more groups, we used the Bonferroni correction with a significance of $p < 0.017$. The presence of a correlation between adiponectin and other parameters was checked using the Spearman correlation coefficient. The effect of other parameters on adiponectin concentration was determined using linear regression with a confidence interval (CI) of 95%.

Results

Our study included 113 subjects divided into two groups: a group of subjects with metabolic syndrome and a control group of subjects. The preliminary analysis did not show differences in gender distribution or average age between the observed groups. As expected, the group with metabolic syndrome had a significantly higher WC, triglyceride, systolic and diastolic blood pressure levels, and significantly lower HDL concentration (Table 1).

Table 1. Baseline characteristics of subjects with metabolic syndrome and the control group

		Control group	Metabolic syndrome	*P*
Gender	M F	15 (30.0%) 35 (70.0%)	26 (41.3%) 37 (58.7%)	0.149*
Age (year)		35.82 ± 10.06	38.90 ± 10.45	0.114**
Waist circumference (cm)		84.79 ± 10.44	106.98 ± 12.85	0.000***
Triglycerides (mmol/l)		1.04 ± 0.41	2.25 ± 1.51	0.000***
HDL (mmol/l)		1.39 ± 0.29	1.14 ± 0.22	0.000***
Systolic TA (mmHg)		115.67 ± 12.41	129.34 ± 17.43	0.000***
Diastolic TA (mmHg)		78.39 ± 7.41	83.23 ± 11.20	0.009**

Note: M – male, F – female, * χ^2 test, ** Independent *T*-test, *** Independent sample, statistical significance $p < 0.05$.

Table 2. Baseline characteristics of patients with metabolic syndrome stratified by gender

Characteristic	Males (n = 26)	Females (n = 37)	*p*
Age (year)	40.38 ± 8.84	37.86 ± 11.44	0.329*
Waist circumference (cm)	112.53 ± 11.99	103.08 ± 12.12	0.004**
Hip circumference (cm)	113.57 ± 12.38	116.29 ± 11.68	0.364**
Height (cm)	183.11 ± 7.17	167.02 ± 7.59	0.000**
BMI (kg/m^2)	31.88 ± 5.76	33.11 ± 6.00	0.406**
Triglycerides (mmol/l)	2.79 ± 2.07	1.91 ± 0.85	0.128**
HDL cholesterol (mmol/l)	1.11 ± 0.24	1.17 ± 0.21	0.279**
Leukocytes (×10^9)	8.26 ± 2.62	7.80 ± 2.03	0.748**
Platelets (×10^9)	243.39 ± 50.96	281.45 ± 54.74	0.005**
Systolic TA (mmHg)	133.61 ± 18.69	126.35 ± 16.06	0.407**
Diastolic TA (mmHg)	84.50 ± 9.61	82.35 ± 12.24	0.459*

Note: * Independent *T*-test, ** Independent sample, statistical significance $p < 0.05$.

Stratification of patients with metabolic syndrome by gender showed a significantly higher waist circumference (112.53 vs 103.08; $p = 0.004$) and height (183.11 vs 167.02; $p = 0.000$) in the male group, while a significantly higher platelets number (243.39 vs 284.45; $p = 0.005$) was observed in the female group. In the other observed characteristics, there were no significant differences between genders (Table 2).

After the analysis of demographic and basic clinical parameters, we divided the group of subjects with metabolic syndrome according to the value of platelet HDL cholesterol ratio below 220 and above 220. The subgroup with a lower ratio was the subgroup with milder disease, while the group with a higher platelet HDL cholesterol ratio was the subgroup with more pronounced metabolic syndrome and prediabetes (HbA1c ≥ 5.7%). The subgroup with a higher platelet HDL cholesterol ratio had significantly higher WC (107.06 vs 84.79; $p = 0.000$), HC (115.20 vs 101.55; $p = 0.000$), CRP (5.65 vs 1.03; $p = 0.000$), fibrinogen (3.53 vs 2.79; $p = 0.000$), total leukocytes (8.64 vs 6.50; $p = 0.000$), neutrophils % (59.77 vs 54.62; $p = 0.002$), neutrophils absolute number (5.30 vs 3.50; $p = 0.000$), platelets number (289.8 vs 250.5; $p = 0.000$), PCT (0.246 vs 0.224; $p = 0.014$), HOMA IR index (2.62 vs 0.91; $p = 0.000$), HbA1c (5.72 vs 5.16; $p = 0.000$), triglycerides (1.88 vs 1.04; $p = 0.000$), nonHDL (4.57 vs 3.59; $p = 0.000$), remnant cholesterol (0.80 vs 0.50; $p = 0.000$), and adiponectin (80.10 vs 65.30; $p = 0.000$) compared to the control group (Table 3 and 4). At the same time, % of lymphocytes (27.15 vs 34.37; $p = 0.003$), HDL concentration (1.04 vs 1.39; $p = 0.000$), and Matsuda index (5.16 vs 12.35; $p = 0.000$) were significantly lower in this subgroup compared to the control group. Although the absolute number of monocyte, Homa beta values, concentration of LDL, and total cholesterol were highest in this subgroup too, the differences did not reach the level of statistical significance.

During the comparison of the parameters of two subgroups of patients with metabolic syndrome, significantly higher levels of CRP (5.65 vs 3.07; $p = 0.001$), total leukocytes (8.64 vs 7.34; $p = 0.015$), and PCT (0.246 vs 0.208; $p = 0.000$) were observed in the group with more pronounced disease, with an expected higher platelets number (289.8 vs 233.8; $p = 0.000$) and a lower HDL (1.04 vs 1.27; $p = 0.000$) (Table 3 and 4).

Table 3. Metabolic characteristics of patients with metabolic syndrome subgroups and control groups

	Control group (n = 50)	Platelets/HDL ratio <220 (n = 33)	Platelets/HDL ratio >220 (n = 30)	*P*	*P* 1vs2	*P* 1vs3	*P* 2vs3
HbA1c (%)	5.16 ± 0.40	5.50 ± 0.41	5.72 ± 0.48	0.000*	0.004	0.000	0.153
Matsuda	12.35 ± 6.72	6.20 ± 5.07	5.16 ± 2.82	0.000**	0.000	0.000	0.928
HOMA IR	0.91 ± 0.45	2.55 ± 1.81	2.62 ± 1.55	0.000**	0.000	0.000	0.705
HOMA Beta	105.39 ± 63.55	116.61 ± 79.86	137.95 ± 79.55	0.291**	0.845	0.102	0.313
LDL (mmol/l)	3.08 ± 0.79	3.65 ± 1.23	3.66 ± 1.09	0.062**	0.105	0.028	0.863
Triglycerides (mmol/l)	1.04 ± 0.41	1.92 ± 0.92	1.88 ± 0.83	0.000**	0.000	0.000	0.098
HDL cholesterol (mmol/l)	1.39 ± 0.29	1.27 ± 0.23	1.04 ± 0.16	0.000*	0.092	0.000	0.002
Total cholesterol (mmol/l)	4.98 ± 0.98	6.04 ± 1.38	5.61 ± 1.27	0.003**	0.001	0.043	0.203
nonHDL cholesterol (mmol/l)	3.59 ± 0.89	4.67 ± 1.40	4.57 ± 1.20	0.000**	0.001	0.000	0.842
Remnant cholesterol (mmol/l)	0.50 ± 0.23	0.99 ± 0.45	0.80 ± 0.28	0.000**	0.000	0.000	0.180
Adiponectin (ng/ml)	65.30 ± 15.99	76.23 ± 14.96	80.10 ± 14.18	0.001**	0.013	0.000	0.240

Note: * ANOVA, ** Kruskal–Wallis Test, statistical significance $p \leq 0.017$.

Table 4. Main anthropometric and blood analysis of patients with metabolic syndrome subgroups and control groups

	Control group (n = 50)	Platelets/HDL ratio <220 (n = 33)	Platelets/HDL ratio >220 (n = 30)	P	P 1vs2	P 1vs3	P 2vs3
Waist circumference (cm)	84.79 ± 10.44	107.63 ± 14.04	107.06 ± 11.98	0.000**	0.000	0.000	0.859
Hip circumference (cm)	101.55 ± 9.00	114.59 ± 12.33	115.20 ± 10.26	0.000*	0.000	0.000	1.00
CRP (ml/l)	1.03 ± 0.69	3.07 ± 3.00	5.65 ± 3.77	0.000**	0.000	0.000	0.001
Fibrinogen (g/l)	2.79 ± 0.47	3.26 ± 0.73	3.53 ± 0.51	0.000*	0.002	0.000	0.239
Leukocytes ($\times 10^9$)	6.50 ± 1.31	7.34 ± 2.20	8.64 ± 2.08	0.000**	0.085	0.000	0.015
Neutrophils (%)	54.62 ± 5.87	58.02 ± 6.61	59.77 ± 10.19	0.01**	0.111	0.003	0.202
Lymphocytes (%)	34.37 ± 5.23	30.53 ± 5.87	27.15 ± 7.15	0.003*	0.202	0.002	0.340
Monocytes (%)	8.02 ± 1.68	7.94 ± 1.48	6.99 ± 1.31	0.084*	1.00	0.124	0.222
Neutrophils ab. number	3.50 ± 0.66	4.36 ± 1.89	5.30 ± 1.58	0.001**	0.179	0.000	0.035
Lymphocytes ab. number	2.20 ± 0.52	2.12 ± 0.53	2.35 ± 0.60	0.432*	1.00	1.00	0.603
Monocytes ab. number	0.51 ± 0.16	0.58 ± 0.25	0.59 ± 0.18	0.382**	0.393	0.187	0.557
Platelets ($\times 10^9$)	250.5 ± 45.5	233.8 ± 43.5	289.8 ± 46.3	0.000**	0.062	0.000	0.000
PCT (%)	0.224 ± 0.032	0.208 ± 0.029	0.246 ± 0.039	0.000**	0.015	0.014	0.000
MPV (femtoliter)	8.59 ± 0.60	8.92 ± 0.85	8.55 ± 0.76	0.126**	0.076	0.442	0.099
PDW (%)	16.19 ± 0.76	16.75 ± 0.61	16.24 ± 0.42	0.002**	0.002	0.809	0.002

Note: * ANOVA, ** Kruskal–Wallis Test, statistical significance $p \leq 0.017$.

Correlation analysis showed a positive correlation between MPV and adiponectin (0.431 p = 0.017) in the subgroup of subjects with metabolic syndrome, higher platelet/HDL ratio, and prediabetes (Table 5).

Linear regression showed that MPV represents an independent predictor [β 0.431; p = 0.018 (95% CI)] of adiponectin concentration in the subgroup of patients with metabolic syndrome, prediabetes, and high platelet/HDL ratio.

Table 5. Correlation of platelets, platelet indices, and adiponectin in patients with metabolic syndrome and the control group

Correlation table (Spearman rho)					
Control group		Platelets/HDL ratio <220		Platelets/HDL ratio >220	
	Adiponectin		Adiponectin		Adiponectin
PDW	0.028 (p = 0.864)	PDW	0.199 (p = 0.310)	PDW	0.312 (p = 0.093)
PCT	–0.053 (p = 0.744)	PCT	0.177 (p = 0.358)	PCT	–0.016 (p = 0.934)
MPV	–0.164 (p = 0.317)	MPV	0.128 (p = 0.508)	MPV	0.431 (p = 0.017)
Platelets	–0.094 (p = 0.562)	Platelets	0.048 (p = 0.806)	Platelets	–0.285 (p = 0.128)

Note: Statistical significance $p < 0.05$.

Discussion

To our knowledge, this is the first study to show a significant conditional association between MPV and adiponectin in patients with prediabetes; a specific stage of metabolic syndrome with a significant prothrombogenic risk.

Metabolic syndrome is a pathological condition with a continuously increasing incidence globally. This condition represents a significant proinflammatory and procoagulant state. In addition to numerous ways of dividing patients with metabolic syndrome into subgroups (shown by the ratio of various laboratory parameters), from a pathophysiological point of view, the platelets/HDL is one of the most accurate ways to divide patients according to the severity of the disease (Jialal et al., 2021). Some authors consider platelets/HDL to be a nascent index in the future research of metabolic syndrome, given that it consists of two parameters that are significantly disturbed in the later stages of this syndrome. Patients with lower platelets/HDL ratio represent a group with a less severe disease, while patients with a higher ratio represent a group with a more severe disease.

Over the last decade, research on platelets has overturned the previous view that they are important solely for the coagulation process. Although their function in the process of coagulation is the most important, it is believed that platelets have significant functions in enhancing the process of inflammation (Hottz et al., 2022; Margraf and Zarbock, 2019). Determination of the number of platelets and platelet indices is part of routine clinical practice. In this sense, platelet indices can provide data about the appearance of platelets, which is related to their function. The increased average platelet volume repre-

sents an index indicating that younger, more voluminous, and active platelets were created (Noris et al., 2016). Such enlarged platelets are more active than normal and have greater prothrombogenic potential (Korniluk et al., 2019). Increased prothrombogenic potential is especially important in conditions that are accompanied by inflammation, hyperlipidemia, hyperinsulinemia, and hyperglycemia, such as metabolic syndrome (Devaraj et al., 2004). In obesity related diseases, activated platelets amplify inflammatory processes through their interactions with vascular and immune cells (Rayes et al., 2019).

Data from the literature show that insulinemia level affects the level of aggregability of platelets, and that insulin resistance followed by hyperinsulinemia leads to hyperactivity of platelets. Also, in conditions of compensated hyperinsulinemia, platelet adhesiveness is increased (Gerrits et al., 2010). Some data have shown that obesity can cause resistance to antiplatelet therapy (Puccini et al., 2023). These hypotheses have been confirmed by the observed improvement in the effect of anti-aggregation drugs in patients who lost weight.

On the other side, the role of adiponectin in the pathogenesis of metabolic syndrome depends on the stage of the disease. Adiponectin, an adipokine that is predominantly produced in white adipose tissue, has a dominant antidiabetogenic effect (Yanai and Yoshida, 2019). It is considered to act by reducing inflammation and simultaneously enhancing insulin production during insulin resistance (Nguyen, 2020; Ohashi et al., 2012). It is believed that adiponectin has a protective effect on the process of atherosclerosis (Ekmekci and Ekmekci, 2006).

Some authors believe that adiponectin is an adipokine that appears early in the metabolic syndrome, during the onset of initial disorders, where the increase in adiponectin production attempts to neutralize the initial disorders (Matsuzawa et al., 2004). The results of our previous study showed the association between the concentration of regulatory cytokine interleukin 33 and the level of adiponectin in patients at the early stages of metabolic syndrome (Nesic et al., 2022).

Numerous studies have shown an adiponectin anticoagulant effect. Kato et al. (2006) *in vitro* and *in vivo* demonstrated rapid thrombus formation and greater platelet aggregation in adiponectin knockout mice, after blood vessel injury. The authors also showed the increased platelet aggregation on a type I collagen-coated surface, when blood of adiponectin-deficient mice was used.

Some studies have hypothesized that platelet function can be modulated by adiponectin and that normal or higher adiponectin levels decreased the platelet-dependent thrombosis. A clinical study by Shoji et al. (2006) has demonstrated that the adiponectin level was negatively associated with platelet activation independent of other risk factors.

Hara et al. (2007) showed that adiponectin levels are inversely related to the severity of coronary artery diseases, even in nondiabetic patients.

One hypotheses of how adiponectin inhibits the effect of platelets attributes this to its ability to stimulate the production of endothelial NO and vasodilatation (Ebrahimi-Mamaeghani et al., 2015). Although most data support the anticoagulant effect of adiponectin, some support the claim that adiponectin can activate platelets (Riba et al., 2008).

On the other hand, a study by Okamoto et al. (2013) showed that adiponectin reduces the thrombogenic potential of macrophages by inhibiting tissue factor expression and activity. The results of this study could indicate a potential link between low adiponectin levels and thrombotic complications in patients with obesity-related diseases.

In addition to investigating the role of adiponectin in obesity-related diseases, the anticoagulant role of adiponectin has also been investigated in autoimmune diseases such as antiphospholipid syndrome. In their paper, Bećarević et al. (2019) provided a complete review – supported by experimental models and clinical studies – on the potential antithrombogenic effect of adiponectin in patients with antiphospholipid syndrome.

However, despite all the above-mentioned studies, the causal relationship between adiponectin and platelet indices is yet to be examined. The results of our study showed that in patients with metabolic syndrome and prediabetes, changes in MPV are associated with changes in adiponectin concentration.

In a recent study investigating the effect of recombinant adiponectin on platelet activation and thrombus formation, significant anticoagulant effects of this molecule on platelet function in humans (*in vitro*) and mice (in a model of chemically induced carotid damage) were demonstrated (Zhou et al., 2023).

Based on the already confirmed assumption that platelet activity observed through the change of MPV is a very good prognostic parameter in infections associated with micro thrombotic events (Beceren et al., 2023), the results of our study highlighted the importance of simultaneous determination of MPV and adiponectin for the timely application of recombinant adiponectin in clinical trials of later stages. This can be especially important for the population with metabolic syndrome and prediabetes, where there are a greater number of prothrombogenic factors. Due to this simultaneous effect of several factors, a certain percentage of these patients develop a thrombotic event, even before receiving the diagnosis of a glucose metabolism disorder.

Strengths and limitations

The main strength of our study is the data about the specific population that could be used for future clinical studies for investigating the protective effect of recombinant adiponectin in patients with a significant prothrombogenic risk. The main limitation is a non-exclusive number of patients per subgroup.

Conclusion

Adiponectin and MPV are significant markers of metabolic syndrome in patients with prediabetes, which should be routinely determined to assess the condition of patients with prediabetes and increased risk. Our results can be a starting point for further research to determine the best time for testing and/or therapeutic application of recombinant adiponectin in patients with obesity-related diseases such as metabolic syndrome and T2DM.

Statement

Materials that can be freely found on the Internet, which are not protected by the copyright of third parties, were used.

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Ethical aspects and conflict of interest

The authors have no conflict of interest to declare.

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