ORIGINAL ARTICLE

CONTENTS

Holter ECG monitoring and platelets characteristics in patients with coronary artery disease and atrial fibrillation

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ABSTRACT

Aim: To check the relationships between platelet characteristics and Holter ECG monitoring results in patients with atrial fibrillation (AF) and coronary artery disease (CAD).

Materials and Methods: 300 investigated patients were separated into three groups: I (CAD) – 149 patients with CAD without arrhythmias, II (CAD and AF) – 124 patients with CAD and AF paroxysm, and the control group (CG) – 27 patients without CAD and arrhythmias.

Results: In the II group was detected an increase in mean platelet volume (MPV) (9.30%) and platelet-to-leucocyte ratio (PLR) (41.12%) and a decrease in platelet count (PC) (12.20%) in comparison with the I group, $P<0.05$. Also, in the II group was found an increase in platelet leucine (12.63%), isoleucine (10.73%), and a decrease in serine (5.06%), threonine (23.05%), valine (30.83%), glycine (32.21%) levels in comparison with the I group, $P<0.05$. PC, MPV, and PLR ratios were correlated with supraventricular extrasystoles per hour ($r=-0.352$, $r=0.308$, and $r=0.359$, consequently), $P<0.05$. Platelets distribution width (PDW) was correlated with ST-segment changes ($r=0.371$), $P<0.05$. Platelet threonine, serine, glycine, alanine, and valine levels were correlated with total supraventricular extrasystoles ($r=-0.374$, $r=-0.358$, $r=-0.402$, $r=-0.307$, $r=-0.312$, consequently) and supraventricular extrasystoles per hour ($r=-0.374$, $r=-0.358$, $r=-0.402$, $r=-0.307$, $r=-0.312$, consequently), $P<0.05$. Platelet lysine, taurine, cysteine, and phenylalanine levels were correlated with ST-segment changes ($r=-0.319$, $r=-0.344$, $r=-0.376$, and $r=0.317$, consequently), $P<0.05$.

Conclusions: Platelet features (PC, MPV, PDW, PLR, and amino acid spectrum) are significantly correlated with supraventricular arrhythmias and ST-segment episodes, which shows their role in AF and CAD pathogenesis.

KEY WORDS: coronary artery disease, atrial fibrillation, electrocardiography, platelets, amino acids

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INTRODUCTION

There is no doubt that pathogenetically atrial fibrillation (AF) and coronary artery disease (CAD) are characterized by prothrombotic state and platelet activation. Adequate anticoagulation is the first step and the main basis in the management of AF paroxysms [1, 2]. Platelet conditions represent hemostatic balance and can directly affect the prothrombotic state, which plays a major role in the supraventricular arrhythmia development. Increased mean platelet volume (MPV) is the known marker of platelet activation. Also, AF is significantly associated with reduced platelets count (PC), which can be explained by their overuse and synthesis decrease. The rise of platelets distribution width (PDW) also is common for cardiovascular pathology and some metabolic states, like diabetes mellitus [3]. Platelets also can represent prothrombotic potential and atherosclerotic plaque composition. Platelet activation in CAD patients is connected with increased integrin αIIbβ3 levels [4], which also can be promoted by circulatory branched-chain amino acids (AA) [5, 6].

Holter ECG monitoring is indicated for patients with AF paroxysms for the determination of the best treatment strategy or heart rate control management. For stable CAD patients, it is only reasonable in case of ischemia cardiac clinical features [7]. So, connections between Holter ECG monitoring findings: rhythm abnormalities, ST-segment changes, QTs-interval differences, and platelets morphological and biochemical characteristics are still unexplored.

AIM

The aim of this study was to investigate the relationships between Holter ECG monitoring findings and platelet characteristics in patients with atrial fibrillation paroxysm and coronary artery disease.

MATERIALS AND METHODS

300 patients were separated into three groups: I (CAD) – 149 patients with CAD without arrhythmias, II (CAD and

Table 1. Baseline characteristics of the study groups, mean ± standard error

Characteristic /group	I group	II group	CG
Age (years)	67.71±3.90	67.96±0.94	56.25±2.18
Men (%)	48.99	47.97	48.15
Smoking (%)	51.01	41.46	40.74
History of myocardial infarction (%)	30.87+	26.02#	0
History of stroke (%)	8.72+	8.13#	0
Diabetes mellitus (%)	18.12+	14.63#	0
Obesity (%)	8.84+	12.0#	0
BMI (kg/m^2)	27.02±0.33	26.93±0.43	27.12±2.10
Total bilirubin (mmol/l)	11.3±0,09	12.4±0,08	11.7±0.11
Uric acid (mmol/l)	380.5±28.16+	404.9±36.11#	310.2±29.12
GFR (ml/min)	62.03±2.31+	67.73±1.98#	84.01±5.48
TC (mmol/l)	5.73±0.37+	6.18±0.31#	4.32±0.21

Notes: +-p<0.05 I group – CG; #-p<0.05 II group – CG

AF) – 124 patients with AF paroxysm and CAD, and the control group (CG) – 27 patients without arrhythmias and CAD. Investigated patients were hospitalized and observed in the cardiological and therapeutic departments in the Kyiv City Clinical Hospital No. 12 in 2018-2023 years. Diagnosis CAD was based on the history of coronary artery stenotic changes during invasive coronary angiography. Diagnosis of AF paroxysm was based on 12 leads electrocardiography at rest. These diagnoses were matched the resent ESC guidelines [1, 2]. Heart failure in stage B or C was found in the I and II group of patients [8]. Exclusion criteria included heart failure Class III to IV (by New York Heart Association), ejection fraction <40%, valvular AF, thyroid pathology, chronic kidney disease (Glomerular Filtration Rate, GFR <60 mL/min), reported malignancies, pregnancy, inflammatory bowel disease and irritable bowel syndrome, probiotics or antibiotics usage for a month before the study, vegetarians. Informed consent was signed by the all subjects according to the Declaration of Helsinki. The study was performed at the base and got approval of the Kyiv City Clinical Hospital No. 12 ethical commission (protocol # 8 from 22/08/2018).

Holter ECG monitoring (Cardiosens_K, Kharkiv, 2014) in V1, aVF, and V5 leads during 24 hours was performed for the patients with AF within 24 hours after sinus rhythm restoration, and for the patients without AF on the first day of observation. PC, MPV, PDW, and platelets-to-leucocytes ratio (PLR) were obtained from the common blood count. Platelet AA level was detected by the method of ion exchange liquid column chromatography. Patients' blood sampling was made from the cubital vein fasted before treatment on the first day of hospitalization.

Results have been introduced as mean ± standard error for continuous variables or [95% confidence interval (CI)] as a number for categorical variables. Normality distribution was checked by the Pearson criterion. Data comparison was performed by Wilcoxon signed-rank test or Student t-test with two critical regions depending on the distribution type. Correlation analysis was done by the Spearman's coefficient [9]. All calculations were done in MATLAB R2014a (License number 271828, MathWorks, Inc., USA).

RESULTS

In investigated groups, significant differences in age and gender, total bilirubin, body mass index (BMI), and smoking history were not checked. In the I and II groups uric acid (by 22.66% and 30.53% respectively) and total cholesterol (TC) (by 32.64% and 43.06% respectively) levels were significantly higher and glomerular filtration rate (GFR) (by 26.16% and 19.38% respectively) were lower versus CG, P<0.05. Also, CG patients did not have obesity, stroke, diabetes mellitus, or myocardial infarction history, as the I and II groups patients. Data are presented in Table 1.

The average Holter monitoring lasted for 22,13±0.22 hours in average. The I and II groups were characterized by significant decrease in minimum heart rate (HR) (13.82% and 11.36%, consequently) and average (9.38% and 14.14%, consequently) versus the CG, P<0.05. In the II group had a significant rise in supraventricular ectopic beats (SVEs) per hour, total SVEs, single SVEs, pair SVEs, ventricular ectopic beats (VEs) per hour, total VEs, single VEs, and pair VEs, AF paroxysm, and its duration versus the I group, P<0.05. ST -segment deviations were not found in the CG. It was no significant difference in ST-segment changes between I and II groups, P<0.05. The data are presented in Table 2.

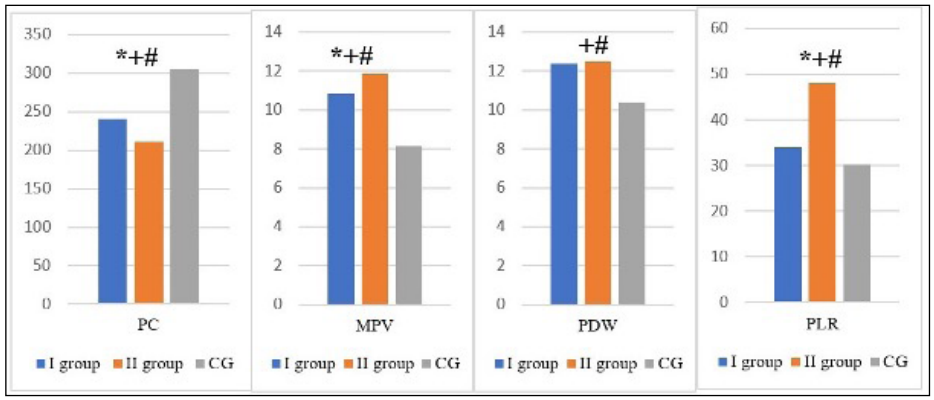

Fig. 1. Platelet morphological characteristics in investigated patients.
Notes: *-P<0.05 I-II groups; +-P<0.05 I group – CG; #-P<0.05 II group – CG.

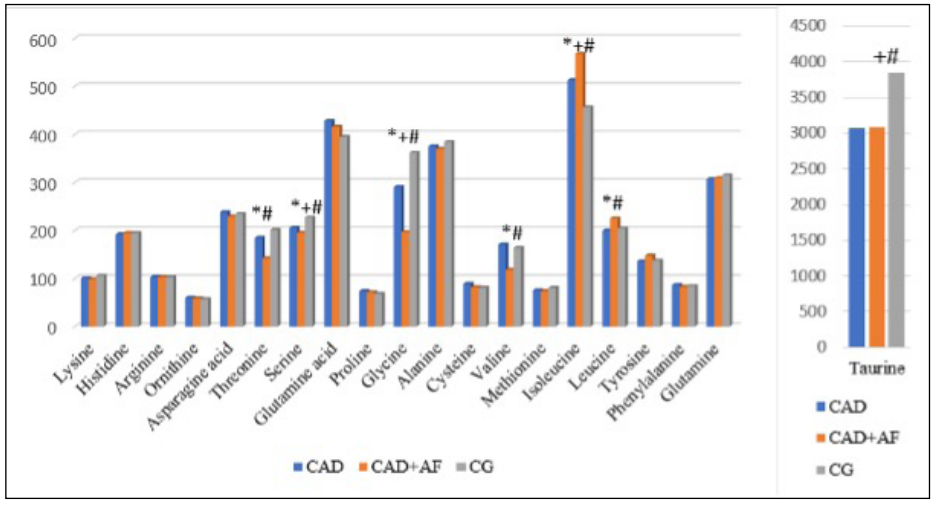

Fig. 2. Platelets amino acids profile in investigated patients, μmol/l.
Notes: *-P<0.05 I-II groups; +-P<0.05 I group – CG; #-P<0.05 II group – CG.

In the II group, a significant depletion in PC (12.20%) and a rise in MPV (9.30%) and PLR (41.12%) was revealed versus the I group, P <0.05. In the I group, a significant decline in PC (21.25%) and a growth in MPV (33.58%), PDW (20.31%), and PLR (12.37%) was detected versus the CG, P <0.05. In the II group, a significant decrease in PC (30.85%) and a rise in PDW (20.31%), MPV (46.00%), and PLR (58.58%) was observed versus the CG, P <0.05. The data are shown in Fig. 1.

In the II group, a significant rise in isoleucine (10.73%), and leucine (12.63%) and a decline in serine (5.06%), threonine (23.05%), valine (30.83%), glycine (32.21%) levels were found versus the I group, P <0.05. In the I group was found a significant growth in isoleucine (12.41%) and a decline in serine (9.31%), glycine (19.73%), and taurine (20.26%), levels versus the CG, P <0.05. In the II group, a significant increase in leucine (10.20%), isoleucine (24.47%), and a fall in serine (13.90%), taurine (19.84%), valine (27.87%), threonine (29.37%), and glycine (45.59%) levels were obtained versus the CG, P <0.05. The data are presented in Fig. 2.

The correlation analysis between platelets morphological characteristics, amino acids spectrum, and Holter ECG monitoring indexes is shown in Table 3 and Table 4.

DISCUSSION

Holter ECG monitoring is a significant part of the investigation in patients with AF paroxysms and CAD [7]. In our study, we selected patients with CAD and without arrhythmias and CG using Holter ECG monitoring. That's why, these groups had significantly lower levels of supraventricular and ventricular rhythm abnormalities, and CG had no ST episodes. According to our data patients with AF and CAD are characterized by a rise in MPV and PLR and a decrease in PC. These results were expected according to the literature data [4, 5]. Platelet characteristics are deeply connected with inflammation, myocardial fibrosis, and remodeling [10]. Also, PC, MPV, and PLR significantly correlated with supraventricular arrhythmias. According to the literature data, an increase in PLR can be an independent indicator of ventricular repolarization and depolarization heterogeneity [11]. The rise of MPV is associated with platelet activation, which is characterized by intracellular calcium exchange disturbances and can lead to electrolyte disbalance [12]. In animal experiments, platelet activation is connected with cellular hypoxia [13], which is also important in arrhythmia pathogenesis [1]. At the same time, PDW is mostly correlated with ST-segment changes. According to some data, PDW

Table 2. Holter ECG monitoring indexes in investigated groups, mean ± standard error or mean [95% CI]

Characteristic /group	I group	II group	CG
Maximum HR, bpm	110.20±2.48	106.6±3.89	109.8±3.97
Minimum HR, bpm	45.6±1.68	46.9±1.66 #	52.91±1.30 +
Average HR, bpm	66.98±0.99 *	63.46±1.24 #	73.91±2.20 +
SVEs total	36 [95% CI 24-43] *	729 [95% CI 331-982] #	7 [95% CI 0-15] +
SVEs single	32 [95% CI 24-43] *	502 [95% CI 307-766] #	7 [95% CI 0-15] +
SVEs pair	0 [95% CI 0-3] *	27 [95% CI 8-42] #	0 +
SVEs group	0 [95% CI 0-1]	5 [95% CI 0-9] #	0 +
SVT	0 [95% CI 0-1]	0 [95% CI 0-1] #	0 +
Longest SVT, sec.	0 [95% CI 0-16]	0 [95% CI 0-42] #	0 +
SVEs per hour	8 [95% CI 3-17] *	38 [95% CI 11-112] #	0 [95% CI 0-2] +
AF paroxysm	0 *	0 [95% CI 0-1] #	0
Longest AF paroxysm, sec.	0 *	0 [95% CI 0-44] #	0
VEs total	0 [95% CI 0-3] *	3 [95% CI 0-15] #	0 [95% CI 0-1] +
VEs single	0 [95% CI 0-3] *	3 [95% CI 0-15] #	0+
VEs pair	0 [95% CI 0-2] *	3 [95% CI 0-15] #	0+
VEs group	0 [95% CI 0-1]	0 [95% CI 0-2] #	0+
VT	0	0	0
Longest VT, sec.	0	0	0
VE's per hour	14 [95% CI 5-19] *	32 [95% CI 17-41] #	0 [95% CI 0-1] +
Pauses more than 3 sec	0	0	0
Longest pauses, sec.	0	0	0
Changes ST segment, quantity episodes	0 [95% CI 0-3]	0 [95% CI 0-6] #	0 +
Maximum ST depression, μV	0 [95% CI 0-118]	0 [95% CI 0-124] #	0 +
Maximum ST elevation, μV	0 [95% CI 0-133]	0 [95% CI 0-112] #	0 +
Maximum ST episode duration, minutes	2 [95% CI 1-5]	2 [95% CI 1-5.5] #	0 +

Notes: +-p<0.05 I group – CG; #-p<0.05 II group – CG; *-p<0.05 I-II groups; HR – heart rate; AF – atrial fibrillation; SVE – supraventricular ectopic beats; VE - ventricular ectopic beats; SVT – supraventricular tachycardia, VT – ventricular tachycardia.

is directly connected with GPIIb/IIIa receptor activity [14], which is associated with increased risks of MI [15].

Besides, patients with AF and CAD had a significant increase in platelet isoleucine, and leucine and a significant decrease in threonine, serine, glycine, and valine levels in our study. Platelet glycine, alanine, serine, threonine, valine, and leucine levels are mostly correlated with arrhythmias due to obtained data. According to the previous data, an increase in circulating levels of leucine and tyrosine and a decrease in glycine, serine, and alanine levels are associated with cardiovascular diseases. Serine is a precursor of glycine synthesis. Glycine has antihypertensive, antioxidative, anti-inflammatory, and metabolic effects [6]. According to some data, glycine can counteract angiotensin II, which prevents left ventricular hypertrophy and stimulates growth factor β and endothelin-1, which prevents myocardial fibrosis [16]. Moreover, activation of myocardial glycine receptors provides ischemic conditioning in experiments [17]. Also, alanine, serine, threonine, and their exchange violations regulate Ca2+ dependent kinase 2 activity and myocardial sarco/endoplasmic reticulum (SR) Ca^{2+} ATPase pump, which changes Ca2+ handling proteins exchange, reduce Ca2+ uptake, and prevent O-GlcNAcylation induced increase in Ca^{2+} leak [18, 19]. Leucine participates in electrical remodeling processes by modulation of L-type Ca2+ channels and excitation-contraction activity [20]. Valine is responsible for fatty acid oxidation in cardiomyocytes, which leads to antioxidative properties, but on the other hand, sometimes it can suppress glucose oxidation in cardiac tissue [21].

Table 3. Correlation matrices between Holter ECG monitoring indexes and platelet morphological characteristics

Holter ECG monitoring indexes / Platelet morphological characteristics	PC	MPV	PDW	PLR
Maximum HR	0,196	-0,050	0,145	0,153
Minimum HR	0,347*	-0,188	-0,214	0,116
Average HR	0,377*	-0,360*	-0,012	0,382*
SVE total	-0,377*	0,374*	0,272	-0,119
SVE single	-0,399*	0,374*	0,247	-0,154
SVE pair	-0,301*	0,366*	0,130	-0,014
SVE group	-0,047	0,363*	0,196	0,002
SVT	0,043	0,197	0,008	0,326*
Longest SVT	0,052	0,194	0,008	0,329*
SVEs per hour	-0,352*	0,308*	0,211	0,359*
AF paroxysm	-0,164	0,451*	0,163	0,357*
Longest AF paroxysm	-0,155	0,456*	0,178	0,341*
VE total	-0,323*	0,420*	0,172	-0,203
VE single	-0,364*	0,434*	0,270	-0,131
VE pair	0,047	0,050	0,136	0,115
VE group	0,041	0,020	0,075	0,041
VE's per hour	-0,123	0,159	0,035	-0,221
Changes ST segment	0,028	0,101	0,371*	-0,096
Maximum ST depression	0,053	0,098	0,385*	-0,08
Maximum ST elevation	0,070	0,084	0,271	-0,08
Maximum ST episode duration	0,041	0,092	0,308*	-0,08

Notes: *- correlations with moderate or strong force (r>0.3 or r<-0.3), P<0.05. HR – heart rate; AF – atrial fibrillation; SVE – supraventricular ectopic beats; VE - ventricular ectopic beats; SVT – supraventricular tachycardia, VT – ventricular tachycardia.

We established that platelet lysine, taurine, cysteine, and phenylalanine levels correlated with ST-segment episodes. Cysteine is a precursor of taurine, they are sulfur contains amino acids. As reported, taurine and cysteine have strong anti-ischemic properties. Taurine is a trigger for osmotic preconditioning, by its antioxidant properties. Cysteine inhibits vascular endothelial growth factor and hypoxia-inducible factor 1-alpha [22, 23]. Also, according to the latest data in experiments lysine can prevent cardiac fibrosis and apoptosis by influencing cardiomyocytes mitochondria, sarcolemma, and architecture [24]. In animal models, an increase in circulated phenylalanine is closely associated with cardiac aging: fibrosis, ectopic activity, and inflammation [25].

So, the role of platelets' morphological and biochemical features in arrhythmia pathogenesis in CAD patients is important and needs further investigation.

CONCLUSIONS

The features of platelet characteristics, Holter ECG monitoring indexes, and their correlations in patients with coronary artery disease and atrial fibrillation were described in our study:

1. Patients vwith atrial fibrillation paroxysm and coronary artery disease characterized by a significant increase in mean platelet volume (9.30%) and platelet-to-leucocyte ratio (41.12%) and a significant decrease in platelets count (12.20%), P<0.05;
2. Patients with atrial fibrillation paroxysm and coronary artery disease characterized by a significant increase in platelet isoleucine (10.73%), leucine (12.63%), and a significant decrease in serine (5.06%), threonine (23.05%), valine (30.83%) and glycine (32.21%) levels in comparison with coronary artery disease patients without atrial fibrillation, P<0.05;
3. Platelets count, mean platelet volume, and platelet-to-leucocyte ratio correlated with supraventricular extrasystoles per hour (r=-0.352, r=0.308, and r=0.359, consequently), P<0.05;
4. Platelet distribution width correlated with ST-segment changes (r=0.371), P<0.05;
5. Platelet threonine, serine, glycine, alanine, and valine levels negatively correlated with supraventricular arrhythmias: total supraventricular extrasystoles (r=-0.374, r=-0.358, r=-0.402, r=-0.307, r=-0.312, respectively) and supraventricular extrasystoles per hour (r=-0.374, r=-0.358, r=-0.402, r=-0.307, r=-0.312, respectively), P<0.05;

Table 4. Correlation matrices between Holter ECG monitoring indexes and platelets morphological characteristics, P<0.05

Holter ECG monitoring indexes / Platelet amino acids	Maximum ST episode duration	Maximum ST elevation	Maximum ST depression	Changes ST segment	VE's per hour	VE group	VE pair	VE single	VE total	Longest AF paroxysm	AF paroxysm	SVEs per hour	Longest SVT	SVT	SVE group	SVE pair	SVE single	SVE total	Average HR	Minimum HR	Maximum HR
Lysine	**-0,320***	**-0,307***	**-0,326***	**-0,319***	0,071	0,089	0,074	0,187	0,189	-0,102	-0,111	-0,135	-0,073	-0,065	-0,213	-0,165	-0,107	-0,115	0,098	-0,008	**-0,329***
Histidine	-0,128	-0,109	-0,118	-0,134	-0,022	0,128	0,009	0,024	0,027	0,068	0,066	-0,109	0,028	0,030	0,056	0,060	-0,096	-0,097	-0,153	-0,054	-0,030
Arginine	-0,18	-0,120	-0,183	-0,177	-0,030	0,015	-0,099	-0,038	-0,037	0,038	0,012	0,020	0,186	0,168	0,015	-0,011	0,009	0,009	0,020	0,042	-0,110
Ornithine	-0,18	-0,089	-0,179	-0,175	-0,162	-0,028	-0,015	-0,142	-0,142	0,214	0,232	0,075	-0,016	-0,036	0,023	-0,042	-0,001	0,024	0,109	0,008	-0,079
Taurine	**-0,356***	-0,296	**-0,343***	**-0,344***	-0,078	0,045	-0,115	-0,252	-0,253	-0,043	-0,031	-0,180	-0,052	-0,071	-0,035	-0,102	**-0,324***	-0,186	**0,488***	0,114	0,027
Asparagine acid	-0,016	-0,055	-0,028	-0,013	0,009	0,069	-0,024	-0,176	-0,175	-0,094	-0,104	-0,133	-0,077	-0,074	-0,206	-0,211	-0,192	-0,172	-0,022	-0,001	0,007
Threonine	-0,111	-0,132	-0,127	-0,125	-0,153	0,050	-0,050	-0,205	-0,207	-0,223	**-0,328***	**-0,374***	-0,116	-0,115	**-0,357***	**-0,382***	**-0,333***	**-0,358***	0,083	0,046	0,075
Serine	-0,034	-0,085	-0,032	-0,033	-0,024	-0,061	0,034	**-0,234***	-0,23	-0,298	-0,318	**-0,358***	-0,163	-0,175	-0,145	-0,176	-0,211	**-0,318***	0,126	0,067	0,107
Glutamine acid	-0,052	-0,124	-0,072	-0,063	-0,020	0,022	0,022	0,124	0,124	-0,018	-0,033	-0,091	0,131	0,148	-0,039	-0,095	-0,074	-0,091	-0,136	0,075	-0,086
Proline	0,070	0,079	0,070	0,066	-0,097	0,006	-0,019	-0,182	-0,178	0,002	0,022	0,065	0,085	0,084	0,161	0,111	0,056	0,065	-0,060	**-0,384***	0,113
Glycine	0,048	0,104	0,046	0,045	-0,102	0,017	0,019	**-0,406***	**-0,403***	-0,4	**-0,494***	**-0,402***	**-0,338***	**-0,344***	**-0,316***	**-0,376***	**-0,484***	**-0,479***	**0,394***	-0,066	0,098
Alanine	-0,171	-0,192	-0,187	-0,178	0,048	0,024	0,035	-0,045	-0,046	-0,149	-0,139	**-0,307***	**-0,331***	**-0,323***	**-0,325***	**-0,375***	-0,191	**-0,312***	**0,357***	0,154	0,085
Cysteine	**-0,386***	0,281	**-0,379***	**-0,376***	0,013	-0,076	0,035	-0,068	-0,065	-0,009	0,004	0,295	0,104	0,104	0,131	0,119	0,213	0,215	-0,140	**0,302***	-0,058
Valine	0,067	0,020	0,072	0,068	-0,078	0,087	0,015	-0,238	-0,235	**-0,376***	**-0,341***	**-0,312***	**-0,311***	**-0,328***	**-0,319***	**-0,375***	**-0,308***	**-0,389***	0,090	-0,134	-0,050
Methionine	0,118	0,095	0,104	0,118	-0,065	-0,049	-0,006	0,025	0,022	-0,017	-0,011	-0,140	-0,038	-0,042	0,001	-0,106	-0,186	-0,192	0,120	-0,054	0,057
Isoleucine	-0,064	-0,117	-0,069	-0,061	0,019	0,013	0,041	0,152	0,150	0,049	0,034	-0,038	0,060	0,073	-0,005	-0,053	-0,015	-0,032	-0,033	0,073	0,059
Leucine	0,078	0,144	0,078	0,074	0,134	0,028	0,119	0,291	0,292	0,117	0,123	0,048	**0,308***	**0,395***	0,152	0,196	0,163	0,150	-0,018	0,162	0,007
Tyrosine	-0,059	-0,048	-0,075	-0,067	0,071	0,086	-0,047	0,124	0,123	-0,096	-0,109	-0,077	0,012	0,018	-0,197	-0,151	0,002	-0,013	0,047	0,113	0,084
Phenylalanine	**0,321***	0,279	**0,319***	**0,317***	0,015	0,061	0,060	0,011	0,018	-0,02	-0,020	-0,106	-0,173	-0,167	-0,013	-0,148	-0,118	-0,108	-0,033	-0,215	0,082
Glutamine	-0,191	-0,145	-0,198	-0,201	-0,114	0,056	0,087	0,009	0,013	0,064	0,052	-0,230	-0,109	-0,109	-0,177	-0,160	-0,210	-0,207	0,096	0,161	0,012

Notes: *- correlations with moderate or strong force (r>0.3 or r<-0.3), P<0.05.

6. Platelet lysine, taurine, cysteine, and phenylalanine levels correlated with ST-segment changes (r=-0.319, r=-0.344, r=-0.376, and r=0.317, consequently), P<0.05.

The role of platelet amino acids spectrum abnormalities should be deeply investigated in further studies and possible approaches to their correction.

REFERENCES

1. Hindricks G, Potpara T, Dagres N et al. ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). European Heart Journal. 2020;42:373498. doi:10.1093/eurheartj/ehaa612. DOI
2. Knuuti J, Wijns W, Saraste A et al. ESC Guidelines for the diagnosis and management of chronic coronary syndromes. European Heart Journal. 2020;41:407477. doi:10.1093/eurheartj/ehz425. DOI
3. Weymann A, Ali-Hasan-Al-Saegh S, Sabashnikov A et al. Platelets Cellular and Functional Characteristics in Patients with Atrial Fibrillation: A Comprehensive Meta-Analysis and Systematic Review. Med Sci Monit Basic Res. 2017;23:58-86. doi:10.12659/msmbr.902557. DOI
4. Pasalic L, Wang SS, Chen VM. Platelets as Biomarkers of Coronary Artery Disease. Semin Thromb Hemost. 2016;42(3):223-233. doi:10.1055/s-0036-1572328. DOI
5. Xu Y, Jiang H, Li L et al. Branched-Chain Amino Acid Catabolism Promotes Thrombosis Risk by Enhancing Tropomodulin-3 Propionylation in Platelets. Circulation. 2020;142(1):49-64. doi:10.1161/CIRCULATIONAHA.119.043581. DOI
6. Hu S, Lin Z, Hu MJ et al. Causal relationships of circulating amino acids with cardiovascular disease: a trans-ancestry Mendelian randomization analysis. J Transl Med. 2023;21(1):699. doi:10.1186/s12967-023-04580-y. DOI
7. Sandau KE, Funk M, Auerbach A et al. Update to Practice Standards for Electrocardiographic Monitoring in Hospital Settings: A Scientific Statement From the American Heart Association. Circulation. 2017;136(19):e273-e344. doi:10.1161/CIR.0000000000000527. DOI
8. Malik A, Brito D, Vaqar S, Chhabra L. Congestive Heart Failure. In StatPearls. StatPearls Publishing. 2023.
9. Faizi N, Alvi Y. Biostatistics Manual for Health Research. Elsevier. 2023.
10. Schütte JP, Manke MC, Hemmen K et al. Platelet-Derived MicroRNAs Regulate Cardiac Remodeling After Myocardial Ischemia. Circ Res. 2023;132(7):e96-e113. doi:10.1161/CIRCRESAHA.122.322459. DOI
11. Abus S, Koparal M, Kaya H et al. Evaluation of frontal QRS-T angle values in electrocardiography in patients with chronic rhinosinusitis. BMC Cardiovasc Disord. 2023;23(1):160. doi:10.1186/s12872-023-03175-1. DOI
12. Kong Y, Chiu J, Passam FH. "Sticki-ER": functions of the platelet endoplasmic reticulum. Antioxid Redox Signal. 2024. doi:10.1089/ars.2024.0566. DOI
13. Iring A, Baranyi M, Iring-Varga B et al. Blood oxygen regulation via P2Y12R expressed in the carotid body. Respir Res. 2024;25(1):61. doi:10.1186/s12931-024-02680-x. DOI
14. Akbarinia A, Kargarfard M, Naderi M. Aerobic training improves platelet function in type 2 diabetic patients: role of microRNA-130a and GPIIb. Acta Diabetol. 2018;55(9):893-899. doi:10.1007/s00592-018-1167-2. DOI
15. Gasperi V, Catani MV, Savini I. Platelet Responses in Cardiovascular Disease: Sex-Related Differences in Nutritional and Pharmacological Interventions. Cardiovasc Ther. 2020;2342837. doi:10.1155/2020/2342837. DOI
16. Lu Y, Zhu X, Li J et al. Glycine prevents pressure overload induced cardiac hypertrophy mediated by glycine receptor. Biochem Pharmacol. 2017;123:40-51. doi:10.1016/j.bcp.2016.11.008. DOI
17. José Alburquerque-Béjar J, Barba I, Valls-Lacalle L et al. Remote ischemic conditioning provides humoural cross-species cardioprotection through glycine receptor activation. Cardiovasc Res. 2017;113(1):52-60. doi:10.1093/cvr/cvw242. DOI
18. Shanmugam M, Li D, Gao S et al. Cardiac specific expression of threonine 5 to alanine mutant sarcolipin results in structural remodeling and diastolic dysfunction. PLoS One. 2015;10(2):e0115822. doi:10.1371/journal.pone.0115822. DOI
19. Okolo CA, Khaing EP, Mereacre V et al. Direct regulation of the cardiac ryanodine receptor (RyR2) by O-GlcNAcylation. Cardiovasc Diabetol. 2023;22(1):276. doi:10.1186/s12933-023-02010-3. DOI
20. Santamaria-Herrera MA, Ríos-Pérez EB, de la Rosa JA et al. MDIMP, a novel cardiac Ca(2+) channel blocker with atrial selectivity. Eur J Pharmacol. 2016;781:218-228. doi:10.1016/j.ejphar.2016.04.027. DOI
21. Li Y, Xiong Z, Yan W et al. Branched chain amino acids exacerbate myocardial ischemia/reperfusion vulnerability via enhancing GCN2/ATF6/PPAR-α pathway-dependent fatty acid oxidation. Theranostics. 2020;10(12):5623-5640. doi:10.7150/thno.44836. DOI
22. Duan Q, Dong A, Cheng H et al. Inhibition of Taurine-upregulated Gene 1 Upregulates MiR-34a-5p to Protect against Myocardial Ischemia/Reperfusion via Autophagy Regulation. Comb Chem High Throughput Screen. 2024. doi:10.2174/0113862073267559231106074309. DOI
23. Chao WW, Chao HW, Lee HF, Chao HM. The Effect of S-Allyl L-Cysteine on Retinal Ischemia: The Contributions of MCP-1 and PKM2 in the Underlying Medicinal Properties. Int J Mol Sci. 2024;25(2):1349. doi:10.3390/ijms25021349. DOI
24. Cai W, Xu D, Zeng C et al. Modulating Lysine Crotonylation in Cardiomyocytes Improves Myocardial Outcomes. Circ Res. 2022;131(5):456-472. doi:10.1161/CIRCRESAHA.122.321054. DOI

25. Czibik G, Mezdari Z, Murat Altintas D et al. Dysregulated Phenylalanine Catabolism Plays a Key Role in the Trajectory of Cardiac Aging. Circulation. 2021;144(7):559-574. doi:10.1161/CIRCULATIONAHA.121.054204. DOI

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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