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PLASMA AMINO ACIDS PECULARITIES AND CARDIOMETABOLIC RISK FACTORS IN PATIENTS WITH CORONARY ARTERY DISEASE AND ATRIAL FIBRILLATION

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Studies targeting small molecule metabolites (amino acids, sugars, nucleotides, lipids) in connections with gut microbiota metabolites that impact the host metabolome give a possibility to define a special metabolic signature of different diseases. Plasma amino acids (AA) profile is known to be a new promising biomarker for the screening of coronary artery disease (CAD) pathogenesis connected with gut dysbiosis. The aim of our study was to estimate the spectrum of plasma amino acids in CAD patients with atrial fibrillation (AF) and to check their connections with the gut microbiota metabolites. 300 patients were divided into three groups: CAD – 149 patients with CAD but without arrhythmias, CAD+AF – 123 patients with CAD and AF paroxysm and control group– 28 patients without CAD and arrhythmias. Plasma AA level was detected by ion exchange liquid column chromatography. Significant changes in the content of plasma Glutamate, Glutamine, Glycine, Alanine, Valine and Tyrosine and combinations Isoleucine+Leucine/Valine, Glycine+Serine, Glycine/Methionine, Phenylalanine/Tyrosine, Glutamine/Glutamate in CAD+AF patients were detected. A strong reliable connection between plasma AA spectrum and gut microbiota metabolites trimethylamine, trimethylamine-N-oxide and total amount of fecal short chain fatty acids was determined. The highly validated plasma AA combinations Isoleucine – Glycine (area under ROC-curve 0.8122) and Phenylalanine – Glycine (area under ROC-curve 0.8061) that can be used as the early markers of AF paroxysm in CAD patients were proposed.

K e y w o r d s: coronary artery disease, atrial fibrillation, cardiometabolic risk factors, gut microbiota metabolites, plasma amino acids.

Metabolomics studies targeting small molecule metabolites (sugars, nucleotides, amino acids, lipids) that impact the host metabolome and their biochemical functions have shown promise for studying host-gut microbiota interactions. Today new diagnostic methods give us the possibility to check the special metabolic signatures of different diseases that enable diagnoses, predict disease course, and guide treatment strategies [1].

Gut microbiome regulates different functions in the host organism, including lipid and protein metabolism. Some studies have proven connection of gut dysbiosis with cardiovascular pathology, such as atherosclerosis, arterial hypertension, heart failure, platelet hyperactivity, vascular dysfunction [2]. The gut-heart axis can be altered that leads to hyperactivation of sympathetic heart innervation through trimethylamine-N-oxide action (TMAO) [3]. Gut microbiota affects our health through its metabolites: TMAO and trimethylamine (TMA), short chain fatty acids (SCFA), bile acids, uremic toxins, lipopolysaccharide [4, 5]. Gut microbiota plays an important role in coronary artery disease (CAD) pathogenesis through several mechanisms: foam cell formation, inflammation, lipid metabolism, platelet hyperreactivity and thrombosis, endothelial dysfunction [7]. Several studies also classify plasma amino acids (AA) as gut microbiota metabolites, especially branched-chain and aromatic acids [6, 7].

Atrial fibrillation (AF) is the most common arrhythmia in the world. CAD is also a widely spread cardiovascular pathology disorder. Their combination is associated with increasing risk of morbidity

and mortality. Both of them are characterized by similar risk factors such as dyslipidemia, obesity, inflammatory diseases, heart failure, diabetes mellitus, arterial hypertension etc. All these factors are associated with special metabolic profile [4, 8]. Several studies analyzed plasma AA profiles in AF patients, but their data are controversial [8-10].

Plasma AA profile investigations are a new promising approach for the detection and screening AF paroxysm development in CAD patients [8-10]. Its changes are associated with different cardiovascular and endocrine pathology, that are known AF and CAD risk factors [10-12]. In to the previous studies, CAD was associated with alterations in tyrosine, glycine, threonine and valine levels [9, 12]. Also, changes in branched-chain AA metabolism are commonly associated with CAD [12], aromatic AA changes are connected with diabetes mellitus [13], but recent controversial data on concomitant AF prompted us to further investigate AF patients' metabolic profiles [8, 9]. So, deeper pathophysiological investigations of AF paroxysm development are promising and have actual scientific interest.

The aim of our study was to estimate the peculiarities of plasma amino acid (AA) spectrums in coronary artery disease (CAD) patients with atrial fibrillation (AF) and check their connections with other gut microbiota metabolites and known cardiometabolic risk factors – trimethylamine (TMA), trimethylamine-N-oxide (TMAO), the total amount of fecal short chain fatty acids (SCFA), lipids profile, inflammatory markers.

Materials and Methods

300 patients were enrolled in the study. They were divided into 3 groups: group I (CAD) – 149 patients with CAD but without arrhythmias, group II (CAD+AF) – 124 patients with CAD and AF paroxysm and control group – 27 patients without CAD and arrhythmias. CAD and AF diagnoses were based on the latest ESC guidelines [14, 15]. Inclusion criteria were based on results of objective clinical investigation (typical patients' compliance and history), resting 12 lead electrocardiogram (ECG), transthoracic echocardiography, ultrasound of the carotid arteries, lipid profile, invasive coronary angiography. We selected patients who had atherosclerotic plaques in coronary arteries during invasive coronary angiography by anamnesis morbi for CAD diagnosis decision. AF paroxysm was found by resting 12 lead ECG. The mean duration of AF paroxysm was 2 [1, 3] days. Patients with paroxysmal and persistent AF were included in our study. ECG was done using CardioLab ECG complex (Kharkiv, 2017). Carotid ultrasound and echocardiography were done using Toshiba Aplio 400 color Doppler ultrasound system (Japan, 2016). Exclusion criteria includes: reported malignancies, chronic kidney disease (Glomerular Filtration Rate, GFR <60 ml/min), valvular AF, heart failure Class III to IV (by New York Heart Association), left ventricular dysfunction (ejection fraction < 45%), thyroid pathology, inflammatory bowel disease, irritable bowel syndrome, vegetarians and vegans, pregnancy, taking probiotics and antibiotics for a month before the study. No significant difference in risk factors at baseline was seen between investigated groups, they were compatible ($P > 0.05$). Informed consent was obtained from all subjects in accordance with the Declaration of Helsinki. The study was conducted at the base and was approved by the ethical commission of the Kiev City Clinical Hospital No. 12 (protocol # 8 from 22/08/2018). Baseline characteristics of the studed samples are shown in Table 1.

Plasma AA level was detected by method of ion-exchange liquid column chromatography – the following AAs were identified: lysine, histidine, arginine, ornithine, taurine, asparaginate, threonine, serine, glutamate, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, glutamine, ammonia. Blood sampling from patients was performed on an empty stomach from the cubital vein on the day of hospitalization.

The cardiometabolic risk factors explored were: total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), lipoprotein α (Lpα), apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB), C-reactive protein (CRP), interleukin 6 (IL-6), TMA and TMAO. Also, ApoB/ApoA1 and TMA/TMAO ratios were checked. The level of TMAO, TMA plasma was determined by gas chromatography with mass electron detection. They were extracted from blood plasma into acid by adding internal standards. The patients' blood sampling was performed on an empty stomach from the cubital vein on the day of hospitalization. Hymalyzer 2000 was used for the detection of TC, TG, HDL, LDL (reagent produced by HUMAN GmbH), ApoA1, ApoB, Lpα and CRP (reagent produced by Dialab) – by flow cytometry. Hymareader 2106 (ELISA) was used for the detection of IL-6 – reagents produced by Vector Best.

Table 1. Baseline characteristics of the studied samples, mean ± standard error

Characteristic	Groups					
	I	II	CG	P1-2	P2-CG	P1-CG
Age, years	67.71±3.90	67.96±0.94	56.25±2.18	$P > 0.05$	$P > 0.05$	$P > 0.05$
Men, %	48.99	47.97	48.15	$P > 0.05$	$P > 0.05$	$P > 0.05$
Smoking, %	51.01	41.46	40.74	$P > 0.05$	$P > 0.05$	$P > 0.05$
History of myocardial infarction, %	30.87	26.02	0	$P > 0.05$	$P < 0.05$	$P < 0.05$
History of stroke, %	8.72	8.13	0	$P > 0.05$	$P < 0.05$	$P < 0.05$
BMI, kg/m^2	27.02±0.33	26.93±0.43	28.12±2.10	$P > 0.05$	$P > 0.05$	$P > 0.05$
Uric acid, mmol/l	380.50±28.16	404.90±36.11	310.20±29.12	$P > 0.05$	$P < 0.05$	$P < 0.05$
Total bilirubin, mmol/l	11.30±0.09	12.40±0.08	11.70±0.11	$P > 0.05$	$P > 0.05$	$P > 0.05$
GFR, ml/min	62.03±2.31	67.73±1.98	84.01±5.48	$P > 0.05$	$P < 0.05$	$P < 0.05$

Results were presented as mean ± standard error for continuous variables or median [95% confidence interval (CI)] for categorical variables. Variable distribution for normality was checked using the Pearson criterion. Data were compared using Kruskel-Wallis rank univariate analysis. Pearson's rank correlation coefficient was calculated. ROC-curve analysis for lipid and inflammatory indexes and linear regression model were done [16, 17]. All calculations were done in MATLAB R2014a (License number 271828).

Results

At first, we analyzed the well-known cardiometabolic risk factors in CAD patients with and without AF and compared them with CG (group of patients without CAD and AF). The obtained results are presented in Fig. 1.

In group II, significant increase in ApoB (29.91%), CRP (40.93%), IL-6 (22.93%), TMA (16.13%), TMAO (57.54%) levels, ApoB/ApoA1 ratio (49.25%) and decrease TMA/TMAO ratio (26.16%) were detected in comparison with group I. In groups I and II, there was a significant increase in TC (32.64 and 43.06%, respectively), TG (80.36 and 55.36%, respectively), LDL (70.78 and 72.73%, respectively), Lpα (41.17 and 54.95% respectively), ApoB (85.12 and 140.50% respectively), CRP (136.26 and 232.97%, respectively), IL-6 (65.22 and 103.11%, respectively), TMA (22.50 and 42.25%, respectively), TMAO (50.00 and 136.31%, respectively) and decreasing HDL (16.09 and 29.31%, respectively) compared with CG ($P < 0.05$). TMA/TMAO ratio was significantly lower in groups I (18.59%) and II (39.89%) than in CG ($P < 0.05$).

Also, plasma AA spectrums in CAD patients with and without AF were compared with CG (group of patients without CAD and AF). A general overview of the investigated groups plasma AA levels is provided in Table 2.

In group I patients, in comparison with CG, a decrease in glycine (83.5%), valine (18.10%) and alanine (74.86%) levels was detected ($P < 0.05$). In group II patients, in comparison with CG, an increase glutamate (43.60%) and a decrease in glycine (85.16%), valine (25.75%), alanine (72.73%), tyrosine (63.55%) and glutamine (68.47%) levels were found ($P < 0.05$). In group II, in comparison with group I, increasing glutamate (35.14%) and decreasing absolute glycine (10.07%) levels was detected ($P < 0.05$).

For a deeper understanding of pathogenetic ways of the amino AA exchange in patients with CAD and AF, different plasma AA groups were investigated. Their meanings are shown in Table 3.

In groups I and II, in comparison with CG, there was a decrease in Isoleucine+Leucine/Valine ratio (42.68 and 45.86%, respectively), Glycine+Serine sum (77.27 and 78.88%, respectively), Glycine/Methionine ratio (19.38 and 55.01%, respectively) and increase of Phenylalanine/Tyrosine ratio (31.88 and 66.67%, respectively) ($P < 0.05$). Glycine/Methionine ratio was lower in group II (44.19%) in comparison with group I ($P < 0.05$). Phenylalanine/Tyrosine ratio in group II was higher (26.37%) than in group I ($P < 0.05$). Glutamine/glutamate ratio in-

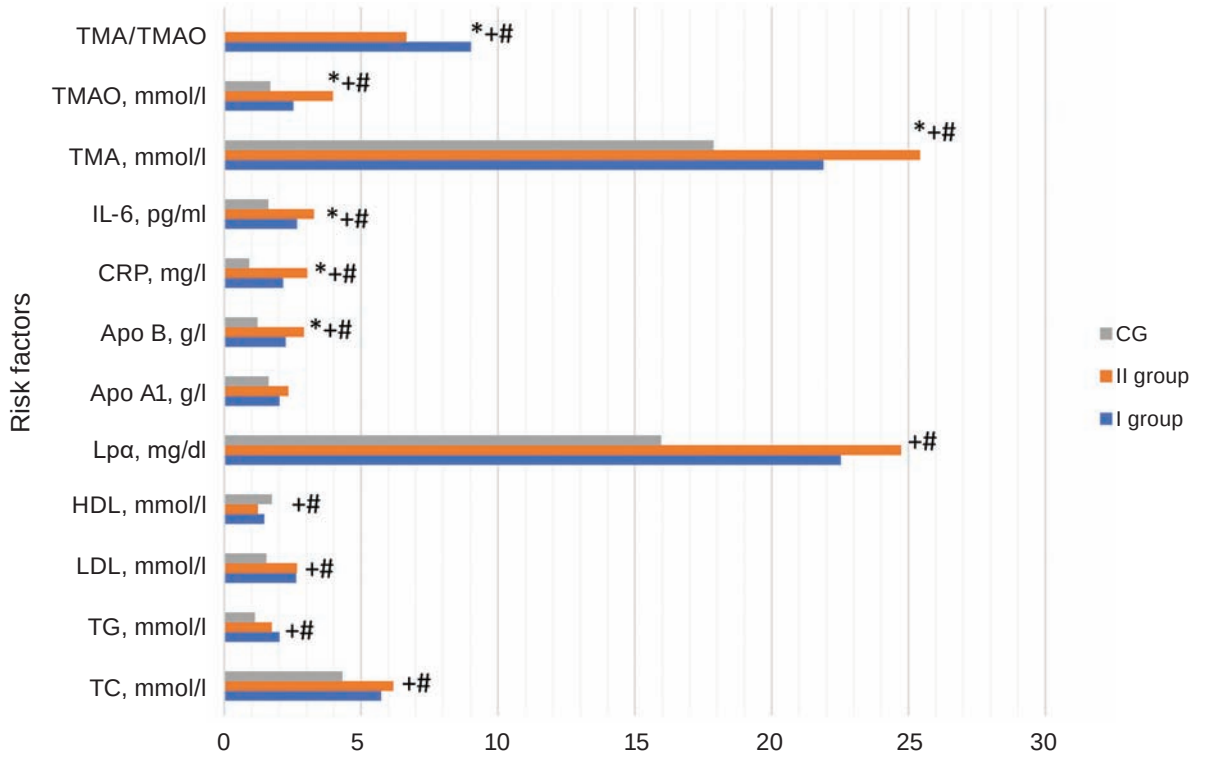

*Fig. 1. Cardiometabolic risk factors in investigated groups. *P < 0.05 I-II groups; +P < 0.05 group I – CG; #P < 0.05 group II – CG*

crease in group II compared with I (37.60%) and CG (94.71%) ($P < 0.05$).

The correlation analysis between plasma AA spectrums and cardiometabolic risk factors of the examined groups was done. Spearman's correlation analysis was used to explore their correlations with species abundance. All correlations are shown in Fig. 2.

The largest amount of correlations was checked between plasma AA spectrum and such clinical characteristics as the total amount of fecal SCFA (total number = 12), ApoB (total number = 10), CRP (total number = 9), TMAO (total number = 8) and TMA (total number = 8) levels. At the same time, the highest amount of correlations was between glycine (total number = 9), valine (total amount = 8), arginine (total number = 7), glutamate (total number = 7), isoleucine (total number = 7), alanine (total number = 6), methionine (total number = 6) and clinic-laboratory changes.

In opinion, significant changes in plasma AA spectrum levels should be a promising prognostic marker for AF paroxysm among CAD patients. ROC-analysis was performed individually for each plasma AA and their combinations for further validation of their diagnostic values. We found that optimal plasma AA combinations can be used as prognostic markers of risk AF paroxysm in CAD patients. The area under the ROC curve exceeded 0.75 for different AA and their combinations, while the P value was significant ($P < 0.05$). The ROC-analysis, therefore, further validated the prognostic value of the plasma levels of AA in AF and CAD. It was made for CAD/AF. Results are shown in Fig. 3.

2,44 * Isoleucine – Glycine and 3,16 * Phenylalanine – Glycine show an excellent evaluation opportunity for AF paroxysm diagnostic and prediction through CAD patients. Moreover, it showed the importance of glycine, alanine, BCAA (isoleucine, valine) and AAA (phenylalanine) in AF paroxysm development in CAD patients, that further validated the diagnostic value of listed AA.

Discussion

Obtained cardiometabolic risk factors changes – significant increase in ApoB, CRP, IL-6, TMA, TMAO levels and decreased TMA/TMAO ratio in patients with CAD and AF in comparison with CAD patients without arrhythmias are predictable according to the literature data [18].

Table 2. Plasma amino acid spectrums in CAD patients with or without AF compared with the control group, mean [95% CI], mμmol/l

Characteristic	Groups					
	I	II	CG	*P*1-2	*P*2-CG	*P*1-CG
Lysine	25.35 [19.44; 133.33]	29.84 [19.36; 112.24]	91.83 [17.18; 181.32]	*P*>0.05	*P*>0.05	*P*>0.05
Histidine	11.52 [9.48; 53.04]	10.32 [9.60; 46.48]	46.49 [5.56; 63.38]	*P*>0.05	*P*>0.05	*P*>0.05
Arginine	13.13 [8.57; 87.5]	22.96 [9.12; 79.55]	62.09 [6.63; 119.32]	*P*>0.05	*P*>0.05	*P*>0.05
Ornithine	16.04 [10.01; 122.22]	22.09 [11.78; 88.00]	75.59 [7.85; 179.89]	*P*>0.05	*P*>0.05	*P*>0.05
Taurine	12.04 [4.8; 29.41]	7.87 [4.30; 45.29]	23.97 [3.28; 53.37]	*P*>0.05	*P*>0.05	*P*>0.05
Asparaginate	4.82 [1.42; 6.08]	3.95 [1.83; 4.39]	4.43 [0.79; 9.39]	*P*>0.05	*P*>0.05	*P*>0.05
Threonine	21.19 [12.87; 63.22]	17.65 [14.23; 69.54]	61.82 [10.97; 91.46]	*P*>0.05	*P*>0.05	*P*>0.05
Serine	15.08 [13.7; 52.17]	20.64 [13.49; 29.37]	60.18 [11.51; 103.45]	*P*>0.05	*P*>0.05	*P*>0.05
Glutamate	18.67 [15.64; 29.41]	25.23 [21.51; 36.76]	17.57 [7.34; 20.15]	*P*<0.05	*P*<0.05	*P*>0.05
Proline	25.00 [16.33; 63.46]	23.33 [16.67; 82.50]	80.23 [13.33; 115.38]	*P*>0.05	*P*>0.05	*P*>0.05
Glycine	31.18 [20.95; 147.90]	28.04 [21.50; 44.82]	189.0 [56.56; 281.40]	*P*<0.01	*P*<0.01	*P*<0.05
Alanine	57.86 [45.64; 145.29]	56.25 [48.31; 131.65]	206.28 [40.47; 345.24]	*P*>0.05	*P*<0.01	*P*<0.05
Cysteine	6.52 [5.32; 78.95]	5.69 [5.21; 39.47]	44.83 [5.32; 88.45]	*P*>0.05	*P*>0.05	*P*>0.05
Valine	28.56 [22.44; 142.86]	25.89 [19.48; 137.50]	34.87 [13.97; 82.86]	*P*>0.05	*P*<0.05	*P*<0.05
Methionine	2.71 [2.07; 9.18]	3.97 [2.64; 11.09]	6.03 [2.37; 16.13]	*P*>0.05	*P*>0.05	*P*>0.05
Isoleucine	8.33 [5.78; 31.5]	11.02 [6.86; 36.17]	31.38 [5.34; 46.88]	*P*>0.05	*P*>0.05	*P*>0.05
Leucine	16.35 [12.70; 61.54]	23.07 [12.90; 63.46]	51.87 [12.90; 92.31]	*P*>0.05	*P*>0.05	*P*>0.05
Tyrosine	8.01 [5.84; 35.71]	7.69 [5.96; 15.07]	21.10 [9.57; 44.12]	*P*>0.05	*P*<0.05	*P*>0.05
Phenylalanine	6.79 [6.08; 23.53]	12.14 [6.69; 24.12]	17.64 [5.56; 29.41]	*P*>0.05	*P*>0.05	*P*>0.05
Glutamine	78.22 [57.14; 337.26]	74.01 [51.19; 164.44]	234.79 [96.18; 398.53]	*P*>0.05	*P*<0.05	*P*>0.05
Ammonia	15.00 [11.22; 77.78]	27.97 [17.50; 66.95]	36.985 [9.06; 83.76]	*P*>0.05	*P*>0.05	*P*>0.05

Table 3. Plasma AA spectrums combinations in CAD patients with or without AF compared with the control group, mean [95% CI], mμmol/l

Characteristic	Groups					
	I	II	CG	*P*1-2	*P*2-CG	*P*1-CG
Isoleucine+ Leucine/ Valine	0.90 [0.70; 0.96]	0.85 [0.78; 0.98]	1.57 [1.11; 2.86]	*P*>0.05	*P*<0.05	*P*<0.05
Glycine+ Serine	47.40 [34.78; 188.10]	56.55 [39.73; 95.82]	208.52 [28.07; 363.95]	*P*>0.05	*P*<0.05	*P*<0.05
Glycine/ Methionine	11.11 [8.37; 16.59]	6.20 [4.91; 10.16]	13.78 [10.69; 25.67]	*P*<0.05	*P*<0.05	*P*<0.05
Phenylalanine/ Tyrosine	0.91 [0.72; 1.16]	1.15 [0.98; 1.40]	0.69 [0.45; 1.04]	*P*<0.05	*P*<0.05	*P*<0.05
Glutamine/ Glutamate	5.08 [3.90; 8.18]	6.99 [6.17; 9.08]	3.59 [2.13; 7.80]	*P*<0.05	*P*<0.05	*P*>0.05

This study evaluates the plasma AA spectrum as an important part of metabolic profile and their network in pathogenesis of AF paroxysm in CAD patients. Their role was checked by the following observations: several plasma AAs (glutamate, glutamine, glycine, alanine, valine, tyrosine) and their combinations (Isoleucine+Leucine/Valine, Glycine+Serine, Glycine/Methionine, Phenylala-

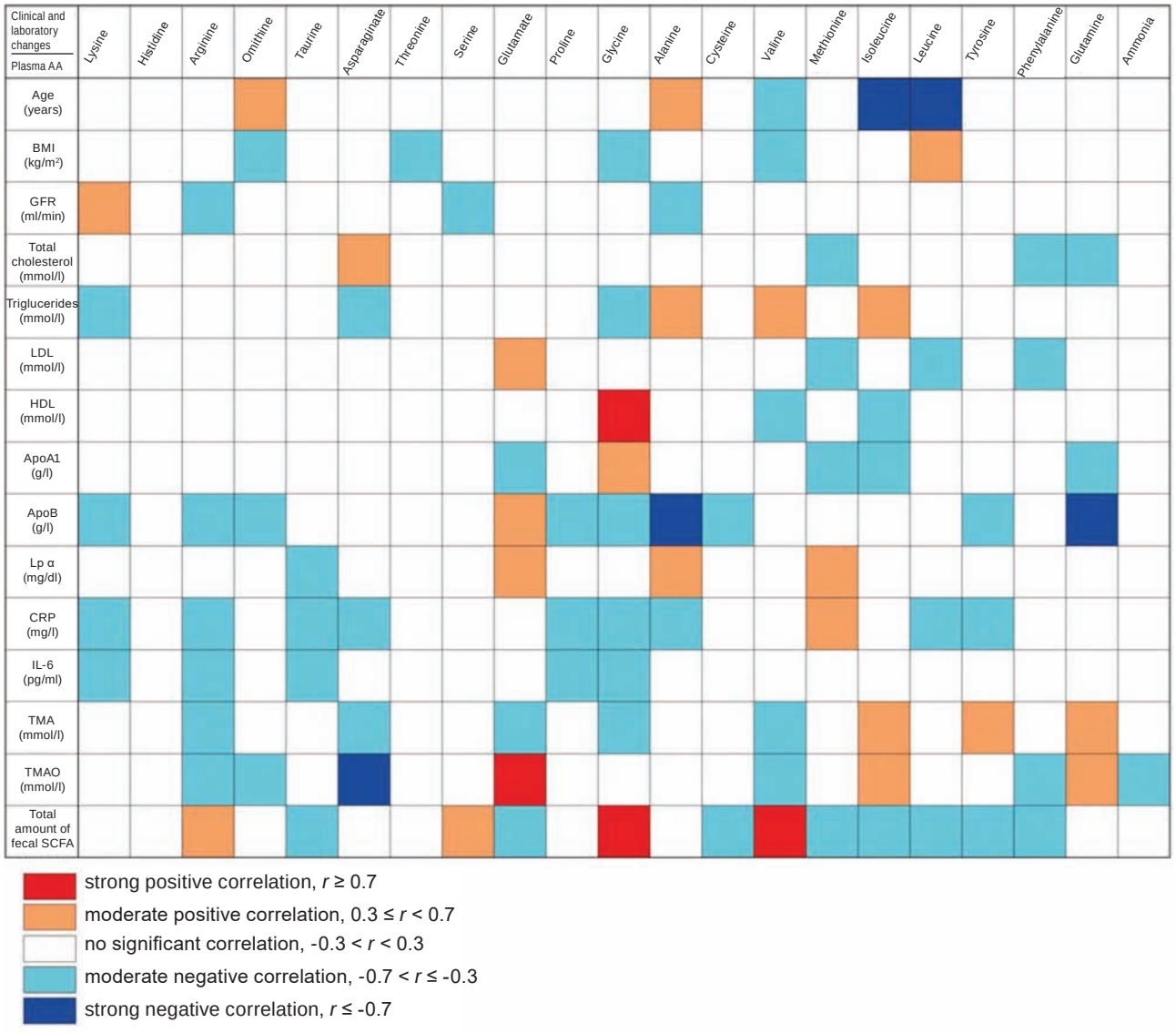

Fig. 2. Heatmap correlation matrices between plasma AA levels and cardiometabolic risk factors, P < 0.05

nine/Tyrosine, Glutamine/Glutamate) changes in CAD+AF patients; their strong correlations with mean clinic-laboratory groups characteristics (glycine, valine, arginine, glutamate, isoleucine, alanine, methionine); highly validated role of some AA combinations as a marker of AF paroxysm through CAD patients (2,44 * Isoleucine – Glycine; area under ROC-curve 0.8122 and 3,16 * Phenylalanine – Glycine, area under ROC-curve 0.8061).

The plasma AA spectrum is an important marker of human metabolism. Its changes are common for different pathological conditions, including AF [8-10] and atherosclerosis [11, 12]. But the obtained data are still staying controversial in different studies, that understands an importance of further investigations. Moreover, in our work, we detected the optimal AA combinations that can help us to predict AF paroxysm in CAD patient that was not done before.

According to the published data, branched-chain amino acids (BCAA) metabolism plays an important role in the development of diabetes mellitus and dyslipidemia [9, 13]. Aromatic amino acids (AAA) are closely associated with lipid exchange alterations [21] and atherosclerosis [22]. BCAA (isoleucine, valine, leucine) and AAA (phenylalanine, tyrosine) metabolism are closely linked with gut microbiota conditions [23], in our study, they correlated with such gut microbiota metabolites as TMA, TMAO and the total amount of fecal SCFA. Glutamine/glutamate ratio was closely connected with BCAA metabolism [19].

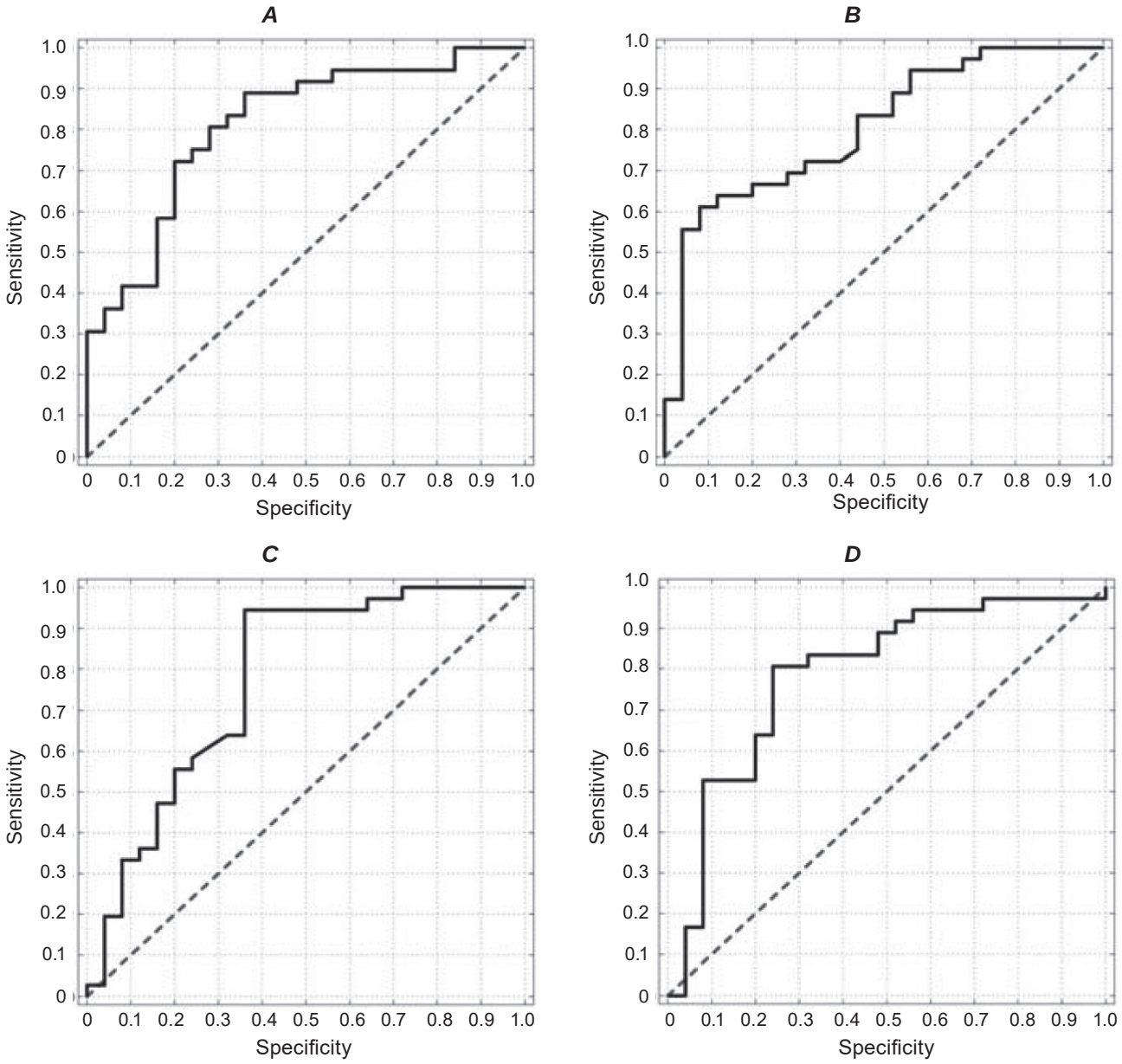

Fig. 3. ROC-curve analysis for respective AA and their combinations in CAD and CAD+AF groups, P < 0.05. ***A*** *– 2.44 * Isoleucine – Glycine, area under ROC-curve 0.8122;* ***B*** *– 3.16 * Phenylalanine – Glycine, area under ROC-curve 0.8061;* ***C*** *– 106 * Valine/Glycine – Alanine, area under ROC-curve 0.7750;* ***D*** *– Glycine – 19.4 * Alanine/Isoleucine, area under ROC-curve 0.7889*

Also, the role of glycine, serine and methionine in lipid exchange, gut microbiota condition is still interesting [9, 12, 20]. In our study, alterations in glycine metabolism play an important role in AF paroxysm pathogenesis. According to published data, about 30% of glycine supplied with food is metabolized by the microbiota of the small intestine, and by both gram-positive and gram-negative flora. However, what determines the activity of glycine degradation by intestinal microbiota is still unknown. For example, the activity of glycine degradation increases in patients with type 2 diabetes. It was found that patients who took probiotics (bifido and lactobacilli) had a lower concentration of glycine in their feces. An increase in the content of formic acid in the stool is a sign of increased glycine degradation under the influence of the gut microbiome. On the other hand, the state of the intestinal microbiome can influence the metabolism of glycine in the host's body due to changes in the expression of en-

zymes. It was estimated that intestinal dysbiosis has an effect on the development of NASH by reducing the content of circulating glycine. Also, obesity and metabolic syndrome are closely associated with a decrease in circulating glycine and disruption of the gut microbiome [24].

Study limitations. Further verification of obtained data requires a prospective study of CAD patients without arrhythmia. The patients with first time occurred AF paroxysm may have other AA profile. However, they are poorly investigated due to commonly asymptomatic course.

Conclusions. Plasma AA spectrum evaluation can be a new promising metabolic marker/pattern for AF paroxysm in CAD patients. Moreover, altered AA levels might have considered the depth of pathogenetic changes during AF paroxysm formations as it was characterized by violations in BCAA (isoleucine, leucine, valine), AAA (phenylalanine, tyrosine), glutamine/glutamate, glycine/serine and glycine/methionine metabolism. A strong reliable connection between plasma AA spectrum and known gut microbiota metabolites (TMA, TMAO, total amount of fecal SCFA) was detected. Also, we proposed the highly validated plasma AA combinations that can be used as an early marker for AF paroxysm in CAD patients ($P < 0.05$): 2.44 * Isoleucine – Glycine; area under ROC-curve 0.8122 and 3.16 * Phenylalanine – Glycine, area under ROC-curve 0.8061.

Conflict of interest. The authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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ОСОБЛИВОСТІ АМІНОКИСЛОТНОГО СПЕКТРА ПЛАЗМИ ТА КАРДІОМЕТАБОЛІЧНІ ФАКТОРИ РИЗИКУ У ПАЦІЄНТІВ ІЗ ІШЕМІЧНОЮ ХВОРОБОЮ СЕРЦЯ ТА ФІБРИЛЯЦІЄЮ ПЕРЕДСЕРДЬ

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Відомо, що профіль амінокислот (АК) плазми крові є новим перспективним біомаркером для скринінгу патогенезу ішемічної хвороби серця (ІХС), пов’язаної з дисбактеріозом кишечника. Метою нашого дослідження було оцінити спектр амінокислот плазми крові у пацієнтів з ІХС та фібриляцією передсердь (ФП) і перевірити їх зв’язок із метаболітами мікробіоти кишечника. Для визначення спектра амінокислот у плазмі крові 300 пацієнтів було розподілено на три групи: ІХС – 149 пацієнтів з ІХС, ІХС+ФП – 123 пацієнти з ІХС та пароксизмом ФП і контрольна група – 28 пацієнтів без ІХС та аритмій. Рівень АА в плазмі визначали за допомогою іонообмінної рідинної колонкової хроматографії. Виявлено суттєві зміни вмісту глутамату, глутаміну, гліцину, аланіну, валіну, тирозину та комбінацій ізолейцин+лейцин/валін, гліцин+серин, гліцин/метіонін, фенілаланін/тирозин, глутамін/глутамат у плазмі крові хворих на ІХС+ФП. Встановлено достовірний зв’язок між спектром АК плазми крові та метаболітами мікробіоти кишечника – триметиламіном, триметиламін-N-оксидом та загальною кількістю коротколанцюгових жирних кислот у фекаліях. Було запропоновано високо валідовані комбінації амінокислот плазми ізолейцин – гліцин (площа під ROC-кривою 0,8122) та фенілаланін – гліцин (площа під ROC-кривою 0,8061), які можуть бути використані як ранні маркери пароксизму ФП у хворих на ІХС.

Ключові слова: ішемічна хвороба серця, фібриляція передсердь, метаболіти мікробіому кишечника, амінокислоти плазми.

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