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Research Article

New-onset atrial fibrillation in patients with SARS-CoV-2 pneumonia as a manifestation of acute myocardial injury

Tatiana I. Makeeva, Elizaveta V. Zbyshevskaya, Mark V. Mayer, Faiz A. Talibov, Sergey A. Saiganov

North-Western State Medical University named after I.I. Mechnikov, Saint Petersburg, Russia

BACKGROUND: Over the past 3 years, the prevalence of atrial fibrillation (AF) has increased significantly worldwide, which was associated with the pandemic caused by SARS-CoV-2. It is accompanied by an increase in the cases of ischemic stroke, myocardial infarction, and development of heart failure due to acute myocardial injury. Given the high lethality of SARS-CoV-2 infection (COVID-19), studying the characteristics of new-onset AF is essential.

AIM: The study aims at determining the predictors of new-onset AF in patients with COVID-19 pneumonia and at analyzing the clinical and pathophysiological characteristics of acute myocardial injury.

MATERIALS AND METHODS: In 36 patients aged 44–82 years (average 68.0) with COVID-19 pneumonia, AF paroxysms were recorded for the first time. All of them underwent computed tomography of the chest, electrocardiography, and echocardiography. The left ventricular ejection fraction was calculated using the Simpson method. Oxygen saturation was determined as blood oxygen saturation. Clinical blood tests were performed, C-reactive protein (CRP), ferritin, D-dimer, fibrinogen, and troponin I levels were measured.

RESULTS: Along with the well-known predictors of AF development (arterial hypertension, coronary heart disease, left ventricular myocardial hypertrophy, and left atrial dilatation), with COVID-19 pneumonia, new-onset AF paroxysms were recorded in patients of the middle, elderly, and late-life age. In 44.4% of patients with AF, cardiomegaly occurred with dilatation of both atria and ventricles. With decreased left ventricular ejection fraction, the incidence of AF paroxysms reached 61.5%. With preserved ejection fraction, AF paroxysms occurred much less frequently (27%). In patients with AF, the extent of lung damage is on average 62.5% (20–80%) with oxygen support saturation of 93% (76–97%). Serum troponin I levels of > 2000 ng/L indicated acute myocardial injury. CRP and blood ferritin values confirmed the presence of a pronounced inflammatory component in myocardial injury. High concentrations of blood fibrinogen and D-dimer, reaching 16,301 ng/mL, were associated with a tendency to hypercoagulation in patients with AF and COVID-19 pneumonia.

CONCLUSIONS: COVID-19 has a direct damaging effect on the myocardium and probably persists for a long time, which may induce AF in patients with acute pneumonia.

Keywords: atrial fibrillation; SARS-CoV-2; predictors.

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Научная статья

Впервые возникшая фибрилляция предсердий у пациентов с SARS-CoV-2-пневмонией как манифестация острого повреждения миокарда

Т.И. Макеева, Е.В. Збышевская, М.В. Майер, Ф.А. Талибов, С.А. Сайганов

Северо-Западный государственный медицинский университет им. И.И. Мечникова, Санкт-Петербург, Россия

Актуальность. За последние три года в мире существенно выросла распространенность фибрилляции предсердий (ФП), что связывают с пандемией, вызванной вирусом SARS-CoV-2. Это сопровождается увеличением количества ишемических инсультов, инфарктов миокарда, развитием сердечной недостаточности вследствие острого повреждения миокарда. В связи с высокой летальностью пациентов, инфицированных SARS-CoV-2, изучение особенностей впервые возникшей ФП является крайне необходимым.

Цель — определить предикторы впервые возникшей ФП у пациентов с SARS-CoV-2-пневмонией, изучить клинические и патофизиологические особенности острого повреждения миокарда.

Материалы и методы. У 36 пациентов в возрасте 44–82 лет (в среднем 68,0 года) с SARS-CoV-2-ассоциированной пневмонией впервые были зафиксированы пароксизмы ФП. Всем выполнялась компьютерная томография грудной клетки, электрокардиографическое, эхокардиографическое обследование; расчет фракции выброса левого желудочка (ФВ ЛЖ) проводили по методу Симпсона. Определяли сатурацию (SpO_2) — насыщение крови кислородом, клинический анализ крови, С-реактивный белок (СРБ), ферритин, Д-димер, фибриноген, тропонин I.

Результаты. Было показано, что наряду с общеизвестными предикторами развития ФП (артериальная гипертензия, ишемическая болезнь сердца, гипертрофия миокарда ЛЖ, расширение левого предсердия) при SARS-CoV-2-пневмонии впервые возникшие пароксизмы ФП регистрировались у пациентов среднего, пожилого и старческого возраста. У 44,4 % пациентов с ФП имела место кардиомегалия с дилатацией обоих предсердий и желудочков и снижением фракции выброса левого желудочка, при этом частота пароксизмов ФП достигала 61,5 %; при сохраненной фракции выброса пароксизмы ФП развивались значительно реже — в 27 % случаев. Установлено, что у пациентов с ФП объем поражения легких составляет в среднем 62,5 % (20–80 %) при сатурации на кислородной поддержке 93 % (76–97 %). Об остром повреждении миокарда свидетельствовали уровни тропонина I в сыворотке крови, превышающие отметку в 2000 нг/л. Показатели СРБ и ферритина крови подтверждали наличие выраженного воспалительного компонента при повреждении миокарда. Высокие концентрации фибриногена крови и Д-димера, достигающие 16301 нг/мл, ассоциировались с наклонностью к гиперкоагуляции у пациентов с ФП на фоне SARS-CoV-2-пневмонии.

Заключение. Коронавирус SARS-CoV-2 оказывает прямое повреждающее воздействие на миокард и, вероятно, длительно персистирует, что может быть причиной развития ФП у больных острой формой пневмонии.

Ключевые слова: фибрилляция предсердий; SARS-CoV-2; предикторы.

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ЭКО•ВЕКТОР

BACKGROUND

At the turn of the 20th – 21st centuries, an emergence of a pandemic of any infection could not be supposed. All pandemics seemed to become history. It was speculated that vaccinating the general population, using high-tech diagnostic methods, and prescribing new anti-infective drugs could reliably protect everyone. The Spanish influenza epidemic was probably the last largest one in Europe. In 1918–1919, over 18 months, more than 550 million people, or 29.5% of the global population, fell ill. Moreover, 50–100 million people died from it, which was 2.7–5.3% of the number of cases. In the Russian Soviet Federative Socialist Republic, approximately 3 million people died from the Spanish influenza, and this amounted to 3.4% of the country's total population [1].

In December 2019, an outbreak of pneumonia of unknown etiology was registered among residents of Wuhan City, China. The study of bronchoalveolar secretions and blood samples of patients identified the pathogen as an RNA-containing coronavirus (SARS-CoV-2). The disease was named Coronavirus disease-19 (COVID-19). In March 2020, the World Health Organization declared COVID-19 a pandemic. As of May 2023, more than 765 million people had COVID-19, and nearly 7 million died, globally.

Having quickly recovered from the first shock caused by high mortality rates, the entire global medical community started to investigate the new disease. Thus, in a comprehensive analysis of 700 autopsies of patients who died from this new coronavirus infection, Rybakova et al. (2020) established that in 43% of cases, COVID-19 was the only underlying cause of death. The major thanatogenetic mechanisms in COVID-19 were acute respiratory, pulmonary heart failure (HF) and multiple organ dysfunction. The most common comorbid pathology in patients with COVID-19 included cardiovascular diseases, diabetes mellitus, and obesity [2].

Katsoularis et al. (2021) analyzed 86,742 COVID cases in Sweden. They compared the obtained results with the incidence of myocardial infarction (MI) and ischemic strokes in 348.481 patients in the control group. They concluded that MI and ischemic stroke were part of the clinical presentation of COVID-19, and their risk remained significantly increased during the first 2 weeks after recovery [3].

Cardiac arrhythmias occur in 19–21% of patients with severe COVID-19 [4, 5], whereas the incidence of new-onset AF in patients with COVID-19 varies from 3.6% to 6.7% [6, 7]. Thus, in the study by Bhatia et al. (2021), who analyzed 644 patients with severe COVID-19, AF episodes on electrocardiography (ECG) were recorded for the first time in 3.6% of cases [8]. In a meta-analysis, Romiti et al. (2021) examined 187.716 patients with COVID-19 and revealed that the prevalence of AF with COVID-19 was approximately two times higher than in the general population [9].

According to Rosenblatt et al. (2022), 27.851 of 30.999 patients hospitalized with COVID-19 had no AF history. In 1517 (5.4%) patients atrial fibrillation developed for the first time during their COVID-19 course. The presence of AF was associated with higher rates of overall mortality (45.2% versus 11.9%) and mortality due to MI, stroke, cardiogenic shock, and HF (23.8% versus 6.5%) [10].

Wollborn et al. (2022) compared the incidence of AF in 5005 patients from the pre-pandemic cohort and 2283 patients with COVID-19. They found that the incidence of AF was 1.57 times higher in the COVID-19 group than in the pre-pandemic group [11].

The aim of the study was to identifying predictors of new-onset AF in patients with COVID-19 pneumonia as well as at determining the clinical and pathophysiological characteristics of acute myocardial injury (AMI).

MATERIALS AND METHODS

This controlled nonrandomized cohort study enrolled 216 patients aged 23-82 years with PCR-diagnosed COVID-19 pneumonia. All patients were hospitalized in the acute period of the disease, i.e., on days 2–7 (average 5.2). Of these, 32 patients aged 52–86 (mean 78.6) years died from severe bilateral viral pneumonia on days 6–10 of the hospital stay. 30 patients with paroxysmal AF that occurred before COVID-19 diagnoses were excluded from the sample.

In 36 patients (group I) aged 44–82 years (average, 68 years, Table 1) with COVID-19 pneumonia, AF paroxysms were recorded for the first time during the hospital stay. The duration of the attacks ranged from 35 s to 3 min. In these patients, 2 paroxysms were recorded in 2 patients with CT1, 30 in 22 patients with CT2, 16 in 10 patients with CT3, and 6 in 2 patients with CT4, which totaled 54 paroxysms.

All patients had arterial hypertension (AH), and 23 of 36 patients (63.9%) had a history of coronary heart disease (CHD), including 8 patients with MI. Out of 36 patients, 7 (19.4%) had diabetes mellitus type II (DM2), and the body mass index (BMI) was 33.1 (22–43) kg/m^2.

Moreover, 64 patients with COVID-19 pneumonia without AF paroxysms constituted the control group (group II). The age of the patients ranged from 23 to 64 years, with a mean of 41 years. Group I patients were older than group II patients (p = 0.0036), and they significantly more often experienced CHD, AH, and DM2. In group II, AH was determined in 20 of 64 patients (31.2%), CHD was registered in 3 patients (4.7%), and DM2 was noted in 3 patients (4.7%). BMI was 26,9 (18–36) kg/m^2, which was significantly lower than in group I (p = 0.0458).

Echocardiography (echoCG) was performed on Philips EnVisor (Philips Electronics N.V.) and Toshiba Artida (Toshiba Medical Systems) devices on day 1 of the hospital stay. The study was performed according to the standard method using B and M scanning modes, as well as pulsed-wave, and continuous-wave modes. Left ventricular ejection fraction (LVEF) was calculated using the Simpson method.

HF with preserved EF (⩾ 50%), HF with moderately reduced EF (40–49%), and HF with low EF (< 40%) were identified.

In all patients, cardiospecific enzyme troponin I, C-reactive protein (CRP), ferritin, D-dimer, fibrinogen, and creatinine levels were determined, and clinical blood test was performed in the clinical laboratory of St. Petersburg City Hospital Pokrovskaya.

Statistical analysis was performed using the non-parametric Mann–Whitney test. A p-value < 0.05 was considered significant. Spearman's coefficient was applied

Table 1. Clinical characteristics of the patients

Parameters	Atrial fibrillation patients, Group I, *Me* (IQR)	*n* = 36	Patients without atrial fibrillation, Group II, *Me* (IQR)	*n* = 64	*p*
Age, years	68 (44–82)	–	57 (23–64)	–	0.0036
⩽ 44	44	1	38 (35–43)	29	–
45–59	57 (46–59)	10	47 (45–54)	17	0.043
60–74	70 (65–74)	17	61 (60–68)	18	0.038
75–89	82 (75–82)	8	–	–	–
Sex, M/F, *n*	20/16	–	40/24	–	–
Body mass index, kg/m^2	33.1 (22–43)	36	26.9 (18–36)	64	0.0458
Coronary heart disease	63.9%	23	4.7%	3	0.0001
History of MI	22.2%	8	3.1%	2	0.0002
Arterial hypertension	100%	36	31.2%	20	0.0001
Diabetes mellitus	19.4%	7	4.7%	3	0.0283
CT (%)	41 (20–80)	36	33 (10–79)	64	0.0361
CT1 (%)	23 (20–25)	6	16 (10–24)	37	0.0035
CT2 (%)	40 (30–49)	15	29 (27–45)	17	0.0471
CT3 (%)	59 (52–74)	11	51 (50–61)	7	0.0346
CT4 (%)	79 (75–80)	4	77 (75–79)	3	0.0381
Saturation (SpO_2) (%)	91 (76–97)	–	96 (84–98)	–	0.0001

Note. *n,* number of patients; grade I respiratory failure (RF), SpO_2 of 90-94%; grade II RF, SpO_2 of 75–89%; grade III RF, SpO_2 < 75%; normal saturation index, ⩾ 95%; CT, volume of lung tissue damage; CT1, < 25% of damage; CT2, 25–49% of damage; CT3, 50–75% of damage; CT4, > 75% of damage.

Table 2. Biochemical parameters of the blood in patients examined

Parameters	Atrial fibrillation patients, Group I (*n* = 36), *Me* (IQR)	Patients without atrial fibrillation, Group II (*n* = 64), *Me* (IQR)	*p*
CRP, mg/L norm 0–5	77.4 (30.5–189)	44.7 (9.1–167)	0.0027
Ferritin, μg/L norm 20–250	723.5 (85–3500)	577.4 (56–1104)	0.0349
Troponin I, ng/L norm 0–34.2	289.6 (5.9–2041)	29.4 (2.8–165)	0.0027
D–dimer, ng/mL norm 0–230	2040 (321–16301)	494.6 (125–3831)	0.0001
Fibrinogen, g/L, norm 2–4	5.8 (3.6–8.3)	5.2 (3.4–7.9)	0.048
Creatinine, μmol/L, norm 44–110	116.4 (63–234)	96.1 (55–197)	0.062
Leukocytes, 10^9/L	7.5 (4.0–13.3)	7.9 (3.5–20.1)	0.065
Lymphocytes, n	1.15 (0.8–3.0)	1.3 (0.9–2.8)	0.073
Platelets, 10^9/L	269.4 (50–453)	244.4 (83–411)	0.093
Erythrocytes, 10^{12}/L	4.3 (3.2–5.8)	4.7 (3.6–5.8)	0.084

for the correlation analysis of relationships between the analyzed parameters.

RESULTS

Chest CT revealed that the extent of lung tissue damage in group I was on average 41% (20–80%), which was significantly higher than that in group II, with 33% (10–79%) (p = 0.0361). Moreover, group I recorded the following extent of lung damage: CT1 (p = 0.0035), CT2 (p = 0.0471), CT3 (p = 0.0346), and CT4 (p = 0.0381).

The average oxygen saturation in the air upon hospital admission was significantly lower in patients with diagnosed AF paroxysms with 93% (76–97%) than in the comparison group with 96% (84–98%) (p = 0.0001). Biochemical blood parameters are presented in Table 2.

On analysis of biochemical blood test data, the patients with AF showed higher concentrations of CRP (p = 0.0027), ferritin (p = 0.0349), D-dimer (p = 0.0001), fibrinogen (p = 0.048), and troponin I (p = 0.0027).

An increased risk of thrombogenesis and a higher procoagulatory activity of the hemostasis system in group I, compared to group II, was evidenced by fibrinogen and D-dimer values. This was also confirmed by the low platelet count in groups I (50×10^9/L) and II (83×10^9/L).

The level of troponin I, which indicates the AMI level, was 9.8-12.4 times higher in group I than in group II. No significant difference in blood creatinine levels was found. The severity of COVID-19 was indicated by low lymphocyte counts (1.15 (0.8–3.0) in group I and 1.3 (0.9–2.8) in group II; p = 0.073), which is typical of COVID-19. No significant difference in leukocyte and erythrocyte counts was noted.

EchoCG parameters of patients with LVEF of ⩾50% are presented in Table 3. When comparing echoCG in patients with LVEF of ⩾ 50%, group I had higher LV myocardial mass indices (MMI) (p = 0.032) and left atrial volume index (LAVI) (p = 0.034) than group II. The LV end-diastolic volume indices (EDVI) did not exceed the norm in all patients; however, they were higher in group I than in group II (p = 0.047). In addition, patients with AF were older (p = 0.047).

All patients with LVEF of 40-49% had an increase in LV MMI and LAVI; however, group I had higher values for both LV MMI (p = 0.021) and LAVI (p = 0.003). Group I had higher LV EDVI than group II (p = 0.035). Group I patients were older (62 (55-77) years) than group II years (54 (51–60) years) (p = 0.028) (Table 4).

EchoCG data in patients with LVEF < 40% are presented in Table 5. In group I with LVEF < 40%, all echoCG parameters exceeded the norm and were significantly higher than those in group II. Thus, the LVMMI reached 201 g/m^2, the EDVI was 82 mL/m^2, and the ESVI reached 41 mL/m^2. Both atria were enlarged (LAVI up to 70 mL/m^2, RAVI up to 32 mL/m^2). The difference with the indicators of group II was highly significant. The age of patients with low LVEF ranged from 59 to 82 years, with an average of 70 years (p = 0.041).

Group 1 turned out to be very heterogeneous (Table 6). Thus, in 16 of 36 patients (44.4%) (group IA) with LVEF < 50%, a

Table 3. EchoCG parameters in patients with left ventricular ejection fraction of ⩾ 50%

Parameters	Atrial fibrillation patients, Group I (n = 20), *Me* (IQR)	Patients without atrial fibrillation, Group II (n = 54), *Me* (IQR)	p
LV MMI, g/m^2	119 (112–132)	107 (94–124)	0.032
EDVI, mL/m^2	48 (38–60)	40 (38–52)	0.047
End-systolic volume index (ESVI), mL/m^2	23 (20–27)	19 (18–23)	0.800
LAVI, mL/m^2	44 (37–51)	31 (24–36)	0.034
Right atrial volume index (RAVI), mL/m^2	23 (18–26)	21 (18–24)	0.230
LVEF, %	59 (52–64)	62 (58–65)	0.068
Age, years	63 (44–79)	43 (35–54)	0.047

Table 4. EchoCG parameters in patients with left ventricular ejection fraction of 40–49%

Parameters	Atrial fibrillation patients, Group I (n = 12), *Me* (IQR)	Patients without atrial fibrillation, Group II (n = 8), *Me* (IQR)	p
LV MMI, g/m^2	135 (128–165)	123 (120–141)	0.021
EDVI, mL/m^2	65 (51–74)	51 (43–56)	0.035
End-systolic volume index (ESVI) , mL/m^2	30 (28–37)	26 (22–28)	0.090
LAVI, mL/m^2	50 (40–56)	41 (38–45)	0.003
Right atrial volume index (RAVI), mL/m^2	26 (24–30)	23 (20–28)	0.090
LVEF, %	44 (41–48)	46 (43–49)	0.044
Age, years	62 (55–77)	54 (51–60)	0.028

Table 5. EchoCG parameters in patients with left ventricular ejection fraction (LVEF) < 40%

Parameters	Atrial fibrillation patients, Group I (*n* = 4), *Me* (IQR)	Patients without atrial fibrillation, Group II (*n* = 2), *Me* (IQR)	*p*
LV MMI, g/m^2	154 (141–201)	141 (132–163)	0.005
EDVI, mL/m^2	77 (68–82)	59 (48–74)	0.021
End-systolic volume index (ESVI), mL/m^2	39 (37–41)	32 (28–36)	0.047
LAVI, mL/m^2	60 (56–70)	49 (43–52)	0.0001
Right atrial volume index (RAVI), mL/m^2	34 (31–37)	30 (24–32)	0.043
LVEF, %	36 (35–38)	38 (37–39)	0.038
Age, years	70 (59–82)	65 (60–68)	0.041

Table 6. Comparative analysis of the biochemical parameters of the blood and echoCG parameters in group I with atrial fibrillation and left ventricular ejection fraction (LVEF) < 50% and ⩾ 50%

Parameters	LVEF < 50%, Group IA (*n* = 16), *Me* (IQR)	LVEF ⩾ 50%, Group IB (*n* = 20), *Me* (IQR)	*p*
MMI, g/m^2	154 (128–201)	119 (112–132)	0.0001
EDVI, mL/m^2	73 (51–82)	48 (38–60)	0.001
End-systolic volume index (ESVI), mL/m^2	34 (28–41)	23 (20–27)	0.001
LAVI, mL/m^2	59 (56–64)	44 (37–51)	0.002
Right atrial volume index (RAVI), mL/m^2	33 (24–37)	23 (18–26)	0.010
LV EF, %	40 (35–48)	59 (52–64)	0.001
CRP, mg/L	116 (57–189)	87 (30,5–127)	0.0001
Ferritin, μg/L	947 (232–3500)	567 (85–1504)	0.002
Troponin I, ng/L	546 (5,9–2041)	114 (14–365)	0.0001
D-dimer, ng/mL	2943 (564–16301)	1246 (375–6031)	0.005
Fibrinogen, g/L	5,8 (5,2–8,3)	4,9 (3,6–6,3)	0.0362
Lymphocytes, n	1,08 (0,8–1,3)	1,3 (1,1–3,0)	0.045
Platelets, 10^9/L	277 (50–453)	185 (95–308)	0.038
Age, years	74 (48–82)	63 (44–79)	0.035

Table 7. Results of the correlation analyses between blood biochemical parameters and echoCG parameters in group IA with atrial fibrillation and left ventricular ejection fraction (LVEF) < 50% (*n* = 16)

Parameters		EF < 50%	EDVI	ESVI	LAVI	RAVI
CRP	*r*	–1.00	0.89	0.83	0.85	0.68
	p	0.0001	0.001	0.002	0.004	0.013
Troponin I	*r*	–0.90	0.79	0.76	0.94	0.65
	p	0.0001	0.008	0.002	0.003	0.001
Ferritin	*r*	–0.89	0.84	0.68	0.61	0.81
	p	0.0001	0.003	0.040	0.046	0.002
Fibrinogen	*r*	–0.63	0.80	0.78	0.70	0.71
	p	0.040	0.0001	0.001	0.002	0.002
D-dimer	*r*	–1.0	0.75	0.65	0.64	0.90
	p	0.0001	0.010	0.040	0.010	0.0001

high LVMMI was noted, and cavities of both atria and ventricles were dilated, as evidenced by the EDVI, end-systolic volume, LA volume, and right atrial volume. This group consisted of patients of middle, elderly, and late-life age.

In 20 of 36 patients (55.6%) (group IB) with LVEF of ⩾50%, the LVMMI moderately increased, and the LAVI increased. The EDVI, ESVI, and RAVI were normal, and the difference with group IA was highly significant. Group IB patients were somewhat younger than group IA patients ($p = 0.035$).

Compared to group IB, group IA had significantly higher indicators of the general inflammatory response (CRP and ferritin), procoagulatory activity of the blood (D-dimer and fibrinogen), and AMI level (troponin I). Thus, the CRP level was 1.3–1.5 times higher, ferritin level 1.7–2.3 times higher, D-dimer level 2.4–2.7 times higher, fibrinogen level 1.2 times higher, and troponin I level 4.8–5.6 times higher. Moreover, the blood lymphocytes level was 1.2–2.3 times lower than in group IB, which indicated a more severe viral infection. Indeed, according to CT data, the extent of lung tissue damage reached 62.5% (20–80%) in group IA compared to 43.5% (20–70%) in group IB ($p = 0.0001$). This was accompanied by lower oxygen saturation values, i.e., 92% (76–97%) and 94% (84–97%) ($p = 0.0001$), respectively.

Spearman's rank correlation was used to assess the complex effect of inflammation, hypercoagulation, and AMI on changes in echoCG parameters. Table 7 presents the results of the correlation analysis in group IA.

The role of AMI in the dilatation of the cardiac chambers in group IA was evidenced by a positive correlation between troponin I and EDVI, ESVI, and LAVI.

A close relationship between the dilatation of the cardiac cavities and inflammation was noted by a positive correlation between (1) CRP and EDVI, ESVI, and LAVI, and between (2) ferritin and EDVI and RAVI.

The pathophysiological effect of procoagulatory changes on the development of cardiomegaly was indicated by a positive correlation between the fibrinogen level and EDVI, ESVI, RAVI, and LAVI. In addition, a positive and strong correlation was detected between D-dimer and EDVI; between D-dimer and RAVI.

Microcirculation disorders, acute inflammation, and myocardial damage by COVID-19 were the main cause of the decrease in myocardial contractility. In patients with LVEF < 50% and AF, a very strong and negative correlation was noted between EF and (1) troponin I, (2) CRP and ferritin; and (3) D-dimer (Table 7).

In 20 patients with LVEF of ⩾ 50% and AF in group IB, the influence of the damaging and inflammatory effects of SARS-CoV-2 on the myocardium was noticeably weaker. Thus, a negative correlation was noted between troponin I and EF and between D-dimer and EF. A positive correlation was noted between EF and RAVI. No other statistically significant correlations were observed.

In 10 of 64 patients (15.6%) of group II (without AF) with LVEF < 50%, a moderately strong and negative correlation was detected between the CRP level and LVEF and between the D-dimer level and EF, and a significantly positive correlation was observed between the D-dimer level and RAVI.

In ⩾ 50%, blood biochemical parameters did not affect the size and the systolic function of the heart.

Thus, only patients with AF and reduced LVEF showed significant AMI and pathophysiological changes in echoCG parameters because of an inflammatory reaction and a tendency to hypercoagulability. In patients with AF and EF of ⩾ 50%, these changes were less pronounced or absent.

DISCUSSION OF RESULTS

Various mechanisms of myocardial injury in COVID-19 are described, namely, (1) direct myocardial injury, when SARS-CoV-2 uses the angiotensin-converting enzyme 2 receptor (ACE2) and CD147 to enter the cell. ACE2 is a membrane protein of the carboxypeptidase family, which is found in many human organs, including heart, kidneys, intestines, and lungs. By using spike proteins to bind to the receptor and enter the cardiomyocytes, SARS-CoV-2 initiates an inflammatory process in the myocardium. Viruses, penetrating target cells, start replication (reproduction) of their kind from the materials of the cell where they parasitize. They damage the genetic apparatus, destroy cell nuclei, and disrupt deeply the intracellular protein metabolism, and the cell may die. The products of the disturbed protein metabolism of cells serve as antigens, causing the emergence of corresponding antibodies and triggering the mechanism of autoimmune myocardial damage. Newly emerged virions invade neighboring cardiomyocytes, infecting them directly [12]; (2) development of an acute systemic inflammatory reaction and a "cytokine storm" with high levels of pro-inflammatory cytokines in the blood; (3) increased myocardial oxygen demand in acute respiratory distress syndrome (ARDS) caused by increasing hypoxia and RF; (4) ischemic damage in the presence of atherosclerotic changes in the coronary arteries and coagulopathy caused by COVID-19; (5) electrolyte imbalance, primarily hypokalemia; and (6) toxic effects of antiviral drugs on the heart [13].

Ruan et al. (2020) analyzed the case histories of 68 patients who died from COVID-19 and noted that they had high blood serum levels of troponin and myoglobin during their lifetime. The levels of troponin I, a highly specific protein released into the bloodstream from cardiomyocytes during structural damage of heart muscles, particularly during viral lesions, myocarditis, pericarditis, and HF, depend directly on the extent of myocardial damage. The authors suggested that fulminant myocarditis was the cause of lethal outcomes; however, no data from myocardial biopsy were provided [14].

In the present study, AMI in patients with AF was evidenced by high levels of troponin I, which were 9.8–12.4 times higher than in patients without AF. Moreover, in patients with AF and LVEF < 50%, the level of troponin I in the blood serum was

4.8–5.6 times higher than in patients with AF and a preserved EF, which indicated a greater amount of myocardial damage. The detected highly significant negative correlation between the level of troponin I and LVEF and the positive correlation between troponin I and indexed atrial and LV volumes in patients with EF < 50% confirmed the AMI attack in patients with AF.

According to Zylla et al. (2021), in patients with COVID-19, the risk of AF in HF is increased by 5 times. They revealed a direct correlation between the HF stage and the incidence of AF. Thus, AF was detected in 30% of cases of Grade II-III chronic heart failure (CHF) (according to the New York Heart Association) and in 30–40% of cases in patients with grade IV CHF [15].

According to our data, 27% of 74 patients with COVID-19 pneumonia and preserved LVEF were diagnosed for the first time with AF paroxysms. In 26 patients with LVEF < 50%, AF paroxysms were recorded in 61.5% of cases, which was 2.3 times more often.

Kogan et al. (2022) presented morphological and immunohistochemical evidence for myocarditis in COVID-19. A morphological study of cardiac autopsy data from 32 elderly patients revealed signs of active myocarditis. Lymphocytic infiltrates and positive PCR confirmed the viral nature of inflammation. Signs of lymphocytic pericarditis, endocarditis and pancarditis with destructive coronary disease, and thrombo-vasculitis with disseminated intravascular coagulation were observed [16]. Moreover, fatal arrhythmias may develop in patients with COVID-19, which are not associated with damage to cardiomyocytes but are caused by arrhythmogenic proinflammatory cytokines [17].

The present study revealed that high levels of inflammation markers in patients with AMI and AF, highly significant correlations between CRP, ferritin, LVEF, and increased indexed atrial, and LV volumes did not allow excluding active myocarditis. During the pandemic, conducting special examinations for diagnosing myocarditis in a large number of patients with severe and extremely severe conditions was quite difficult.

According to Coromilas et al. (2021), in the presence of COVID-19, cardiac arrhythmias occur in 12.9% of cases and 61.5% of them are AF. In such patients, LA appendage thrombus occurs more often than in patients without COVID-19 history and is characterized by parietal localization of the thrombus. This suggested that the impaired integrity and function of the endocardium, caused by its damage during acute infection, is the cause of thrombogenesis [18].

The study of the incidence and characteristics of LA appendage thrombus in 469 patients with persistent nonvalvular AF enabled Mazur et al. (2023) to conclude that parietal thrombi occur 2.5 times more often in patients after COVID-19. Logistic regression analysis showed that the probability of such thrombus formation is independently affected by previous COVID-19 and CHF [19].

According to our data, in patients with AF and LVEF < 50%, a highly significant negative correlation was found between EF and indicators of blood procoagulatory activity, namely, D-dimer, and fibrinogen. In addition, a positive correlation was noted between the levels of fibrinogen, D-dimer, and indexed atrial and LV volumes.

Bhatla et al. (2020) examined nearly 700 patients with COVID-19 and revealed a relationship between elderly age, presence of HF, and AF risk [6]. Peltzer et al. (2020), Podzolkov et al. (2022) noted that AF paroxysms during the acute course of COVID-19 occurred significantly more often in elderly patients and/or in patients with cardiovascular diseases such as AH, CHD, and CHF [20, 21].

Corradi (2006) conducted a morphological analysis of atrial myocardial regions in AF and demonstrated different degrees of their remodeling at the histological and ultrastructural levels [22]. Concomitant cardiovascular disorders contribute to this architectural disorganization of the myocardium, participating in the onset and the perpetuation of AF. The most common causes of AF are considered AH, severe LV hypertrophy, fatty and amyloid infiltration of the atrial tissue with the development of fibrosis, and LA dilatation [7, 22, 23]. Therefore, patients with new-onset AF may already have an existing substrate for the formation of this arrhythmia, and acute COVID-19 may trigger its initiation. AF recurrence in COVID-19 is registered in 23–33% of patients with ARDS and/or sepsis. In approximately 10% AF develops for the first time [24, 25].

Conclusion. In our study, the well-known thesis on the predictors of AF development (AH, CHD, LV myocardial hypertrophy, and LA dilatation) was confirmed. Besides, it was shown that having COVID-19 pneumonia, new-onset AF paroxysms were recorded in patients of middle, elderly, and late-life age with a large area of lung damage and low blood oxygen saturation. AF paroxysms occur in 27% of cases with a preserved LV EF and in 61.5% of cases with EF < 50%. Cardiomegaly is detected in 44.4% of patients with AF, and the combination of acute myocardial damage, inflammation, and high blood procoagulatory activity is important in its development mechanisms.

ADDITIONAL INFORMATION

Competing interests. The authors declare that they have no competing interests.

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AUTHORS INFO

***Tatiana I. Makeeva,** Dr. Sci. (Med.), Professor;
ORCID: https://orcid.org/0000-0003-3819-486X;
eLibrary SPIN: 4915-3109; e-mail: tatianamakeeva@gmail.com

Elizaveta V. Zbyshevskaya, PhD, Associate Professor;
ORCID: https://orcid.org/0000-0002-2565-3548;
eLibrary SPIN: 7761-0942; e-mail: zbyshev@hotmail.com

Mark V. Mayer, PhD Student;
ORCID: https://orcid.org/0000-0002-4658-4975;
e-mail: maier-mark@mail.ru

Faiz A. Talibov, PhD Student;
ORCID: https://orcid.org/0000-0002-0284-9521;
e-mail: faiz-talibov@mail.ru

Sergey A. Saiganov, Dr. Sci. (Med.), Professor;
ORCID: https://orcid.org/0000-0001-7319-2734;
eLibrary SPIN: 2174-6400; e-mail: sergey.sayganov@szgmu.ru

ОБ АВТОРАХ

***Татьяна Ивановна Макеева,** д-р мед. наук, профессор;
ORCID: https://orcid.org/0000-0003-3819-486X;
eLibrary SPIN: 4915-3109; e-mail: tatianamakeeva@gmail.com

Елизавета Владимировна Збышевская, канд. мед. наук, доцент; ORCID: https://orcid.org/0000-0002-2565-3548;
eLibrary SPIN: 7761-0942; e-mail: zbyshev@hotmail.com

Марк Витальевич Майер, аспирант;
ORCID: https://orcid.org/0000-0002-4658-4975;
e-mail: maier-mark@mail.ru

Фаиз Альсовбятович Талибов, аспирант;
ORCID: https://orcid.org/0000-0002-0284-9521;
e-mail: faiz-talibov@mail.ru

Сергей Анатольевич Сайганов, д-р. мед. наук, профессор;
ORCID: https://orcid.org/0000-0001-7319-2734;
eLibrary SPIN: 2174-6400; e-mail: sergey.sayganov@szgmu.ru

* Corresponding author / Автор, ответственный за переписку