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Электрокардиографические феномены при COVID-19: анализ теле-ЭКГ-исследований IT-центра ЭКГ г. Москвы

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АННОТАЦИЯ

Обоснование. При новой коронавирусной инфекции (COVID-19) наряду с доминирующим поражением органов дыхания в патологический процесс вовлекается сердечно-сосудистая система. Однако в доступной литературе аналитические оценки электрокардиографических (ЭКГ) феноменов опираются лишь на результаты исследований небольших выборок и описания единичных клинических случаев, что определяет актуальность проведения более масштабных исследований для уточнения характера и распространённости ЭКГ-изменений у лиц с подтверждённой коронавирусной инфекцией.

Цель — структуризация изменений ЭКГ у пациентов с COVID-19, представляющих неселективную популяцию жителей г. Москвы.

Материалы и методы. Проведён ретроспективный анализ электрокардиографических исследований, выполненных у 42 799 пациентов с верифицированным диагнозом COVID-19 в период с 10.03.2020 по 10.03.2021. Все включённые в исследование лица проходили стационарное лечение в клинических больницах г. Москвы, подключённых к IT-центру ЭКГ. Регистрация ЭКГ производилась в 12 стандартных отведениях, после чего путём интернет-соединения информация передавалась на сервер IT-центра ЭКГ с целью формулировки соответствующих заключений.

Результаты. Изменения ЭКГ обнаружены у 54% пациентов. Наиболее частыми аритмиями были наджелудочковая экстрасистолия и фибрилляция предсердий — у 12,6 и 12,0% пациентов соответственно. Признаки перегрузки правых отделов сердца выявлены у 12,5% больных, из них в 1,13% случаев — ЭКГ-паттерн тромбоэмболии лёгочной артерии. Инфарктоподобные изменения на ЭКГ имели место у 4,5% субъектов, в том числе 3 случая паттерна Бругада. Частота встречаемости изменений ST-T составила 2,2% от числа всех исследований. ЭКГ с удлинённым интервалом QT и QTc зарегистрирована у 540 (1,26%) пациентов. Отмечены единичные случаи фибрилляции желудочков, синдрома Фредерика и АВ-блокады различной степени.

Заключение. На основе проведённого анализа получено представление о частоте встречаемости электрокардиографических феноменов у больных COVID-19. Подтверждена высокая инцидентность фибрилляции предсердий — фактора риска тромбоэмболических осложнений. Одновременно установлена значительная распространённость ЭКГ-паттернов перегрузки правых отделов сердца, часть из которых ассоциирована с тромбоэмболией лёгочной артерии. Другие наблюдаемые изменения ЭКГ характеризовались значительно меньшей распространённостью, что, однако, не снижает их клинического значения. Собранный материал в перспективе может служить оптимизации тактики ведения пациентов при коронавирусной инфекции.

Ключевые слова: электрокардиография; COVID-19; сердечно-сосудистые заболевания; аритмии; миокардит; тромбоэмболия лёгочной артерии; ТЭЛА; теле-ЭКГ.

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Electrocardiographic findings in COVID-19: analysis of tele-ECGs in Moscow ECG IT Center

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ABSTRACT

BACKGROUND: Coronavirus disease (COVID-19) affects the cardiovascular system and the primary damage to the respiratory system involved in the pathological process. However, in the available literature, the electrocardiography (ECG) analyses are based only on small-sample studies and case reports, which determine the relevance of larger-scale studies to clarify the nature and prevalence of ECG abnormalities in subjects with confirmed coronavirus infection.

AIM: To determine the distribution of ECG changes in COVID-19 patients representing a non-selective population of Moscow residents.

MATERIALS AND METHODS: We performed a retrospective analysis of ECGs from 42,799 patients from March 10, 2020 to March 10, 2021 with a verified diagnosis of COVID-19. The study included patients admitted to Moscow clinical hospitals connected to the ECG IT Center. A standard 12-lead ECG was obtained and transmitted via an Internet connection to the server of the ECG IT Center, where the ECG interpretation was performed.

RESULTS: ECG changes were detected in 54% of patients. The most common cardiac arrhythmias were supraventricular extrasystole (12.6%) and atrial fibrillation (12.0%) reported in patients. Signs of the overloaded right heart were detected in 12.5% of cases, of which the ECG pattern of pulmonary embolism was confirmed in 485 patients (1.13%). Infarction ECG pattern was observed in 4.5% of patients, among which 3 cases of Brugada ECG pattern were reported. The incidence of ST-T changes was 2.2% of all studies. Prolonged QT and QTc intervals were recorded in 540 patients (1.26%). In addition, individual cases of ventricular fibrillation, Frederick syndrome, and atrioventricular block of various degrees were reported.

CONCLUSION: The distribution of incidence of ECG changes in COVID-19 was shown based on the data obtained. The high incidence of atrial fibrillation, which is a risk factor for thromboembolic complications, was confirmed. Moreover, a significant prevalence of ECG patterns of overloaded right heart was shown, some are associated with pulmonary embolism. Other reported ECG changes were characterized by a significantly lower prevalence, which does not reduce their clinical significance. The data obtained may be used to improve COVID-19 patient management strategy in the future.

Keywords: electrocardiography, COVID-19; cardiovascular diseases; arrhythmias; myocarditis; pulmonary embolism; tele-ECG.

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Covid-19的心电图现象：莫斯科IT中心电视心电图研究的分析

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简评

论证通过新的冠状病毒感染（Covid-19），随着病理过程中呼吸器官的主要损伤，涉及一种心血管系统。然而，在可用文献中，心电图（ECG）现象的分析估计是基于对小样本的研究结果和单一临床病例的描述，这决定了开展更多大规模研究以澄清性质和患病率的相关性ECG改变冠状病毒感染的人。

目标是构建Covid-19患者ECG的变化，代表莫斯科居民的非选择性人口。

材料与方法心电图研究的回顾性分析，42,799名患者在10.03.2020至10.03.2021期间验证了Covid-19验证诊断。 所有包括在研究人员中的所有人都在莫斯科的临床医院通过住院治疗，连接到ECG IT中心。 12根标准导联上进行ECG登记， 然后，通过互联网连接，将信息传输到ECG IT中心服务器，以形成相关结论。

结果。54％的患者中检测到ECG变化。最常见的心律失常是心室外收缩和心房颤动，分别占12.6%和12.0%。12.5%的患者表现出右心室过载的迹象，其中1.13%的患者表现出肺动脉血栓栓塞的心电图模式。 心电图梗死样改变发生在4.5%的受试者中，包括3例Brugada型。ST-T发生变化的发生频率为所有研究的数量的2.2％。 带有细长QT和QTC间隔的ECG在540（1.26％）患者中注册。 报告了不同程度的心室颤动，弗雷德里克综合征和AB阻滞的单位病例.

结论。基于分析，获得了Covid-19患者心电图现象的发生频率的思路。 确认心房颤动的高发病率 - 血栓栓塞并发症的危险因素。 与此同时，建立了右侧心脏部门过载的ECG模式的显着普遍性，其中一些与光动脉的血栓栓塞相关。 其他观察到的ECG变化的特征在于显着较差的患病率，然而，这不会降低其临床意义。 未来的收集材料可以是冠状病毒感染的患者管理策略的优化。

关键词：心电图；新冠肺炎；心血管疾病；心律失常；心肌炎；肺栓塞；tele- 远程心电图。

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BACKGROUND

In December 2019, the first case of a new coronavirus disease (COVID-19) caused by SARS-CoV-2 was reported in Wuhan (Hubei Province, China). The spread of the virus accelerated, and as early as March 2020, the World Health Organization declared an outbreak of the COVID-19 pandemic.

Thus, Wu and McGoogan reported an overall mortality rate of 2.3% from confirmed COVID-19, with a significant increase (by 5.6%–10.5%) among those with comorbidities, reaching 49% in critically ill patients [1]. The clinical signs of the disease range from asymptomatic infection to multiple organ failure leading to death. The upper respiratory tract is the entry point for infection, and involvement of the lungs is the dominant clinical sign of COVID-19, including acute respiratory distress syndrome, according to most reports. However, patients with the new coronavirus infection develop cardiovascular complications [2, 3], which are caused by three factors:

- A history of cardiovascular diseases
- Myocardial damage by an infectious agent
- The cardiotoxic effect of drugs for COVID-19 treatment, which may concomitantly affect the cardiac conduction system

Cardiovascular complications on electrocardiographic examination (ECG) include signs of ischemia, myocarditis, Brugada pattern, various types of arrhythmias (including fatal), thromboembolic complications, and QT and QTc (corrected interval) prolongation and its proarrhythmogenic value [3–5]. Such myocardial damage is associated with negative disease outcomes, prolongation of the recovery period, and aggravation of the prognosis [2, 6–9]. Therefore, clinical specialists must pay close attention and recognize ECG changes that are characteristic of COVID-19.

Due to published results of clinical studies in small samples and analyses of single clinical cases, data on various types of ECG phenomena in coronavirus infection have already been accumulated in the international and domestic literature [2, 4, 7, 8]. However, no systematization of ECG frequency changes based on larger observations has yet been presented, which is important for determining the tactics of patient management and prognosis.

The goal of the study was to structure ECG changes in COVID-19 patients, who were drawn from a nonselective population of Moscow residents.

MATERIALS AND METHODS

Study design

From March 10, 2020, to March 10, 2021, 42,799 patients were treated for the new coronavirus infection in Moscow medical institutions as part of an observational retrospective study. The ECG findings were obtained from the telemedical system of ECG registration and remote analysis (tele-ECG system) of ATES MEDICA Company (Russia). In addition, the ECG findings received from the tele-ECG system were registered in the Moscow Unified Medical Information and Analysis System.

Eligibility criteria

Inclusion criteria: Persons over the age of 18 with a clinical and laboratory-verified diagnosis of the new coronavirus infection determined in accordance with the Interim Guidelines of the Ministry of Health of the Russian Federation on the COVID-19 Prevention, Diagnosis, and Treatment (based on a positive polymerase chain reaction test and/or the presence of viral pneumonia according to computed tomography)

Exclusion criteria: Patients under the age of 18 and the absence of ECG findings in the tele-EKG system and/or electronic patient records

Setting

Patients were admitted to the Moscow City Health Department's Municipal Clinical Hospital No. 40, as well as clinical departments, a pulmonology center, and a reserve hospital at the Vorokhobov Municipal Clinical Hospital No. 67.

A remote electrocardiography center (ECG IT Center) was established at the Vorokhobov City Clinical Hospital No. 67 of the Moscow City Health Department. In accordance with the guidelines on centralization of ECG descriptions, all ECGs recorded in the abovementioned medical institutions were accumulated in the tele-ECG system of the ECG IT Center to further describe and transfer the findings to the electronic patient records [10]. Morozov et al. reported that such an approach to the centralization of analytical processing of registered ECGs is adequate and allows for the optimization of materials and time costs, which is especially important given the increased load on the public health system during the COVID-19 pandemic [11].

Study duration

This retrospective study was conducted between April and June 2021, based on the ECG findings of coronavirus-infected patients who received inpatient treatment within a year (from March 10, 2020, to March 10, 2021).

Medical intervention

ECGs were recorded in all patients upon admission to the hospital and then every 3 days depending on the clinical situation and baseline ECG changes.

Main study outcome

The main outcome was the ECG recorded in patients with a confirmed COVID-19 diagnosis who received inpatient treatment in clinical departments and structural units of medical organizations that collaborated with the ECG IT Center. The ECG parameters listed below were assessed:

- *Rhythm and conduction disorders:* The grading of supraventricular and ventricular rhythm disorders was performed using the conventional criteria. The QT interval duration was calculated automatically using the ATES MEDICA software, taking into account the variance in

12 leads. When calculating these intervals, the averaged QRST complex of each lead was superimposed on each subsequent lead. The QT interval was calculated by measuring the time between the first point of ventricular depolarization and the last point of T-wave termination. In addition, using Bazett's formula, heart rate data were corrected to obtain the QTc interval value. Thus, the cut-off values for the QTc interval for men and women were 450 and 460 ms, respectively.

- *Morphological abnormalities (ST-T changes):* At 60–80 ms intervals, the ST segment was measured from point J. ST-T abnormality was defined as downsloping and/or horizontal ST segment depression of ≥0.05 mV and/or ST segment elevation of ≥0.10 mV in limb and V_{5-6} leads and/or >0.25 mV in V_{1-3}, with a maximum in V_2 leads. Abnormalities of the T-wave were defined as changes in shape and polarity according to the generally accepted criteria, whereas secondary ST-T changes caused by ventricular premature excitation, intraventricular conduction block, and ventricular stimulation rhythm were not considered.
- *Right heart overload and enlargement:* Standard criteria were used to assess right atrial and right ventricular enlargement as well as the presence of acute pulmonary heart marker and pulmonary embolism, as reflected on ECG by $S_IQ_{III}T_{III}$ pattern and its combination with T-wave inversion in right chest leads, transient right bundle branch block, P-pulmonale, and depressed ST segment in left chest leads.

Subgroup analyses

The sample for this study was a nonselective population of Moscow residents who received hospital treatment for COVID-19. The sample was formed regardless of age, concomitant pathologies, severity of clinical condition, laboratory data, and duration of hospital stay. Retrospectively, patients were divided into two subgroups based on the presence or absence of ECG syndromes.

Any additional subgrouping was not anticipated by the aim and objectives of the study.

Outcome recording methods

The ECG was recorded in 12 standard leads using EASY ECG digital electrocardiographs (ATES MEDICA), which were equipped with modules for remote data transmission and an automatic ECG interpretation function with measurements of the main ECG parameters, such as duration of waves and intervals, voltaic characteristics, and subsequent formation of the preliminary report. When the electrocardiograph was connected to a laptop or tablet, the registered ECG records were visualized with the display of automatic analysis. Then, via Internet connection, the registered ECG was transmitted to the ECG IT Center's server, where functional diagnosticians reviewed the automatic ECG analysis and formulated a final conclusion. Subsequently, the ECG report was transferred to the electronic patient records.

Ethical review

The study was approved by the Independent Ethics Committee of the Moscow Regional Branch of the Russian Society of Roentgenologists and Radiologists, No. 5/2021, on May 20, 2021.

Statistical analysis

The statistical analysis included data from all subjects, which were divided into two subgroups based on the presence or absence of the ECG pathological phenomenon. For each subgroup, descriptive statistics of baseline characteristics were provided, with the following parameters: number of missing values (N), minimum value (Min), maximum value (Max), arithmetic mean (M), standard deviation (SD), 95% confidence interval (CI) for the mean, and median (Me).

A t-test was used to compare data between subgroups. For intergroup comparison of categorical baseline characteristics, the chi-square test or Fisher's exact test (if the expected frequency in any of the cells was >5) was used. The level of statistical significance (p) was set at 0.05 (two-sided). All statistical parameters were calculated using Stata 14 software.

RESULTS

Study subjects/participants

The current study included 42,799 patients who had clinical and laboratory-verified COVID-19 infection.

In the primary analysis of ECG findings, 47,292 recordings with or without diagnosed ECG phenomenon were selected. In the subsequent assessment, ECG recordings with no change in previous ECG diagnosis (n = 3927), duplicated patient records (n = 563), and records with incomplete data (n = 3) were excluded from the data analysis. Thus, the exclusion of 4,493 ECG recordings due to baseline material analysis allowed achieving quantitative matching of ECG findings with patients, i.e., one of the findings with a leading ECG diagnosis was considered for each study subject. The total number of registered primary and repeated ECG findings was 34,510 and 8,289, respectively.

Participants in the study ranged in age from 23 to 98 years. The mean age of patients with no pathologic ECG changes was 52.0 ± 14.5 years, whereas that of patients with various pathologic ECG syndromes was 69.6 ± 15.7 years ([p < 0.0001], Table 1).

Female patients (52%) outnumbered male patients in the study, but statistically significant differences between the subgroups for this parameter were not found (Table 2).

Main study results

Pathological ECG phenomena were recorded in 54% (n=23,113) of the study participants, with the percentage calculated based on the total number of patients.

Table 1. Descriptive statistics of the sample age structure

Parameters	Normal ECG	Abnormal ECG	Total
N	19 686	23 113	42 799
Mean	52,0	69,6	61,7
SD	14,5	15,7	17,5
95% ДИ	(47,7; 56,4)	(65,4; 73,9)	(58,2; 65,2)
Min	23	30	23
Max	77	98	98
Med	55	71	62
P (t-test)	<0,0001		-

Table 2. Distribution of examined subjects by gender

Gender	Normal ECG	Abnormal ECG	Total	*p*-value
Female	9626 (48,9%)	12 629 (54,6%)	22 255 (52,0%)	0,299
Male	10 060 (51,1%)	10 484 (45,4%)	20 544 (48,0%)	

The most common cardiac rhythm and conduction disorders were supraventricular arrhythmia and atrial fibrillation, found in 12.6% and 12.0% of the patients examined, respectively. Moreover, sinus tachycardia was found in 7.13% of the patients.

Signs of right heart overload were registered in 12.5% of patients. This was demonstrated by ECG signs of right atrial and ventricular enlargement, diastolic and systolic tension in the right ventricular myocardium, pulmonary hypertension, and $S_IQ_{III}T_{III}$ patterns, which indicated the development of pulmonary embolism. In this study, the ECG pattern of pulmonary embolism was discovered in 485 patients. Figure 1 depicts an example of the $S_IQ_{III}T_{III}$ ECG pattern.

Infarct-like changes were found in 4.5% of the patients, including three cases of the Brugada pattern (Fig. 2).

Signs of acute myocardial ischemia were observed in 0.5% of cases. Further, acute tissue abnormalities manifested by ECG ST-T changes were found in 2.2% of patients. Figure 3 shows a case of ST segment and T-wave changes.

ECGs with prolonged QT and QTc intervals were recorded in 540 patients, accounting for 1.26% of all subjects examined. Notably, all these subjects were treated with azithromycin and hydroxychloroquine.

During the specified time period, single cases of ventricular fibrillation, Frederick's syndrome, and AV blocks of various degrees were recorded (Table 3).

Fig. 1. $S_IQ_{III}T_{III}$ ECG pattern. Male patient, 81 years old. Diagnosis: COVID-19, negative polymerase chain reaction test. Out-of-hospital bilateral polysegmental pneumonia. Computed tomography findings: Pulmonary tissue involvement of approximately 80%. ECG findings of 02/02/2021: First-degree AV block and second-degree AV block type 2 (2:1; 3:1), 61 bpm. Left axis deviation. $S_IQ_{III}T_{III}$ type, ST elevation, and negative T-wave in II, III, AVF, and V_1–V_5 leads

DISCUSSION

Main study result summary

Cardiovascular complications are common in COVID-19 patients and are reflected in altered ECGs. Thus, ECG phenomena were found in 54% of patients. The most common disorders were supraventricular arrhythmia and atrial

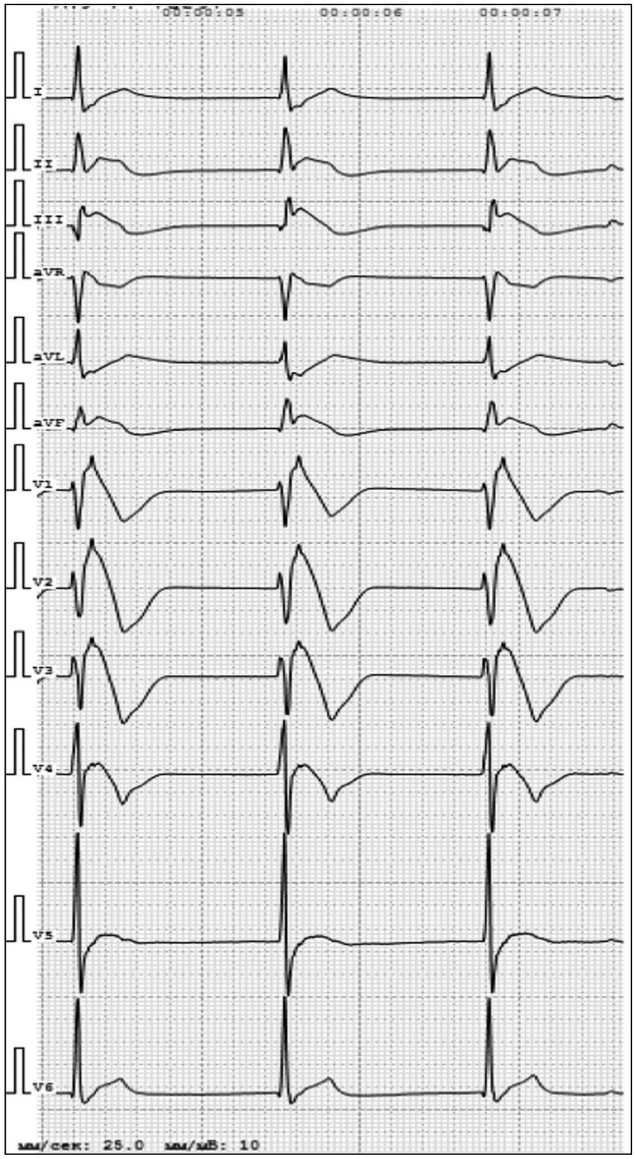

Fig. 2. ECG pattern of Brugada syndrome. Male patient, 67 years old. Diagnosis: COVID-19, positive polymerase chain reaction tests. Out-of-hospital bilateral polysegmental pneumonia. Computed tomography findings: Pulmonary tissue involvement of approximately 75%. ECG findings of 05/22/2020: Wandering of atrial pacemaker. Single supraventricular arrhythmia, 51 bpm. Normal axis. Right bundle branch block. Left ventricular hypertrophy. ST elevation in II, III, AVF, and V_1–V_5 leads

fibrillation, found in 12.6% and 12.0% of patients, respectively. Signs of right heart overload were seen in 12.5% of patients, including 1.13% (485 patients) with ECG pattern of pulmonary embolism. Infarct-like ECG changes occurred in 4.5% of cases, with three patients exhibiting the Brugada pattern. Moreover, ST-T changes were observed in 2.2% of all patients. In 540 patients, ECGs with prolonged QT and QTc intervals were recorded (1.26%).

In addition, single cases of ventricular fibrillation, Frederick's syndrome, and AV blocks of various degrees were observed.

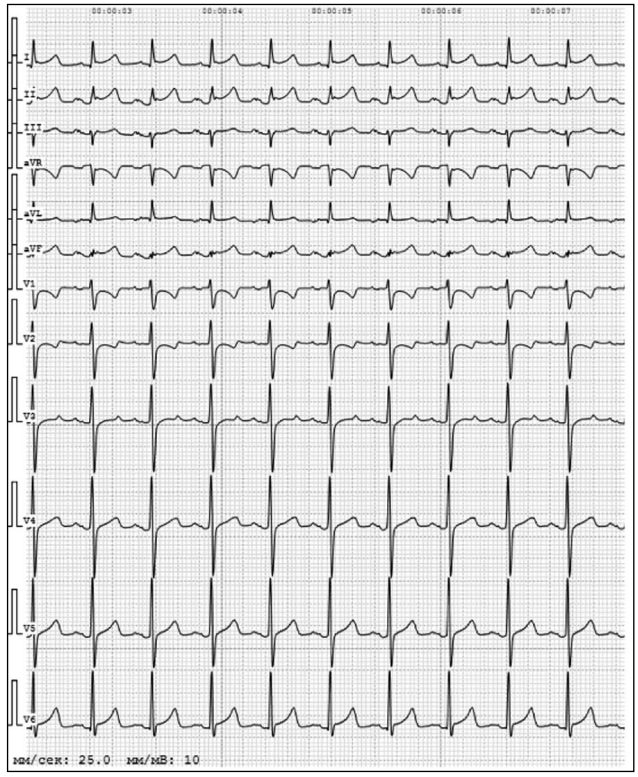

Fig. 3. ST segment and T-wave changes. Female patient, 74 years old. Diagnosis: COVID-19, positive polymerase chain reaction tests. Out-of-hospital bilateral polysegmental pneumonia. Computed tomography findings: Pulmonary tissue involvement of approximately 25% and 50% on the left and right, respectively. ECG findings of 02/25/2021: Sinus tachycardia, 111 bpm. Left axis deviation. ST elevation in I, II, AVL, and AVF leads and ST depression in AVR and V_1 leads

Main study result discussion

The analysis of ECG studies showed that ECG changes are common and occur in more than half (54%) of hospitalized patients with confirmed COVID-19. The obtained data are consistent with global statistics on the prevalence of cardiovascular complications in coronavirus infection and have been confirmed in a number of papers [9, 12–14]. One of the reasons for the high prevalence of cardiovascular complications in COVID-19 is the disease pathogenesis. The binding of the viral surface protein to the angiotensin-converting enzyme 2 (ACE2) receptor is necessary for the infectious process to progress. Moreover, ACE2 receptors located on the membranes of type II pneumocytes are found in high concentrations in the heart and vascular endothelium, including the coronary artery. Thus, the virus causes direct myocardial damage. Cardiovascular complications may develop as a result of molecular mimicry, with immune reactions being activated by a type of "cytokine storm," which is exacerbated by hypoxia due to respiratory failure [6]. In patients with preexisting cardiovascular diseases, SARS-CoV-2 infection aggravates the underlying disease (even if it was previously well controlled by drug therapy) due to pulmonary hypertension, impaired immune regulation, and the direct

Table 3. Structure of ECG phenomena in COVID-19

ECG phenomena	Patients (*n* = 42799)	
	n	%
Supraventricular arrhythmia	5401	12,6
Tachyarrhythmias:		
• Atrial fibrillation	5142	12,0
• Sinus tachycardia	3050	7,13
• Ventricular tachycardia	3	0,007
Bradyarrhythmias:		
• Atrioventricular block (varying degrees)	19	0,04
• Sinus bradycardia	7	0,016
ST-T changes	924	2,2
Brugada-like changes	3	0,007
$S_IQ_{III}T_{III}$ pattern	485	1,13
Infarct-like changes	1941	4,5
Acute myocardial ischemia	214	0,5
Right heart overload	5338	12,5
QT-QTc prolongation	540	1,26
Other ECG changes (ventricular fibrillation, Frederick's syndrome, etc.)	46	0,11

effect of the viral agent, resulting in a more severe course of COVID-19, including prolonged hospitalization, increased risk of death, and transfer to the intensive care unit [2, 6, 12, 15]. Thus, the link between COVID-19 and cardiovascular disease becomes evident, with preexisting pathologies exacerbating the course of the infectious disease and SARS-CoV-2 contributing to or resulting in acute cardiovascular events [6].

Systematization of ECG phenomena in COVID-19 patients using a large dataset allowed for the identification and categorization of various electrocardiographic changes by prevalence, which is characteristic of rhythm and conduction disorders, myocarditis, ischemia, right heart overload, pulmonary embolism, and cardiotoxic effect of drugs in the 4-aminoquinoline derivatives group.

Supraventricular arrhythmia was the most common ECG phenomenon in COVID-19 patients. In clinical practice, it is one of the most common arrhythmias, regardless of gender or age, and develops in the presence of cardiovascular, endocrine, and bronchopulmonary diseases, as well as other disorders, leading to the involvement of the cardiovascular system in the pathological process. Remarkably, supraventricular arrhythmia may occur in a relatively healthy patient when exposed to a stressor or physical activity, or due to the use of drugs, caffeine, and smoking. Direct or mediated exposure of the SARS-CoV-2 viral agent to the myocardium and metabolic disorders caused by the coronavirus infection contribute to the development of supraventricular arrhythmia. In addition, other authors state that it is the most common arrhythmia in COVID-19 patients [2, 6, 9, 12].

In the structure of ECG phenomena, atrial fibrillation took the lead among tachyarrhythmias and was recorded in 12% of patients with confirmed COVID-19. In the general population, the prevalence of atrial fibrillation ranges between 1% and 2% [16]. Its occurrence in a viral process is linked to the pathophysiological mechanisms of arrhythmia, which requires a trigger and a substrate for its maintenance [16]. In the context of coronavirus infection, systemic inflammatory response, fever, and COVID-induced hypoxemia may be triggers for arrhythmia [12, 14, 17]. According to our findings, the mean age of patients with abnormal ECG changes was 69.6 ± 15.7 years, which is a risk factor for atrial fibrillation because the probability of developing atrial fibrillation increases in persons over the age of 40, according to numerous clinical studies. Moreover, age is 1 of the 15 key factors in determining the risk of thromboembolic complications [16]. The prevalence of concomitant cardiovascular and endocrine pathologies, which also contribute to the development of atrial fibrillation, increases with age. The authors of several studies concluded that the presence of atrial fibrillation in patients with coronavirus pneumonia significantly worsens the prognosis of the disease [9, 13, 17, 18]. Thus, Wang et al. analyzed clinical features in 319 patients with severe and extremely severe course of COVID-19 [18]. Male patients predominated among the extremely severe group, whereas females prevailed among the subjects with a severe course of the disease ($p < 0.05$). The proportion of stroke patients in the group of critically ill patients was significantly higher than in the group with a severe course of

the disease ($p < 0.05$). The frequency of increased levels of cardiac-specific troponin I, natriuretic peptide (NT-proBNP), D-dimer, C-reactive protein, and hypocalcemia was higher in critically ill patients than in those with a severe disease ($p < 0.001$). Multivariate logistic regression analysis showed that increased NT-proBNP levels and age were independent predictors of atrial fibrillation, which was then an independent risk factor for hospital mortality (OR = 3.857, 95% CI 1.506–9.879) and artificial respiration (OR = 4.701, 95% CI 1.864–11.856) [18]. Based on the results of studies indicating an increased risk of thromboembolic complications and death in the severe course of coronavirus infection, careful selection of anticoagulant therapy in patients with COVID-19 and concomitant atrial fibrillation is necessary to balance the risk of thromboembolism and possible bleeding.

Furthermore, sinus tachycardia is a common ECG syndrome in coronavirus infection. Thus, the overall prevalence of sinus tachycardia in COVID-19 patients was 7.13%. In a study by D. Wang et al., which included 138 patients hospitalized for COVID-19, tachycardia was found in 17% of cases, and the frequency of arrhythmia reached 44.4% in severely ill patients and those in the intensive care unit, but did not exceed 6.9% in other hospitalized patients [19]. Sinus tachycardia has a negative impact on the clinical course and prognosis of the disease. Y. Wang et al. reported that sinus tachycardia was found to be an independent risk factor for hospital mortality (OR = 6.545, 95% CI 3.166–13.531, and $p < 0.001$) and artificial respiration (OR = 4.804, 95% CI 2.322–9.941, and $p < 0.001$) [18]. In addition, the functional reserve of the left ventricle in long-term tachycardia may decrease due to a weakening of its pumping function, increasing the risk of tachycardia-induced cardiomyopathy.

Bradyarrhythmias were much less common. Thus, out of 23,113 subjects with coronavirus infection and registered ECG abnormalities, sinus bradycardia and atrioventricular blocks of varying degrees were found in 7 and 19 cases, respectively.

In the conducted study, right heart overload was confirmed by signs of right atrial and ventricular hypertrophy, diastolic and systolic tension of the right ventricular myocardium, pulmonary hypertension, and patterns of pulmonary embolism. Signs of right ventricular overload were recorded in 12.5% of COVID-19 patients. The most common manifestation of right heart overload was diastolic overload in the form of right bundle branch block, most of which was incomplete. Thus, Ryabykina investigated the signs of electrocardiographic right ventricular stress in COVID-19 patients and, when analyzing 150 ECGs, discovered that the most common signs of right ventricular dysfunction were incomplete right bundle branch block (42.6%), right atrial phase of P-wave (41.3%), $S_IQ_{III}T_{III}$ ECG type (33.3%), and right ventricular hypertrophy, mostly represented by increasing of $S_{V5–6}$ waves (14.7%) [7]. The registration of the $S_IQ_{III}T_{III}$ pattern as a marker of acute cor pulmonale and pulmonary embolism required special attention due to the right atrial changes. According to the literature, registration of $S_IQ_{III}T_{III}$, complete right bundle branch block, and ST elevation in $V_{1–4}$ chest leads is associated with a high risk of death [20]. This ECG pattern was observed in 485 patients who were later diagnosed with pulmonary embolism. Thus, given the acute damage to the pulmonary tissue and the preexisting hypercoagulable syndrome associated with COVID-19, acute pulmonary thromboembolism should be ruled out first when recording ECG patterns of right heart involvement in the pathological process.

Moreover, markers of acute myocardial damage and infarct-like changes revealed on ECG are noteworthy. Myocarditis caused by the coronavirus infection is a common phenomenon, and its pathogenesis is associated with an active immune response to the myocardium affected by the virus [2, 3, 6, 8, 19, 20]. Acute myocardial damage correlates with an increased risk of hospital mortality. Thus, Shi et al., as a result of the analysis of clinical, laboratory, and instrumental data of 416 hospitalized patients with confirmed coronavirus infection, revealed that those with signs of myocardial damage had a higher in-hospital mortality rate when compared to patients without such signs (51.2% vs. 4.5% [$p < 0.001$]) [2]. Patients with myocardial damage had a higher risk of death compared to those without such a complication, both from the onset of symptoms (OR = 4.26, 95% CI 1.92–9.49) and from admission to the endpoint (OR = 3.41, 95% CI 1.62–7.16) [2].

ECG signs of myocarditis include reduced wave amplitude in limb leads, ST segment elevation predominant in the lower and lateral leads, and ST segment depression with T-wave inversion in V_1 and aVR leads [20]. In our study, such ST-T patterns were observed in 2.2% of patients. Notably, myocarditis can cause life-threatening arrhythmias, bundle branch blocks, QT interval prolongation, and infarct-like changes [3, 6, 20].

Special attention should be given to Brugada-like ECG changes, which include pseudoblocks of the right bundle branch and persistent ST segment elevation in $V_{1–2}$ leads [7]. In the analyzed material, three such cases were found. True Brugada syndrome is a genetic disorder that increases the risk of fatal arrhythmias and sudden death. In COVID-19 patients, existing long-term fever, metabolic disorders, and viral myocardial damage may result in ECG patterns similar to Brugada syndrome; however, unlike true Brugada syndrome, these disorders are transient and disappear when the overall disease pattern improves. Nevertheless, Brugada-like ECG changes significantly complicate diagnostic and clinical strategies, because they are frequently associated with chest pain, mimicking acute myocardial infarction [4, 20]. Coronary artery thrombosis and hyperactivation of coagulation cascade are the primary causes of acute myocardial ischemia in coronavirus infection [6, 7]. Therefore, the patient's history and the data of coronary angiography and laboratory markers of myocardial damage are important for differential diagnosis. In this study, ECG patterns of acute ischemia were detected in 0.5% of patients.

QT and QTc interval prolongation was reported as one of the possible causes of life-threatening arrhythmias in 1.26% of patients who were hospitalized for COVID-19. Remarkably, off-label patients were given antimalarials such as chloroquine and hydroxychloroquine, as well as azithromycin (a macrolide antibiotic). These drugs have a pro-arrhythmogenic effect because of their direct influence on cellular transmembrane potential, which is expressed by QT and QTc interval prolongation, potentially leading to the development of pirouette-type tachycardia [5, 7, 20]. In addition, macrolide use is associated with QT interval prolongation and may lead to pirouette-type tachycardia, especially when combined with concomitant bradycardia, hypokalemia, and hypomagnesemia [20]. Given these peculiarities of pharmacological effects of the aforementioned drugs, continuous monitoring of the QT interval for timely correction of drug therapy and prevention of life-threatening arrhythmias may be recommended for all patients who receive such therapy.

Study limitations

There were some limitations to the study.

The current study used a nonselective sample of patients with confirmed COVID-19 infection, regardless of concomitant pathology, severity of clinical condition, data of laboratory and other instrumental examinations, and duration of hospital stay. This approach to sampling is relevant in the context of the present study's aim because it allows for the primary structuring of ECG changes in the population of Moscow residents. However, stratification of the risk of death, time to complete recovery, and the risk of transferring patients to the intensive care unit are of broad practical interest. Therefore, a future study with subgrouping of patients for the aforementioned analysis is planned.

Importantly, when ranking ECG phenomena among tachyarrhythmias, atrial fibrillation was considered as a single nosology, without differentiating its forms. The revealed ECG changes peculiar to right heart overload, myocarditis, and coronary heart disease are often insufficiently specific, necessitating verification with laboratory tests and instrumental diagnostic methods.

CONCLUSIONS

Based on the analysis, the frequency of ECG phenomena in COVID-19 patients was determined. In addition, a high incidence of atrial fibrillation, which is a risk factor for thromboembolic complications, especially in the elderly, was associated with activation of the hemostasis system due to the coronavirus infection. Simultaneously, a significant prevalence of ECG patterns of right heart overload, including some associated with pulmonary thromboembolism, was established and may be associated with COVID-induced pulmonary tissue lesions. The remaining ECG changes were characterized by a much lower prevalence. However, this does not reduce their clinical significance given the risk to the patients' health and quality of life.

ECG remains the most convenient and accessible method for assessing the pathology of the cardiovascular system in COVID-19 patients, which is explained by the ECG technical simplicity and low cost, as well as the ability to remotely evaluate the obtained results.

The information gathered may serve to optimize the management tactics of patients with coronavirus infection in the long-term.

ADDITIONAL INFORMATION

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