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Holter ECG monitoring and gut microbiota composition in coronary artery disease patients with atrial fibrillation

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Abstract. ***The aim:*** to analyze and find the connections between Holter ECG monitoring indexes and gut microbiota composition in patients with coronary artery disease and atrial fibrillation. ***Materials and methods.*** 300 patients were divided into 3 groups: first (CAD) — 149 patients with CAD but without arrhythmias, second (CAD+AF) — 124 patients with CAD and AF paroxysm, and the control group — 27 patients without CAD and arrhythmias. ***Results.*** The II group patients are characterized by an increase in *Pseudomonadota* (by taxonomic analysis), *Actinobacter spp.* and a decrease in *Blautia spp., Bacteroides thetaiotaomicron* in comparison with the I group, p<0.05. Total supraventricular extrasystoles are significantly correlated with *Verrucomicrobiota* (*Akkermansia muciniphila*, r=–0.340), p<0.05. Total VE is significantly correlated with *Pseudomonadota* (r=0.356), F/B ratio (r=–0.468) — by phylum analysis, *and* by species analysis — *Blautia spp.* (r=–0.336), *Actinobacter spp.* (r=0.325), *Eubacterium rectale* (r=–0.327), and *Roseburia inulinivorans* (r=–0.317), p<0.05. The AF paroxysm occurrence is significantly correlated with *Actinobacter spp.* (r=0.309) and *Eubacterium rectale* (r=–0.328), p<0.05. *ST*-segment changes are correlated only with *Streptococcus spp.* (r=0.369), p<0.05. ***Conclusion.*** Gut microbiota species (*Akkermansia muciniphila, Blautia spp., Actinobacter spp., Eubacterium rectale, Roseburia inulinivorans, Streptococcus spp.)* are significantly correlated with rhythm abnormalities (supraventricular and ventricular) and *ST*-segment changes.

Key words: coronary artery disease, atrial fibrillation, heart rhythm violations, Holter ECG monitoring, gastrointestinal microbiome.

Introduction

In recent years, growing evidence suggests that gut microbiota plays a crucial role in coronary artery disease (CAD) pathogenesis. CAD development depends on chronic vascular inflammation and endothelial injury, which are closely associated with gut microbiota conditions. Gut microbiota provides our metabolic health — lipids, proteins, carbohydrates exchange, and energy metabolism. Gut dysbiosis underlies inflammatory, neurological, cardiovascular, and metabolic diseases and cancer. Gut microbiota composition regulates intestinal barrier integrity and leakage of intestinal metabolites in blood bloodstream, which leads to microbial endotoxemia and chronic low-grade inflammation persistence [1].

Recent preclinical studies have implicated gut dysbiosis as a contributor to atrial fibrillation (AF). It stimulates the progression of a multiplicity of cardiovascular risk factors: dyslipidemia, obesity, atherosclerosis, CAD, arterial hypertension, heart failure, etc. Impairment of the intestinal barrier and circulating gut microbiota metabolites disbalance leads to electrical and structural atrial remodeling. Nowadays, some small observational studies identify the gut microbiota peculiarities in patients with AF, but their results are still controversial. Unfortunately, the effects of gut microbiota change on AF pathogenesis are poorly understood [2, 3].

Holter ECG monitoring is a widely used and reliable diagnostic method. It is prescribed to patients with AF paroxysms to determine the best treatment strategy or heart rate control management and for stable CAD patients with a new episode of ischemia clinical features. It is used for rhythm abnormalities and *ST*-segment change detection [4].

Thus, searching for a significant association between heart rhythm abnormalities, *ST*-segment changes, and gut microbiota features is a contemporary scientific problem.

The aim: to check the connections between Holter ECG monitoring indexes and gut microbiota composition in patients with coronary artery disease and atrial fibrillation.

Materials and methods

In our study, 300 patients were divided into 3 groups: I (CAD) — 149 patients with CAD but without arrhythmias, II (CAD+AF) — 124 patients with CAD and AF paroxysm, and the control group (CG) — 27 patients without CAD and arrhythmias. CAD and AF diagnoses were based on the latest ESC guidelines [5, 6]. All patients were treated in the Kyiv City Clinical Hospital № 12 in cardiological and therapeutic departments in 2018–2023 years. Diagnosis CAD was confirmed by a history of coronary artery stenotic changes during invasive coronary angiography. AF paroxysm was checked by resting 12 leads electrocardiography. All patients had heart failure stage B or C [7].

Exclusion criteria were: 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), 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. The study was conducted at the base and was approved by the ethical commission of the Kyiv City Clinical Hospital № 12 (protocol № 8 from 22/08/2018). Informed consent was obtained from all subjects by the Declaration of Helsinki. Baseline characteristics of the study patients include age, gender, history of myocardial infarction (MI), stroke, diabetes mellitus, obesity, body mass index (BMI), uric acid, total bilirubin, GFR, total cholesterol (TC) levels. Uric acid, total bilirubin, creatinine, and TC were checked by the Kyiv City Clinical Hospital № 12 laboratory (certificate № ПТ — 257/21). Advanced age, obesity, hypercholesterolemia, high stages of chronic kidney disease, gout, and hyperbilirubinemia are known risk factors of AF paroxysm development [5]. That's why these baseline characteristics were analyzed and compared because it can help us to exclude their influence on obtained results.

Holter ECG monitoring 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. A channel Holter ECG monitor («Cardiosens K», Ukraine) was used. We assessed Holter monitoring in V1, aVF and V5 leads during 24 hours. Arrhythmia and conduction abnormalities, *ST*-segment, and QTc monitoring were evaluated by Holter ECG. Studied main indexes were: maximum heart rate (HR, bpm), minimum HR (bpm), average HR (bpm), total number of supraventricular extrasystoles (SVE), number of pairs SVE, number of groups SVE, number of supraventricular tachycardia (SVT) episodes, longest duration of SVT, maximum HR of SVT episode, number of SVE's per hour, number of AF paroxysm, longest duration of AF paroxysm, total number of ventricular extrasystoles (VE), number of pairs VE, number of groups VE, number of ventricular tachycardia (VT) episodes, longest duration of VT, maximum HR of VT episode, number of VE's per hour, number of pauses more than 3 sec, maximum *ST* depression (mkV), maximum *ST* elevation (mkV), maximum *ST* duration (min) [4].

Determination of the gut microbiota composition was carried out using quantitative PCR qRT-PCR using primers for the 16S rRNA gene and taxon-specific primers. Such domains were checked: bacteria — Firmicutes (*Lactobacillus spp., Faecalibacterium prausnitzii, Enterococcus spp., Blautia spp., Streptococcus spp., Eubacterium rectale, Roseburia inulinivorans, Ruminococcus spp.*), Bacteroides (*Bacteroides spp., Bacteroides thetaiotaomicron, Prevotella spp.*), Actinomycetota (*Bifidobacterium spp.)*, Verrucomicrobiota (*Akkermansia muciniphila*), Pseudomonadota (*Escherichia coli, Acinetobacter spp.)* and Archaea (*Methanobrevibacter smithii and Methanosphaera stadmanae*). Also, *Firmicutes/Bacteroides* (F/B) ratio was compared [1–3].

Results were presented as mean±standard error or [95% confidence interval (CI)] for continuous variables or as a number for categorical variables. The Pearson criterion checked variable distribution for normality. Data were compared using the Wilcoxon signed-rank test or Student t-test with two critical regions by the type of distribution; Spearman's rank correlation coefficient [8]. All calculations were done in MATLAB R2014a (License № 271828).

Results

We checked the baseline characteristics in the investigated groups. Significant differences in age, gender, BMI, total bilirubin, and smoking history were not found, p<0.05. In the I and II groups were patients with obesity, diabetes mellitus, stroke, or MI history, such cases were absent in CG. In the I and II groups uric acid (by 22.66% and 30.53%, respectively) and TC (by 32.64% and 43.06%, respectively) levels were higher and GFR (by 26.16% and 19.38%, respectively) was lower than in CG, p<0.05. The data are shown in Table 1.

Holter ECG monitoring results were investigated in our study. The average Holter monitoring duration has lasted for 22,13±0.22 hours. The supraventricular and ventricular arrhythmia and *ST*-segment changes have significant differences between the investigated groups.

Supraventricular rhythm abnormalities are characterized by changes in HR, SVE, and AF paroxysms. The I and II groups were characterized by significant depletion in average (9.38% and 14.14%, consequently) and minimum HR (13.82% and 11.36%, consequently) in comparison with the CG, p<0.05. The II group had a significant decrease in average HR (5.26%) in comparison with the I group, p<0.05. In the I group patients a significant increase in SVEs per hour, total SVE, single SVE, pair SVE, group SVE, SVT, and its duration were detected in comparison with the CG, p<0.05. In the II group patients a significant increase in SVEs per hour, total SVE, single SVE, pair SVE, group SVE, SVT, its duration, AF paroxysm, and its duration were detected in comparison with the CG, p<0.05. In the II group patients a significant increase in SVEs per hour, total SVE, single SVE, pair SVE, AF paroxysm, and its duration were detected in comparison with the I group, p<0.05.

Ventricular arrhythmias presented VE and VT. In the I group patients a significant increase in VEs per hour, total VE, single VE, pair VE, and group VE were detected in comparison with the CG, p<0.05. In the II group patients a significant increase in VEs per hour, total VE, single VE, pair VE, and group VE were detected in comparison with the CG, p<0.05. In the II group patients a significant increase in VEs per hour, total VE, single VE, and pair VE were detected in comparison with the I group, p<0.05. At the same time, VT episodes and pauses of more than 3 s were not detected in the investigated groups.

ST-segment changes include *ST* elevation and depression, and their duration. *ST* elevation and depression episodes were not observed in the CG and a significant difference in *ST*-segment changes was not found, p<0.05. The data are shown in Table 2.

Gut microbiota composition was analyzed in investigated groups. The F/B ratio was not significantly different in the investigated groups, p>0.05. By the taxonomic analysis in the I and II groups was a significant increase in *Pseudomonadota* and a decrease in *Actinomycetota* and *Verrucomicrobiota* compared with CG, p<0.05. In the II group compared with the I group was a significant rise in *Pseudomonadota*, p<0.05. By the species analysis in the I and II groups comparing with CG were the significant

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

Characteristic /group	I group	II group	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
Diabetes mellitus, %	18.12	14.63	0	p>0.05	p<0.05	p<0.05
Obesity, %	8.84	12.0	0	p>0.05	p<0.05	p<0.05
BMI, kg/m^2	27.02±0.33	26.93±0.43	27.12±2.10	p>0.05	p>0.05	p>0.05
Total bilirubin, mmol/l	11.3±0.09	12.4±0.08	11.7±0.11	p>0.05	p>0.05	p>0.05
Uric acid, mmol/l	380.5±28.16	404.9±36.11	310.2±29.12	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
TC, mmol/l	5.73±0.37	6.18±0.31	4.32±0.21	p>0.05	p<0.05	p<0.05

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

Characteristic/group	I group	II group	CG	P1–2	P2–CG	P1–CG
Maximum HR, bpm	110.20±2.48	106.6±3.89	109.8±3.97	p>0.05	p>0.05	p>0.05
Minimum HR, bpm	45.6±1.68	46.9±1.66	52.91±1.30	p>0.05	p<0.05	p<0.05
Average HR, bpm	66.98±0.99	63.46±1.24	73.91±2.20	p<0.05	p<0.05	p<0.05
SVE total	36 [95% CI 24–43]	729 [95% CI 331–982]	7 [95% CI 0–15]	p<0.05	P<0.05	p<0.05
SVE single	32 [95% CI 24–43]	502 [95% CI 307–766]	7 [95% CI 0–15]	p<0.05	p<0.05	p<0.05
SVE pair	0 [95% CI 0–3]	27 [95% CI 8–42]	0	p<0.05	p<0.05	p<0.05
SVE group	0 [95% CI 0–1]	5 [95% CI 0–9]	0	p>0.05	p<0.05	p<0.05
SVT	0 [95% CI 0–1]	0 [95% CI 0–1]	0	p>0.05	p<0.05	p<0.05
Longest SVT, s	0 [95% CI 0–16]	0 [95% CI 0–42]	0	p>0.05	p<0.05	p<0.05
SVEs per hour	8 [95% CI 3–17]	38 [95% CI 11–112]	0 [95% CI 0–2]	p<0.05	p<0.05	p<0.05
AF paroxysm	0	0 [95% CI 0–1]	0	p<0.05	p<0.05	p>0.05
Longest AF paroxysm, s	0	0 [95% CI 0–44]	0	p<0.05	p<0.05	p>0.05
VE total	0 [95% CI 0–3]	3 [95% CI 0–15]	0 [95% CI 0–1]	p<0.05	p<0.05	p<0.05
VE single	0 [95% CI 0–3]	3 [95% CI 0–15]	0	p<0.05	p<0.05	p<0.05
VE pair	0 [95% CI 0–2]	3 [95% CI 0–15]	0	p<0.05	p<0.05	p<0.05
VE group	0 [95% CI 0–1]	0 [95% CI 0–2]	0	p>0.05	p<0.05	p<0.05
VT	0	0	0	p>0.05	p>0.05	p>0.05
Longest VT, s	0	0	0	p>0.05	p>0.05	p>0.05
VE's per hour	14 [95% CI 5–19]	32 [95% CI 17–41]	0 [95% CI 0–1]	p<0.05	p<0.05	p<0.05
Pauses more than 3 s	0	0	0	p>0.05	p>0.05	p>0.05
Longest pauses, s	0	0	0	p>0.05	p>0.05	p>0.05
Changes *ST* segment, quantity episodes	0 [95% CI 0–3]	0 [95% CI 0–6]	0	p>0.05	p<0.05	p<0.05
Maximum *ST* depression, mkV	0 [95% CI 0–118]	0 [95% CI 0–124]	0	p>0.05	p<0.05	p<0.05
Maximum *ST* elevation, mkV	0 [95% CI 0–133]	0 [95% CI 0–112]	0	p>0.05	p<0.05	p<0.05
Maximum *ST* episode duration, minutes	2 [95% CI 1–5]	2 [95% CI 1–5.5]	0	p>0.05	p<0.05	p<0.05

increase in *Bacteroides spp., Faecalibacterium prausnitzii, Actinobacter spp., Streptococcus spp. and* decrease in *Lactobacillus spp., Bifidobacterium spp., Akkermansia muciniphila, Eubacterium rectale,* p<0.05. In the I group in comparison with CG was a significant rise in *Ruminococcus spp.,* p<0.05. In the II group in comparison with CG was a significant decrease in *Roseburia inulinivorans*, p<0.05. In the II group in comparison with the I group was a significant rise in *Actinobacter spp.* and decrease in *Blautia spp., Bacteroides thetaiotaomicron*, p<0.05. The data are shown in the Figure.

The correlation analysis between gut microbiota phylum and Holter ECG monitoring findings was done in our study. Spearman's correlation analysis was used to explore their correlations. *Verrucomicrobiota* is significantly correlated with total SVE (r=–0.340), single SVE (r=–0.348), and SVE per hour (r=–0.392), p<0.05. *Pseudomonadota* is significantly correlated with total VE (r=0.356) and single VE (r=0.356), p<0.05. The F/B ratio is significantly correlated with total VE (r=–0.468) and single VE (r=–0.467), p<0.05. The data are presented in Table 3.

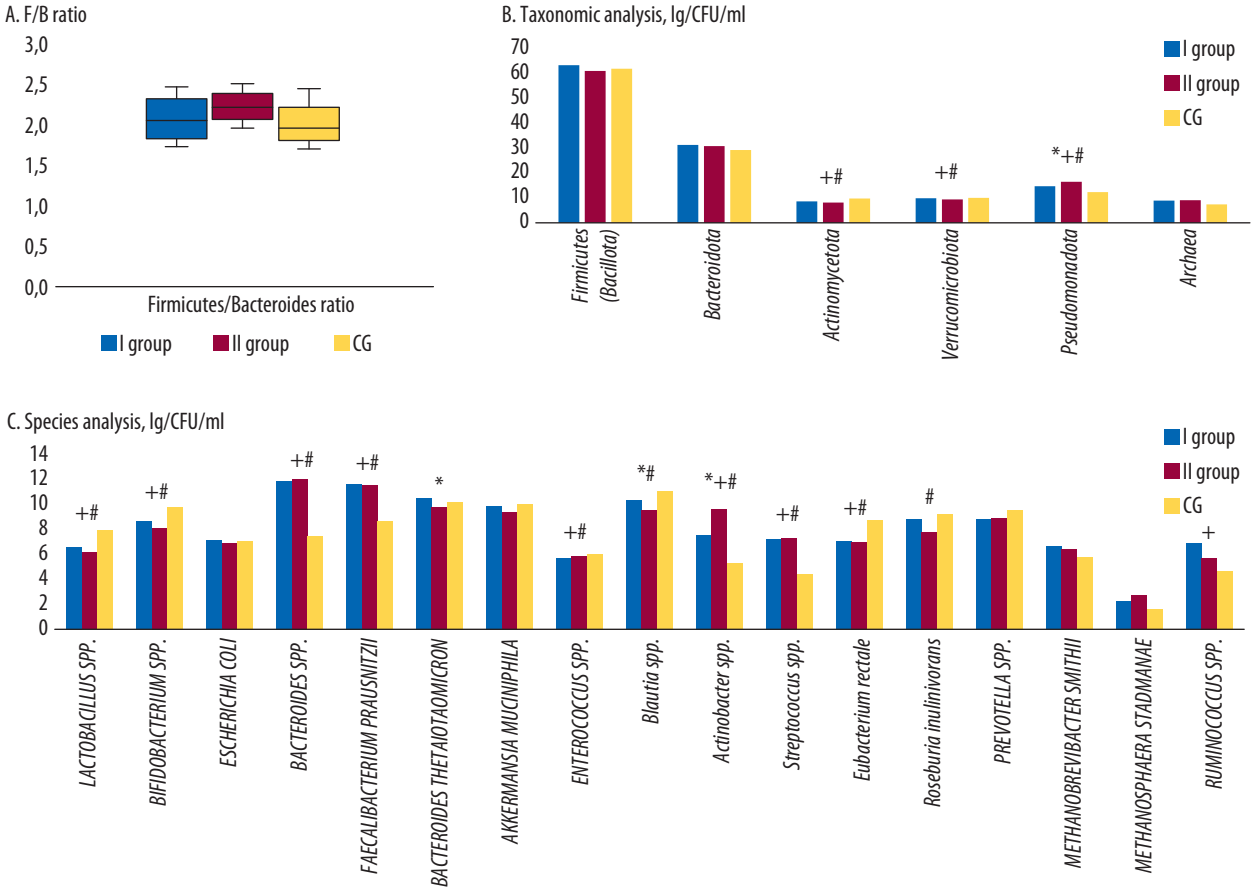
The correlation analysis between gut microbiota species and Holter ECG monitoring findings was done in our work. Spearman's correlation analysis was used to explore their correlations. The largest amount of correlations was checked between Holter ECG monitoring indexes and *Eubacterium rectale* (total number=5), *Roseburia inulinivorans* (total number=4), *Actinobacter spp.* (total number=3) and *Akkermansia muciniphila* (total number=3). The highest amount of correlations were found between total VE (total number=4), single VE (total number=4), and gut microbiota species. *Akkermansia muciniphila* is significantly correlated with total SVE (r=–0.340), single SVE (r=–0.348), and SVE per hour (r=–0.392), p<0.05. Total VE is significantly correlated with *Blautia spp* (r=–0.336), *Actinobacter spp.* (r=0.325), *Eubacterium rectale* (r=–0.327), and *Roseburia inulinivorans* (r=–0.317), p<0.05. The AF paroxysm occurrence is significantly correlated with *Actinobacter spp.* (r=0.309) and *Eubacterium rectale* (r=–0.328), p<0.05. *ST*-segment changes are correlated only with *Streptococcus spp.* (r=0.369), p<0.05). The data are presented in Table 4.

Discussion

SVEs are associated with *Akkermansia muciniphila* by obtained data. By the latest data, *Akkermansia muciniphila* is presented as a promising new-generation probiotic. Its decrease is directly associated with a plurality of metabolic disorders: obesity, diabetes mellitus, dyslipidemia, and also cancer and inflammation, which are known as arrhythmogenic states [9]. *Akkermansia muciniphila* provides intestinal barrier permeability, by stimulating mucin synthesis, which involves serine and threonine amino acids [10]. Also, it is short-chain fatty acids producing bacteria, which have cardioprotective properties [1]. According to animal studies, *Akkermansia muciniphila* can reverse trimethylamine (TMA) and trimethylamine-N-oxide (TMAO) levels, decrease atrial macrophage infiltration and prevent AF paroxysm [11]. Also, a decrease in *Akkermansia muciniphila* is associated with cerebral ischemia [12].

VEs are significantly correlated with *Blautia spp., Actinobacter spp., Eubacterium rectale*, and *Roseburia inulinivorans*. Nowadays, *Blautia spp*. are shown potential probiotic properties. It is inversing correlated with most host metabolism-related parameters as glucose and lipids exchange violations. Also, *Blautia spp*. have anti-cancerogenic and anti-inflammatory effects, by decreasing interleukin-8 secretion and nuclear factor–kB expression [13]. *Eubacterium rectale* and *Roseburia inulinivorans* are known as butyrate-producing bacteria, which have strong anti-inflammatory properties [14]. In the experimental studies, butyrate shows cardioprotective and anti-ischemic properties [15]. Moreover,

Figure Gut microbiota composition in investigated groups: A — F/B ratio; B — taxonomic analysis, mean [95% CI], lg/CFU/ml; C — species analysis, mean [95% CI], lg/CFU/ml



*p<0.05 I–II groups; +p<0.05 I group–CG; #p<0.05 II group–CG.

Table 3 Correlation matrices between gut microbiota metabolites and Holter ECG monitoring indexes

Holter ECG monitoring indexes/ Gut microbiota phylum	*Firmicutes*	*Bacteroidota*	*Actinomycetota*	*Verrucomicrobiota*	*Pseudomonadota*	*Archaea*	F/B
Maximum HR	–0.306*	–0.216	–0.097	–0.133	0.127	0.104	–0.181
Minimum HR	0.155	–0.032	0.012	0.105	–0.218	–0.055	0.188
Average HR	0.037	–0.171	0.081	–0.074	–0.219	0.065	0.226
SVE total	0.072	0.150	–0.024	–0.340*	0.046	0.055	–0.050
SVE single	0.043	0.144	–0.054	–0.348*	0.059	0.020	–0.082
SVE pair	–0.006	0.100	–0.128	–0.288	0.151	0.118	–0.100
SVE group	0.162	0.236	0.038	–0.072	0.098	0.087	0.028
SVT	0.024	0.124	–0.007	–0.187	0.153	–0.023	–0.038
Longest SVT	0.030	0.137	–0.018	–0.192	0.154	–0.015	–0.039
SVEs per hour	0.097	0.180	–0.155	–0.392*	0.119	0.072	–0.231
AF paroxysm	–0.092	0.138	–0.118	–0.239	0.236	0.137	–0.178
Longest AF paroxysm	–0.081	0.145	–0.118	–0.231	0.223	0.129	–0.173
VE total	–0.232	0.122	–0.219	–0.110	0.356*	0.046	–0.468*
VE single	–0.232	0.122	–0.219	–0.109	0.356*	0.043	–0.467*
VE pair	–0.015	–0.004	–0.012	0.035	–0.027	–0.042	–0.080
VE group	–0.076	–0.015	–0.062	0.008	0.100	0.092	–0.103
VE's per hour	–0.106	–0.098	–0.113	0.095	0.290	–0.135	–0.245
Changes *ST*-segment	0.173	0.216	0.120	–0.039	–0.137	–0.028	0.037
Maximum *ST* depression	0.181	0.218	0.130	–0.032	–0.143	–0.035	0.047
Maximum *ST* elevation	0.166	0.195	0.184	–0.040	–0.181	–0.020	0.075
Maximum *ST* episode duration	0.162	0.312*	0.107	–0.050	–0.136	–0.033	0.018

*Correlations with moderate or strong force (r>0.3) or r<–0.3), p<0.05.

Table 4 Correlation matrices between gut microbiota metabolites and Holter ECG monitoring indexes

Holter ECG monitoring indexes/Platelet amino acids	*Lactobacillus spp.*	*Bifidobacterium spp.*	*Escherichia coli*	*Bacteroides spp.*	*Faecalibacterium prausnitzii*	*Bacteroides thetaiotaomicron*	*Akkermansia muciniphila*	*Enterococcus spp.*	*Blautia spp.*	*Actinobacter spp.*	*Streptococcus spp.*	*Eubacterium rectale*	*Roseburia inulinivorans*	*Prevotella spp.*	*Methanobrevibacter smithii*	*Methanosphaera stadmanae*	*Ruminococcus spp.*
Maximum HR	0.002	–0.097	0.127	0.090	–0.012	–0.136	–0.133	0.018	–0.261	0.151	–0.182	0.306*	0.301*	–0.429*	–0.123	0.189	–0.129
Minimum HR	–0.160	0.012	0.109	0.011	–0.157	0.008	0.105	–0.063	0.305*	–0.264	–0.016	0.372*	0.337*	0.201	–0.011	–0.045	–0.028
Average HR	0.066	0.081	0.206	–0.035	–0.095	–0.095	–0.074	–0.168	0.161	–0.371*	–0.146	0.248	0.147	0.037	0.060	0.060	–0.087
SVE total	0.106	–0.024	–0.169	0.062	0.100	0.027	–0.340*	–0.279	–0.115	0.047	0.087	–0.082	–0.081	–0.135	0.134	0.078	0.146
SVE single	0.114	–0.054	–0.158	0.076	0.103	–0.004	–0.348*	–0.259	–0.122	0.055	0.041	–0.116	–0.117	–0.128	0.136	0.046	0.131
SVE pair	0.076	–0.128	–0.121	0.054	–0.038	–0.049	–0.288	–0.031	–0.129	0.160	–0.006	–0.119	–0.152	–0.147	–0.001	0.209	0.054
SVE group	0.130	0.038	–0.057	0.014	0.068	0.062	–0.072	–0.094	0.017	0.127	0.186	0.059	0.007	–0.015	0.010	0.130	0.173
SVT	0.044	–0.007	–0.063	0.036	0.032	–0.092	–0.187	–0.058	–0.104	0.181	0.015	–0.017	–0.061	–0.036	–0.037	0.017	0.089
Longest SVT	0.056	–0.018	–0.056	0.044	0.050	–0.091	–0.192	–0.067	–0.104	0.180	0.006	–0.013	–0.063	–0.031	–0.023	0.021	0.084
SVEs per hour	0.108	–0.155	–0.120	0.091	0.118	–0.055	–0.392*	–0.309*	–0.100	0.108	0.074	–0.177	–0.094	–0.101	0.158	0.094	0.148
AF paroxysm	0.249	–0.118	0.169	0.097	0.133	–0.073	–0.239	–0.156	–0.148	0.309*	0.041	–0.328*	–0.213	–0.031	0.210	0.074	–0.209
Longest AF paroxysm	0.245	–0.118	0.160	0.089	0.139	–0.063	–0.231	–0.169	–0.133	0.296	0.053	–0.319*	–0.198	–0.014	0.214	0.066	–0.199
VE total	–0.135	–0.219	0.037	0.013	–0.021	0.108	–0.110	–0.099	–0.336*	0.325*	0.194	–0.327*	–0.317*	–0.078	0.244	–0.093	–0.204
VE single	–0.136	–0.219	0.038	0.011	–0.024	0.108	–0.109	–0.100	–0.335*	0.325*	0.195	–0.325*	–0.316*	–0.077	0.242	–0.095	–0.204
VE pair	0.022	–0.012	–0.073	0.054	0.061	–0.023	0.035	0.031	–0.062	0.035	0.019	–0.131	–0.088	–0.046	0.040	–0.044	–0.031
VE group	0.124	–0.062	–0.070	–0.092	–0.130	0.031	0.008	0.182	–0.108	0.111	0.104	–0.177	–0.192	–0.050	0.008	0.091	0.050
VE's per hour	–0.104	–0.113	0.041	0.066	0.033	–0.129	0.095	0.042	–0.232	0.299	0.021	–0.278	–0.211	–0.107	–0.132	–0.102	–0.090
Changes *ST*-segment	0.166	0.120	–0.076	0.103	0.078	0.112	–0.039	–0.113	0.159	–0.090	0.369*	0.075	0.077	0.011	–0.044	–0.020	0.111
Maximum *ST* depression	0.156	0.130	–0.077	0.087	0.082	0.118	–0.032	–0.115	0.169	–0.099	0.277	0.090	0.096	0.025	–0.044	–0.029	0.113
Maximum *ST* elevation	0.182	0.184	–0.08	0.113	0.078	0.102	–0.040	–0.108	0.152	–0.087	0.157	0.056	0.055	0.012	–0.007	–0.080	0.125
Maximum *ST* episode duration	0.182	0.107	–0.08	0.113	0.078	0.102	–0.050	–0.108	0.152	–0.087	0.157	0.056	0.055	0.012	–0.038	–0.026	0.100

*Correlations with moderate or strong force (r>0.3 or r<–0.3), p<0.05.

butyrate can increase insulin sensitivity and negatively correlate with blood glucose levels [1]. In animal studies, *Eubacterium rectale* and *Roseburia inulinivorans* were able to reduce atherosclerotic plaques, and positively connected with high-density lipoproteins (HDL), and negatively with C-reactive protein [16]. Also, a rise in *Actinobacter spp.* is associated with dyslipidemia and atherosclerosis and prothrombotic condition [17].

ST-segment changes are correlated only with *Streptococcus spp.* in our study. An increase of *Streptococcus spp.* in the gut is directly associated with the development of the atherosclerotic process. There are several mechanisms of it. At first, a rise of gut *Streptococcus* leads to increase TMA and TMAO levels in blood flow, what leads to dyslipidemia, prothrombotic state, etc. Secondary, *Streptococcus spp.* abundance contributes to microbial endotoxemia, thereby persist low-grade chronic inflammation, what have proinflammatory and cancerogenic properties. The third, *Streptococcus* DNA is directly found in the atherosclerotic plaque, what directly affects plaque and accelerates atherosclerosis progression [18].

Despite the lack of data about the role of gut microbiota composition in AF pathogenesis, undoubtedly that their closely linked.

Conclusions

The role of gut microbiota peculiarities in heart rhythm disturbances and *ST*-segment changes in patients with coronary artery disease and atrial fibrillation was analyzed in our study:

1. Patients with coronary artery disease and atrial fibrillation are characterized by an increase in *Pseudomonadota* (by taxonomic analysis), *Actinobacter spp.* and a decrease in *Blautia spp., Bacteroides thetaiotaomicron* in comparison with coronary artery disease patients without arrhythmia, p<0.05.

2. In the patients with coronary artery disease and atrial fibrillation an increase in supraventricular and ventricular extrasystoles was checked in comparison with patients with coronary artery disease and without atrial fibrillation, p<0.05.

3. Total supraventricular extrasystoles are significantly correlated with *Verrucomicrobiota* (*Akkermansia muciniphila*, r=–0.340), p<0.05.

4. Total VE is significantly correlated with *Pseudomonadota* (r=0.356), F/B ratio (r=-0.468) — by phylum analysis, *and* by species analysis — *Blautia spp.* (r=–0.336), *Actinobacter spp.* (r=0.325), *Eubacterium rectale* (r=–0.327), and *Roseburia inulinivorans* (r=–0.317), p<0.05.

5. The AF paroxysm occurrence is significantly correlated with *Actinobacter spp.* (r=0.309) and *Eubacterium rectale* (r=–0.328), p<0.05.

6. ST-segment changes are correlated only with *Streptococcus spp.* (r=0.369), p<0.05.

Perspectives of subsequent scientific research

The pathogenetic root of AF paroxysm formation in CAD patients is still unclear. Considering that gut microbiota violations are known basis for most AF and CAD risk factors, the search for gut microbiota phylum and species connected with AF paroxysm formation is a current scientific problem.

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Холтерівський моніторинг електрокардіограми та склад мікробіому кишечнику у пацієнтів з ішемічною хворобою серця та фібриляцією передсердь

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Анотація. ***Мета:*** проаналізувати зв'язок між показниками холтерівського моніторування електрокардіограми та складом мікробіму кишечнику у пацієнтів з ішемічною хворобою серця (ІХС) та фібриляцією передсердь (ФП). ***Об'єкт і методи дослідження.*** 300 пацієнтів розподілені на 3 групи: I — 149 пацієнтів з ІХС, але без ФП, II — 124 пацієнти з ІХС та пароксизмом ФП та контрольна група — 27 пацієнтів без ІХС та ФП. ***Результати.*** У пацієнтів II групи виявлено підвищення рівня *Pseudomonadota* (за таксономічним аналізом), *Actinobacter spp.* та зниження *Blautia spp.*, *Bacteroides thetaiotaomicron* порівняно з I групою, p<0,05. Загальна кількість суправентрикулярних екстрасистол корелює з *Verrucomicrobiota* (*Akkermansia muciniphila*; r=–0,340), p<0,05. Загальна кількість шлуночкових екстрасистол корелює з *Pseudomonadota* (r=0,356), співвідношення F/B (r=–0,468) — за родовим аналізом, за видовим аналізом — з *Blautia spp.* (r=–0,336), *Actinobacter spp.* (r=0,325), *Eubacterium Rectale* (r=–0,327) і *Roseburia inulinivorans* (r=–0,317), p<0,05. Виникнення пароксизму ФП корелювало з *Actinobacter spp.* (r=0,309) та *Eubacterium rectale* (r=–0,328), p<0,05. Зміни сегмента *ST* корелюють з *Streptococcus spp.* (r=0,369), p<0,05. ***Висновок.*** Види кишкової мікробіоти (*Akkermansia muciniphila, Blautia spp., Actinobacter spp., Eubacterium rectale, Roseburia inulinivorans, Streptococcus spp.*) суттєво корелюють з порушеннями серцевого ритму (надшлуночкового та шлуночкового) та змінами сегмента *ST*.

Ключові слова: ішемічна хвороба серця, фібриляція передсердь, порушення серцевого ритму, холтерівський моніторинг ЕКГ, шлунково-кишкова мікробіота.

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