International Journal of General Medicine

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Individuals Recovered from Severe COVID-19 are Predispose to Develop Atrial Fibrillation

Mücahid Yılmaz, Çetin Mirzaoğlu

University of Health Sciences, Elazığ Fethi Sekin City Hospital, Department of Cardiology, Elazığ, Turkey

Correspondence: Mücahid Yılmaz, University of Health Sciences, Fethi Sekin City Hospital, Cardiology Department, Elazığ, Turkey, Tel +905337719783, Email mucahid.yilmaz@hotmail.com

Aim: One of the primary contributors of the development of atrial fibrillation (AF) is autonomic dysfunction. It is suggested that heart rate turbulence (HRT) be utilized to assess autonomic nervous system (ANS) function. In this research, we analyzed the impact of COVID-19 on atrial fibrillation predisposition in the post-recovery period by analyzing atrial HRT measurements of patients who described palpitations in the post-COVID-19 period.

Methods: This study included 407 healthy participants without a positive COVID-19 record and 328 patients having a verified positive COVID-19 record (recovered COVID-19). All subjects were categorized into four groups (controls, recovered mild COVID-19, recovered moderate COVID-19 and recovered severe COVID-19) based on the severity value of their chest CT scan. The atrial HRT analyses were taken from a 24-hour electrocardiography- Holter recording.

Results: This study revealed that atrial HRT Onset values were significantly higher in the recovered severe COVID-19 group than the other groups. A positive association was found between the atrial HRT onset value and the chest CT severity value. However, no relationship was found between the atrial HRT onset value and the number of positive PCR test for COVID-19 or the amount of time that had passed since COVID-19. Regression analysis showed that the chest CT severity score, HT, smoking, and recovery from severe COVID-19, were independent predictors of atrial HRT Onset values and abnormal atrial HRT Onset existence.

Conclusion: Blunted atrial HRT, considered a significant predisposition to the development of atrial fibrillation, is more likely to occur in people who recovered from serious COVID-19 than in individuals who have never had severe COVID-19. These individuals should be carefully evaluated for atrial HRT.

Keywords: recovery from severe COVID-19, atrial heart rate turbulence, autonomic nervous system disorder, atrial fibrillation

Introduction

After first emerging in Wuhan, China, a pandemic was swiftly turned into a novel coronavirus (SARS-CoV-2) toward the end of 2019 and caused severe impacts on health and economic systems worldwide. SARS-CoV-2 is also named COVID-19 and affects the respiratory system most, but the disease effects are not limited to the lungs. Venous thromboembolism, acute kidney and liver damage, the release of cytokines, sepsis, disseminated intravascular coagulation, complications of pregnancy, and cardiac and neurological issues are all possible outcomes of a COVID-19 infection, in addition to pulmonary involvement.[1]

According to a report published in Wuhan, China, arrhythmia was found in 16.7% of hospitalized patients with COVID-19 and 44.4% of those monitored in intensive care.[2] Although some studies conducted to date have revealed some clues about the potential for arrhythmia in individuals who have active disease, as of today, we are far from being able to explain why individuals who have completely recovered from the disease apply to outpatient clinics with complaints of palpitations.[3,4]

Heart rate turbulence (HRT) originates from the principle of accelerating sinus rhythm, which occurs as a reflex due to the short diastole period during ventricular premature beat in patients with sinus rhythm. In a healthy heart, there is an acceleration in ventricular rate and there is a degree of this acceleration. HRT indicates this degree of acceleration. In

Received: 12 April 2025
Accepted: 22 July 2025
Published: 12 August 2025

other words, it shows the autonomic activity of the heart. For an healthy HRT both the sympathetic and parasympathetic pathways of the heart must be intact.[5] Abnormal HRT, which can occur due to many diseases, indicates decreased baroreflex sensitivity and autonomic dysfunction. It is well established that individuals with blunted HRT are more likely to die suddenly and from all causes.[6]

It has been revealed by the recent research on holter and pace that HRT is also impaired after atrial premature stimulation. Impaired HRT values, suggesting that the spontaneous emergence of clinical atrial fibrillation is associated with a brief increase in vagal outflow following early atrial excitement.[7,8]

Conditions where a range of symptoms persist for more than three months after recovery from acute COVID-19 are called Long-COVID.[9] Long-COVID-19 may manifest itself with symptoms, such as chest pain, palpitations, cognitive disorders, breath shortness, fatigue, attention deficit, hair loss, headache, myalgia, and arthralgia.[9–12]

Recently, there has been an increase in the admission of patients who recovered from COVID-19 to the clinic complaining of palpitations and that these patients are referred to another departments with the preliminary diagnosis of somatization or panic disorder. Could a more sensitive assessment be made for these individuals? Could SARS-CoV-2 cause permanent damage to the autonomic nervous system (ANS) and predisposition to atrial fibrillation? This study utilized HRT to analyze the persistent impacts of SARS-CoV-2 on cardiac autonomic function in individuals recovered from COVID-19.

Materials and Method

Study Population

This retrospective study analyzed the records of 10,081 participants who visited the cardiology outpatient clinics at Elazığ Fethi Sekin City Hospital between June 1, 2022, and December 31, 2024, and underwent a 24-hour ECG Holter monitoring.

Inclusion Criteria

A total of 328 patients with a history of positive SARS-CoV-2 test results by at least one Real-Time (RT)-PCR test on nasopharyngeal swabs (Bio-Rad CFX96 RT PCR Detection System, Bio-Rad Laboratories, Inc., Hercules, CA, USA) were included in the Recovered COVID-19 group. A total of 407 individuals with no history of positive (RT)-PCR test results for SARS-CoV-2 during the same time period and no cardiac or systemic disease (other than hypertension) detected by physical examination, laboratory tests, or anamnesis were included in the control group (Figure 1).

Exclusion Criteria

Subjects with inadequate data in their files, were under 17 years old, those with atrial fibrillation, electrolyte imbalance, structural heart disease, heart valve disease, or systemic disease (apart from hypertension), individuals using anti-arrhythmic medications or agents that may lead to arrhythmia (such as terfenadine, probucol, erythromycin, amiodarone, antidepressants, clarithromycin, and antipsychotics), professional athletes, patients with a body mass index (BMI) above than 35, and pregnant women were excluded.

Collection of Data for the Post COVID-19 Period

SARS-CoV-2 was caught at least once and no more than three times by the subjects in the COVID-19 recovery group. Individuals in the recovered COVID-19 group had a minimum of 4 weeks and a maximum of 204 weeks between 24-hour ECG-Holter evaluation and their most recent positive RT-PCR test.

Analysis of COVID-19 Severity with Thorax CT

The recovered COVID-19 group was given a semi-quantitative chest CT severity score for each of the five lung lobes (two on the left and three on the right). Visual assessment was used to determine each lobe's percentage of involvement. The chest severity score was obtained by adding the scores corresponding to the percentage of involvement of each lobe (Table 1).[5]

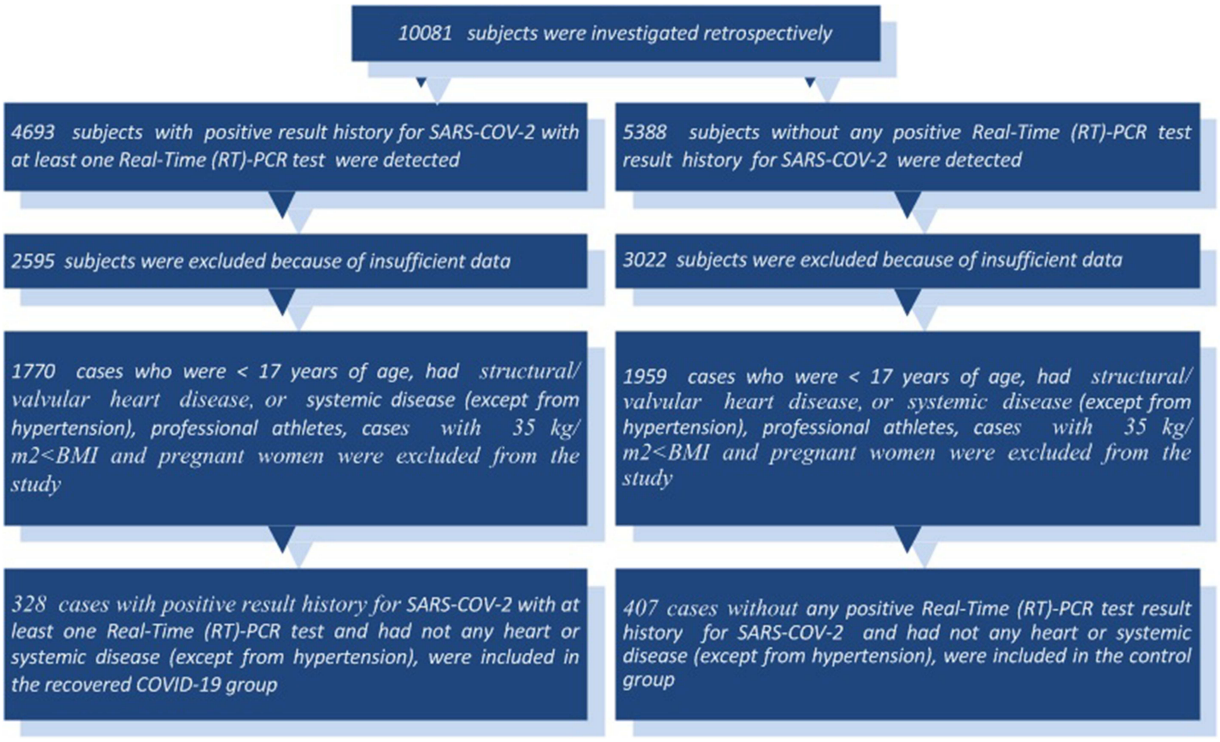

Figure 1 The Subjects inclusion flowchart diagram.

Since COVID-19, which accompanies conditions such as chronic obstructive pulmonary disease and myocardial infarction, can cause severe respiratory distress and arterial blood values <90%, patients with concomitant systemic diseases were excluded from the study before their chest tomography was analyzed. Depending on their chest CT severity score, the recovered COVID-19 group was separated into three subgroups. Mild, moderate, and severe were the classifications assigned to group II (155 instances), group III (56 patients), and group IV (42 patients). Group II (modest): The CT severity score was classified as modest (<8). Group III (Moderate): The CT severity score fell within the moderate range.[8–15] Group IV (Severe): According to Table 1, the CT severity score was rated as severe.[16–25]

The current research was carried out in compliance with the Declaration of Helsinki's tenets. The Ethics Committee of T.C. Fırat University granted the ethical permission (No: 2021/12-45). In compliance with the confidentiality and compliance of patient data, patient consent was waived by the ethics committee due to the retrospective nature of the study and therefore patient consent was not obtained.

Table 1 Semi-Quantitative Chest Computed Tomography (CT) Severity Score and Chest CT Severity Index

Individual Lobar Scores Based on Percentage of Involvement		**COVID-19 Chest CT Severity Index Based on the Involvements of the Five Lobes**	
Lobar involvement	**Score**	**Total Score**	**Severity (Category)**
0-5%	1	<8	Mild
5%-25%	2	8-15	Moderate
26%-49%	3	16-25	Severe
50%-75%	4		
>75%	5		

Description of Supraventricular Ectopic Beats

To describe supraventricular ectopic beats, R-R interval tachograms and 4-lead Holter recordings were simultaneously examined. If, in addition to the presence of definitive evidence of abnormal atrial depolarization, the R-R interval was shortened by at least 20%, an ectopic beat was classified as a supraventricular premature beat. Only isolated premature supraventricular ectopic beats with a significant post-ectopic pause were evaluated.[7]

24-Hour ECG-Holter Monitoring

To evaluate HRT, 24 hour electrocardiography (ECG)-Holter data were evaluated using a 4-lead Holter device (Digitrak XT, Philips Medical Systems, Andover, USA) and Cardioscan II premier software (firmware version C.2). HRT parameters were measured by the method reported by Bauer et al.[6] Turbulence onset (TO), which represents the beginning the sinus rhythm acceleration phase, and turbulence slope (TS) which describes the deceleration phase, were the two numerical IDs employed for the measurement. The start of heart rate turbulence (HRT) was defined as the difference, expressed as a percentage, between the mean of the last 2 sinus rhythm RR intervals before the supraventricular ectopic beat and the mean of the first two sinus rhythm RR intervals following the compensatory pause following the supraventricular ectopic beat. HRT onset was computed with the help of the formula below:

$$TO = [(RR1 + RR2) - (RR-2 + RR-1)/(RR-2 + RR-1)] \times 100(\%)$$

RR −1 and RR-2 refer to the 2 RR intervals immediately before the supraventricular ectopic beat, and RR1 and RR2 refer to the 2 RR intervals immediately after the compensatory pause (Figure 2). The highest positive slope of a regression line assessed across any five consecutive sequences in the first fifteen consecutive sinus intervals following a supraventricular ectopic beat was defined as the turbulence slope (TS), expressed in milliseconds per beat. An HRT Slope of ≤2.5 ms/beat and an HRT Onset of ≥0% were considered abnormal.[7]

Statistical Evaluation

SPSS software (SPSS Inc., Chicago, IL, USA) version 27.0 was used for statistical analysis. The Kolmogorov–Smirnov test was employed to examine the ability of continuous variables to follow a normal distribution. Since all of the continuous variables showed abnormal distribution, for the one-way ANOVA test, Tamhane's T2 correction was employed to analyze these parameters and the variables were shown as median with 25th–75th. For categorical variables, using the chi-square test, variations between groups in baseline characteristics were evaluated and were presented as numbers and percentages. Spearman's Rho and Pearson's correlation analysis were used to analyze the correlation between continuous variables. Binary logistic regression analysis was conducted to detect which variables would independently predict the presence of abnormal atrial HRT onset. Results were presented as hazard ratios and 95% CI. Linear regression analysis was utilized to detect which variables would independently affect atrial HRT onset value. Results were presented as unstandardized and standardized β coefficients. P values were always two-tailed, and statistical significance was defined as values below 0.05.

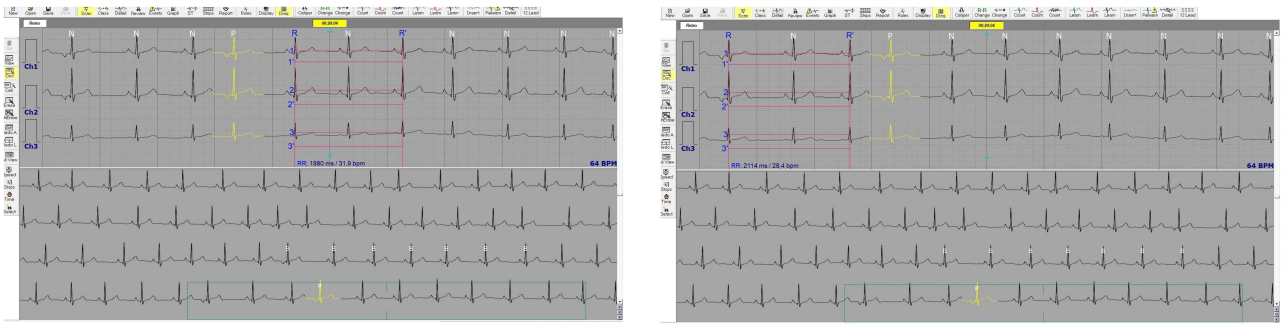

Figure 2 Measurement of the interval between RR1, RR2 and RR −1, RR-2 for supraventricular ectopic beats from 24 Hour ECG-Holter.

Results

Of the 10081 cases whose 24-hour ECG Holter recordings were retrospectively examined, 735 (The controls: 407, The recovered COVID-19 group: 328) were taken in the research. All cases were separated into four groups (controls, recovered mild COVID-19, recovered moderate COVID-19, recovered severe COVID-19). Although the prevalence of abnormal atrial HRT Onset existence and atrial HRT Onset value were significantly higher in the recovered severe COVID-19 group compared to the other groups, no difference was found between the control and other Recovered COVID-19 groups (Table 2) (Figure 3). However, no difference was found among the control group and other Recovered COVID-19 groups in terms of abnormal atrial HRT Slope prevalence, atrial HRT Slope value, HT, smoking, age, and gender (Table 2).

Spearman's rho and Pearson's correlation analyses revealed a positive correlation between atrial HRT Onset and recovered COVID-19 subjects' chest CT severity score and recovered COVID-19 subgroups, while no association was found between atrial HRT Onset and the Number of positive PCR tests for COVID-19 and time elapsed after COVID-19 (Table 3) (Figures 4 and 5).

Regression analyses revealed that recovery from severe COVID −19, recovered COVID-19 subjects' chest CT severity score, HT and smoking were predictors for abnormal atrial HRT onset existence and independently affected atrial HRT onset values (Table 4 and Table 5).

It is clear from the table that the logistic model was developed to ascertain if the independent variables are useful in forecasting the existence of abnormalities. The model's variables have a 19.7% explanatory power in predicting the existence of aberrant atrial HRT onset, and atrial HRT onset is significant (Model-1. $p<0.001$; Nagelke $R^2 = 0.197$) (Table 4). As can be seen from the table, having a history of severe COVID-19 is a 3.851-fold risk factor for abnormal atrial HRT Onset existence compared to not having a history of severe COVID-19 ($p=0.002$).

The developed linear regression model is significant when Model-2 is analyzed, and its explanatory power for the impacts of its variables on the atrial HRT Onset value is 9.2% ($p<0.001$; Nagelke $R^2 = 0.092$) (Table 5). The table shows that the recovered COVID-19 subjects' chest CT severity value variable has a statistically significant effect on the abnormal HRT Onset value. In other words, a 1-point increase in chest severity scores of individuals recovering from COVID-19 increases the atrial HRT Onset value by 0.033 units ($p<0.001$).

Table 2 Comparison of Atrial HRT Parameters Between Recovered COVID-19 Subgroups and the Control Group

	The Controls (Noun: 407)	**Group II (Recovered Mild COVID-19 Group, Noun:186)**	**Group III (Recovered Moderate COVID-19 Group, Noun:87)**	**Group IV (Recovered Severe COVID-19 Group, Noun:55)**	***P***
Age (Years)	43.0(26.0–55.0)	42.0(33.0–49.0)	44.0(39.0–54.0)	46.0(41.0–52.0)	[a]1.0,[b]0.67,[c]0.07,[d]0.60,[e]0.06,[f]0.93
Gender (Male)(%)	48.2	49.5	50.6	54.5	[a]0.77,[b]0.68,[c]0.37,[d]0.86, [e]0.51,[f]0.64
HT(%)	24.8	23.7	25.3	30.9	[a]0.76,[b]1.0,[c]0.42,[d]0.88,[e]0.36,[f]0.59
Smoking(%)	29.5	34.9	35.6	38.2	[a]0.18,[b]0.26,[c]0.25,[d]0.91,[e]0.78,[f]0.89
Atrial HRT Onset(%)	−2.0(-2.2- −1.4)	−2.0(−2.5- −1.0)	−1.99(−2.1- −1.0)	−1.2(−1.9- −0.0)	[a]0.33,[b]0.08,[c]**<0.001**,[d]0.96,[e]**0.01**,[f]**0.02**
Atrial HRT Slope (ms/beat)	12.0(9.0–15.0)	10.2(9.0–15.0)	10.5(8.5–14.2)	12.0(9.0–12.5)	[a]0.86,[b]0.75, [c]<0.18,[d]1.0,[e]0.68,[f]0.95
Abnormal Atrial HRT Onset(%)	5.4	6.5	9.2	23.6	[a]0.75,[b]0.27, [c]**<0.001**,[d]0.57,[e]**<0.001**,[f]**0.03**
Abnormal Atrial HRT Slope(%)	5.2	4.8	5.7	7.3	[a]1.0,[b]0.79, [c]0.52,[d]0.77, [e]0.50,[f]0.73

Notes: [a]p value between control group and group II.; [b]p value between control group and group III; [c]p value between control group and group IV; [d]p value between group II and group III; [e]p value between group II and group IV; [f]p value between group III and group IV. Bold font: $p < 0.05$ indicates statistical significance.

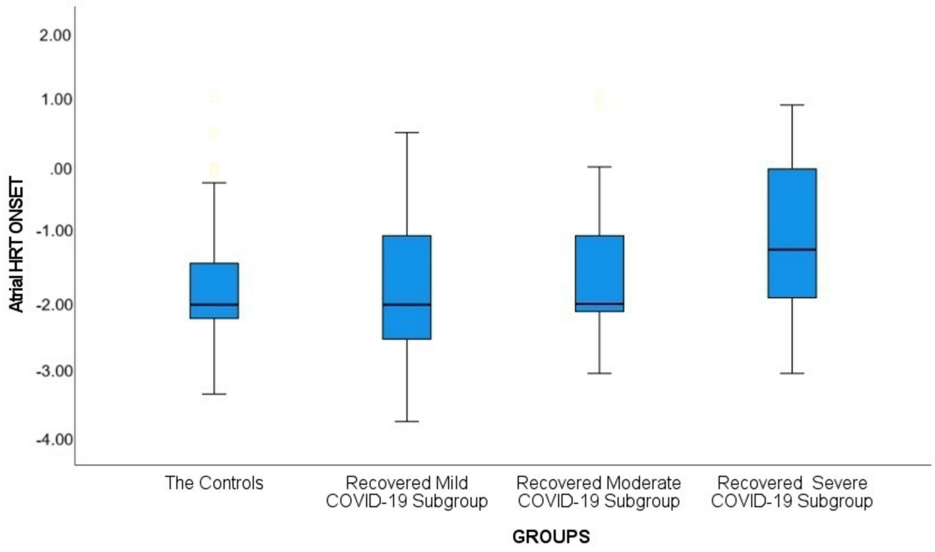

Figure 3 Comparison of Atrial HRT Onset values between the groups.

Discussion

This study revealed that atrial HRT values and the presence of abnormal atrial HRT onset were higher in individuals who had severe COVID-19 and recovered than in other individuals who did not have, while the atrial HRT slope value and the presence of abnormal atrial HRT slope did not differ between the groups (Table 2) (Figure 3). Although a positive connection was found among atrial HRT onset value/abnormal atrial HRT onset presence and subjects' chest severity score and COVID-19 subgroups with correlation analyses, no association was detected between these parameters and having a positive PCR test record for SARS-CoV-2 and the time elapsed since COVID-19 (Table 3) (Figures 4 and 5). Furthermore, analyses of regression showed that recovered COVID-19 subjects' chest CT severity score, recovering from severe COVID-19, smoking and HT were independent predictors of atrial HRT Onset value and abnormal atrial HRT onset presence (Table 4 and Table 5).

SARS-CoV-2 binds to cardiomyocytes, type 2 pneumocytes, macrophages, and perivascular pericytes by binding to transmembrane angiotensin-converting enzyme 2 (ACE2) following proteolytic cleavage of the S-protein by serine

Table 3 Spearman's Rho and Pearson's Correlation Analyses Between Atrial HRT Onset Value and Some Other Variables

Spearman's rho Correlation Analysis Between Atrial HRT Onset Value, the Controls and Recovered COVID-19 Subgroups,	**Atrial HRT Onset value**	
	r	**p**
Recovered COVID-19 subgroups	0.165	<0.001
Pearson's correlation analysis between Atrial HRT Onset and Recovered COVID-19 subjects' chest CT severity score, Post COVID-19 recovery duration and Number of positive PCR tests for COVID-19.		
Number of positive PCR tests for COVID-19	0.005	0.925
Post COVID-19 recovery duration (Week)	−0.019	0.736
Recovered COVID-19 subjects' chest CT severity score	0.253	<0.001

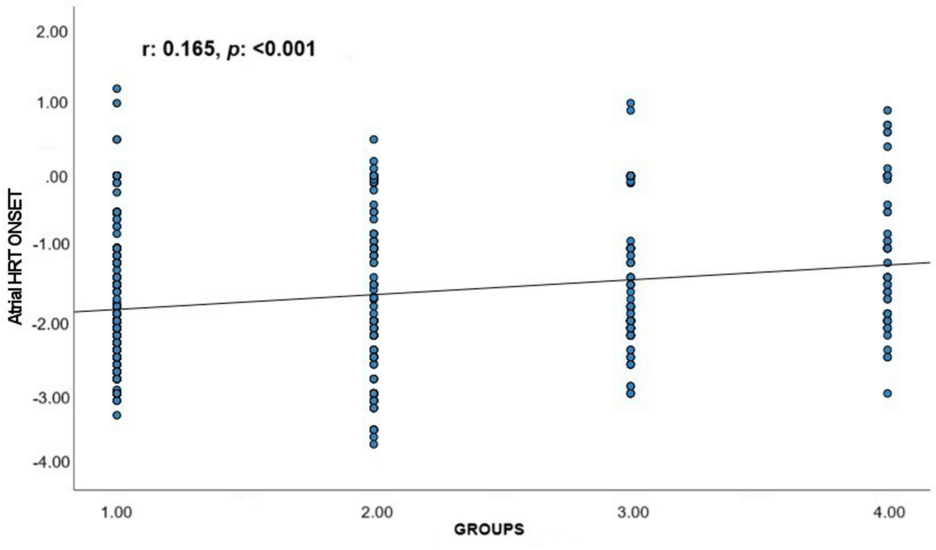

Figure 4 Spearman's rho correlation analyses between Atrial HRT Onset value and groups.

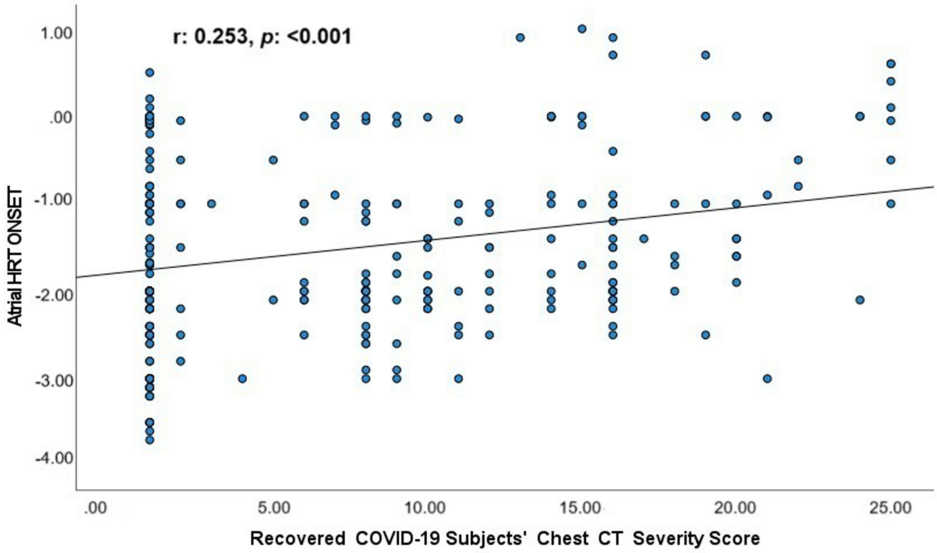

Figure 5 Pearson's correlation analyses between Atrial HRT Onset value and recovered COVID-19 subjects' chest CT severity score.

protease. ACE2 is required for viral invasion, and ACE2 protein is found in many tissues, including the myocardium and central nervous system (CNS).[13,14] In addition to direct viral invasion of myocardial and coronary endothelial cells, systemic inflammation, inappropriate T helper cell response after cytokine storm, increased calcium in myocytes induced by hypoxia causing apoptosis, hypoxia due to cardiac and respiratory failure, increased adrenergic stimulation and increased endogenous stress hormones, electrolyte imbalance, and side effects of medications taken to treat COVID-19 may be shown among the causes of cardiac clinical pictures seen in COVID-19.[15,16] Stromal edema in the heart, secondary to vasculitis resulting from monocyte and lymphocyte infiltration into arterial and venous endothelial cells, is considered another cause.[17] It was thought that SARS-CoV-2 had neural invasion based on genomic sequencing from cerebrospinal fluid (CSF) obtained from patients diagnosed with encephalitis and the isolation of similar viruses in brain tissue during autopsy studies.[18,19] Considering that ACE2 is found in the capillary endothelium, it is thought that

Table 4 Model-1. Binary Logistic Regression for Variables (Dependent Variable: Abnormal Atrial HRT Onset Existence)

	β	S.E.	Hazard Ratio	95% Confidence Interval		*P*
HT	1.253	0.407	3.501	1.576	7.779	0.002
Smoking	0.900	0.401	2.460	1.120	5.401	0.03
Age	0.006	0.019	1.006	0.970	1.043	0.76
(Recovered Severe COVID-19 Group)	1.348	0.428	3.851	1.666	8.903	0.002
Gender	0.677	0.410	0.520	0.232	1.161	0.11
Post COVID-19 recovery duration (Week)	−0.004	0.004	0.996	0.980	1.004	0.34
Number of positive PCR tests for COVID-19	−0.265	0.443	0.768	0.322	1.829	0.55
Constant	−2.318	1.808	0.098			0.20

Notes: Model p<0.001; Nagelke R^2 = 0.197.

Table 5 Model-2. Linear Regression for Variables (Dependent Variable: Atrial HRT Onset Value)

	Unstandardized Coefficients		Standardized Coefficients	t	*P*
	B	Std. Error	Beta		
Gender	0.051	0.111	0.025	0.462	0.65
Smoking	−0.331	0.116	−0.153	−2.844	0.005
HT	−0.351	0.129	−0.148	−2.723	0.007
Age	0.002	0.005	0.020	0.373	0.70
Post COVID-19 recovery duration (Week)	−0.002	0.001	−0.071	−1.335	0.18
Recovered COVID-19 subjects' chest CT severity score	0.033	0.008	0.236	4.393	<0.001
Number of positive PCR tests for COVID-19	−0.005	0.132	−0.002	−0.040	0.97
(Constant)	−0.680	0.494		−1.375	0.17

Notes: Model p<0.001; Nagelke R^2 = 0.092.

COVID-19 can reach the CNS by damaging the blood-brain barrier in this way.[20] Some studies suggest that SARS-CoV -2, like previously reported SARS-CoV, may pass through the cribriform plate of the ethmoid bone into the systemic circulation and the virus may perform central invasion through the microcapillary network between the blood circulation around the ethmoidal bone and the brain.[21,22] According to another view, SARS-CoV-2 has the ability to invade peripheral nerve terminals and slowly progresses through the synapse-related pathway to reach the CNS. In this context, it has been previously shown that when SARS-CoV and MERS-CoV were administered to mice via the nasal route, the virus reached the brain through the olfactory nerves and then affected different brain regions, including the thalamus and brainstem.[20,21] Apart from the direct entry of the virus into the nervous system, COVID-19 infection may cause neurological problems due to widespread cardiopulmonary failure and metabolic abnormalities triggered by infection of SARS-CoV-2 or as a result of autoimmune mechanisms.[23] In particular, by producing more inflammatory cytokines, the cytokine storm that takes place during the illness stimulates T cells, macrophages, and endothelial cells. Then, by triggering vascular leakage, complement activity, and the coagulation cascade, elevated interleukin (IL)-6 release damages neurons and the brain.[24]

Turbulent in heart rate is a phenomena seen in electrocardiograms that reflects momentary hemodynamic disturbances resulting from ventricular premature beats and describes the short-term baroreflex-mediated variations in the duration of the sinus cycle that occur after spontaneous ventricular premature beats. When compared to the rate before the ventricular premature beats, the sinus rate in healthy persons temporarily increases, then decelerates, and finally returns to the basal

rate.[25] A momentary drop in blood pressure due to a ventricular premature beat activates baroreceptors, which in turn causes a decrease in the RR interval cycle lengths as determined by TO and an increase in heart rate brought on by vagal inhibition. Meanwhile, the ANS's sympathetic arc is stimulated by temporary relative hypotension.[26] Vascular resistance and systolic blood pressure gradually rise due to increased sympathetic activity. As a result, vagal activity rises once again and cycle durations are extended which is indicated as TS.[26–29] Heart rate turbulence, therefore, requires a robust interaction of both the vagal and sympathetic systems. A change in either of these systems can result in the absence of normal heart rate turbulence.[29] Some recent studies have shown that the HRT evaluation results performed by evaluating atrial premature beats in patients with supraventricular premature beats indicate blunted HRT and that these patients are prone to atrial fibrillation.[7,8]

A triggering focal activator and alterations in the atrial electrophysiologic characteristics that might sustain AF are both components of the pathophysiology of AF.[30] According to experimental research, parasympathetic activation significantly reduces the atrial effective refractory period, which makes it easier for AF to start and continue.[31,32] Premature beats are necessary in HR turbulence analysis, which examines changes in autonomic control over time. Therefore, by examining the changes in the HR turbulence measurements before the onset of AF, we attempted to test the hypothesis that modified vagal reactions to atrial premature beats might start before the onset of paroxysmal AF.[7] A brief initial acceleration followed by a lengthier period of sinus rhythm slowdown characterizes the considered normal HRT response. This results in a negative TO in individuals with an intact HRT response and a higher TS response than those with an impaired HRT response. Therefore, both TO and TS parameters are considered to be related to the balanced functioning of the ANS and baroreflex sensitivity.[33]

If symptoms and signs persist for more than 12 weeks after COVID-19 infection and other causes are excluded, it is considered Long-COVID-19 syndrome.[9] Although the pathogenesis of this period is not clear, persistent hyperinflammatory process, ongoing viral activity within the viral reservoir of the host, inadequate antibody response and enduring effects of tissue tropism are held responsible for the Long-COVID-19 syndrome. However, the presence and extent of organ damage, the variability in the time required for recovery of all organ systems, the severe acute disease period, intensive care syndromes, complications related to COVID-19 in the acute period, and the side effects of drugs used during the acute disease process are also factors.[34] Long-COVID syndrome, the incidence of which varies between 10% and 60%, may include symptoms that concern many systems, such as fatigue, chest pain, shortness of breath, cough, decreased exercise intolerance, headache, and loss of taste and smell. In addition, palpitations, joint pain, muscle pain and weakness, insomnia, diarrhea, rash or hair loss, issues with balance and movement, issues with memory and focus, and cognitive problems, including deteriorating quality of life, can be observed.[35] In COVID-19 individuals, sinus tachycardia is often the most prevalent arrhythmia.[36] Nonetheless, the most likely pathogenic arrhythmias are ventricular tachycardia, atrial fibrillation, or atrial flutter.[37,38] The pathophysiology of COVID-19-associated AF is not well understood, but some hypotheses that have been proposed include electrolyte and acid-base balance abnormalities that may occur in the acute phase of severe disease, increased adrenergic activation, decreased angiotensin-converting enzyme 2 (ACE2) receptor count, sialic acid-spike protein and CD147 interaction, and myocardial and endothelial damage caused by inflammatory cytokine storm.[39] In the initial phase of severe COVID-19 illness, hypoxia and deficiencies in electrolytes have been commonly documented. These conditions are believed to lead to the emergence of abrupt arrhythmias.[40] An arrhythmia occurring at this stage may persist in the post-COVID period and cause a feeling of palpitations. Several survey-based studies have reported that patients who had COVID-19 reported more complaints of palpitations than patients who had never had COVID-19.[36,41] However, patients' explanations of palpitations are subjective interpretations, differ based on how the questionnaire is designed, and are not supported by concrete electrocardiographic data. A recent study based on an online survey, in which no concrete electrocardiographic data were documented, suggested that the cause of these complaints reported by the participants was postural orthostatic tachycardia syndrome.[36] As of today, objective ECG and Holter-ECG data are needed to show that subjective palpitation complaints described in the post-COVID-19 period indicate specific cardiac arrhythmias. A recently published study analyzing HRT of ventricular extrasystoles suggests that individuals who have recovered from severe COVID-19 may be more likely to develop malignant ventricular arrhythmia than individuals who have never had severe COVID-19.[42] Another recent study examining the effects of the post-COVID-19 period on HRT reported that HRT values were blunted

in the group with positive current COVID-19 test results compared to the group with negative test results.[43] Both studies were based on ventricular extrasystoles. The current study analyzes the HRT of supraventricular ectopic beats and whether individuals who have recovered from COVID-19 are predisposed to developing AF in the future.

Compared to the control group and other recovered COVID-19 subgroups, the recovered severe COVID-19 subgroup in the current investigation had a substantially lower atrial HRT Onset value and a significantly greater prevalence of aberrant atrial HRT Onset (Table 2) (Figure 3). Correlation analyzes revealed that abnormal atrial HRT Onset values were associated with the severity of recovered COVID-19 and chest severity score, but not with the time after recovery or history of positive PCR test results (Table 3) (Figures 4 and 5). Presence of abnormal atrial HRT onset using regression analyses and the atrial HRT Onset value was independently predicted by smoking, HT, recovery from severe COVID-19, and the chest CT severity level of recovered COVID-19 participants. The fact that atrial HRT values in group IV were blunted compared to other groups can be linked to the invasive and medicinal procedures used in the treatment plan for individuals with severe COVID-19 (the use of agents known to have harmful effects on the immune system and myocardium, such as steroids, in high doses eg, Prednisolone 1 gram/day, intubation), prolonged profound hypoxia, as well as to the being infected with high doses of SARS-CoV-2, which is believed to harm the ANS when a patient is unwell. The findings suggest that those have recovered from severe COVID-19 are more likely than those who have not had severe COVID-19 to have blunted atrial HRT and, thus, a greater risk of developing AF.

This investigation demonstrates that the HRT Onset responses to atrial premature impulses are blunted in recovered severe COVID-19 individuals compared with the other groups. ANS dysfunction may be brought on by the neurological, cardiac, and systemic symptoms of COVID-19 and the medications used to treat it, particularly corticosteroids and an ANS dysfunction may result in deviant autonomic reflexes, such as the temporary augmentation of vagal outflow that lessens heart rate variations in response to premature impulses, which explains these deviating HRT reactions to atrial premature beats.

There is a significant increase in the applications of recovered from COVID-19 individuals to psychiatric outpatient clinics with complaints of palpitations. In recently published articles on this subject, a parallel treatment protocol is introduced to the daily routine when palpitations are related to sadness, anxiety, or panic disorder.[44–48] The COVID-19 process, medical and invasive treatment processes may lead to irreversible damage to the heart muscle itself, internal conduction pathways or ANS. It should be kept in mind any potential harm to the heart's tissue, the ANS, or the intrinsic conduction pathways may cause supraventricular arrhythmia and therefore palpitation.

Limitations

Limitations of the study include the long-term effects of COVID-19 vaccines on the myocardium are not yet known and these vaccines were ignored when evaluating the cases, as well as the retrospective nature of the study.

Conclusion

This study demonstrated that abnormal atrial HRT independently was associated with recovering from severe COVID-19. In this context, this research offers verifiable proof of persistent palpitation complaints months after COVID-19 treatment, and it recommends a thorough 24-hour ECG-Holter examination for individuals who have recovered from severe COVID-19 to identify abnormal atrial HRT presence early and prevent AF.

Ethical Approval

The ethical approval was taken from the Ethics Committee of T.C. Fırat University (2021/12–45).

Funding

This article's research, authoring, and/or publishing were all done without any financial assistance to the author/authors.

Disclosure

Regarding the research, authorship, and/or publishing of this paper, the authors have no possible conflicts of interest to report.

References

1. Demirhan R, Çimenoğlu B, Yılmaz E. The effects of hospital organization on treatment during COVID-19 pandemic. *South Clin Ist Euras*. 2020;31:89–95 doi:10.147/scie.2020.32154
2. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585
3. Yenerçağ M, Arslan U, Şeker OO, et al. Evaluation of P-wave dispersion in patients with newly diagnosed coronavirus disease 2019. *J Cardiovasc Med*. 2021;22(3):197–203. doi:10.2459/JCM.0000000000001135
4. Yıldırım Y, Karaca O, Yılmaz FK, Güneş HM, Çakal B. Fragmented QRS on surface electrocardiography as a predictor of cardiac mortality in patients with SARS-CoV-2 infection. *J Electrocardiol*. 2021;66:108–112. doi:10.1016/j.jelectrocard.2021.03.001
5. Bauer A, Malik M, Schmidt G, et al. Heart rate turbulence: standards of measurement, physiological interpretation, and clinical use: international society for holter and noninvasive electrophysiology consensus. *J Am Coll Cardiol*. 2008;52(17):1353–1365. doi:10.1016/j.jacc.2008.07.041
6. Barthel P, Schneider R, Bauer A, et al. Risk stratification after acute myocardial infarction by heart rate turbulence. *Circulation*. 2003;108 (10):1221–1226. doi:10.1161/01.CIR.0000088783.34082.89
7. Vikman S, Lindgren K, Mäkikallio TH, Yli-Mäyry S, Airaksinen KJ, Huikuri HV. Heart rate turbulence after atrial premature beats before spontaneous onset of atrial fibrillation. *J Am Coll Cardiol*. 2005;45(2):278–284. doi:10.1016/j.jacc.2004.10.033
8. Qu XF, Liu L, Guo XN, Piao JY, Gao GY, Huang YL. Investigation of heart rate turbulence after atrial premature beats before onset of paroxysmal atrial fibrillation. *Zhonghua Yi Xue Za Zhi*. 2007;87(40):2840–2842.
9. Abdel-Gawad M, Zaghloul MS, Abd-Elsalam S, et al. Post-COVID-19 syndrome clinical manifestations: a systematic review. *Antiinflamm Antiallergy Agents Med Chem*. 2022;21(2):115–120. doi:10.2174/1871523021666220328115818
10. Carfì A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. *JAMA*. 2020;324:603–635.
11. Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network—United States. 2020. *MMWR Morb Mortal Wkly*. 2020;69(30):993–998. doi:10.15585/mmwr.mm6930e1
12. Mallick D, Goyal L, Chourasia P, Zapata MR, Yashi K, Surani S. COVID-19 induced postural orthostatic tachycardia syndrome (POTS): a review. *Cureus*. 2023;15(3):e36955. doi:10.7759/cureus.36955
13. Singh AK, Gupta R, Misra A. Comorbidities in COVID-19: outcomes in hypertensive cohort and controversies with renin angiotensin system blockers. *Diabetes Metab Syndr*. 2020;14(4):283–287. doi:10.1016/j.dsx.2020.03.016
14. Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *Eur J Intern Med*. 2020;76:14–20. doi:10.1016/j.ejim.2020.04.037
15. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. COVID-19 in critically ill patients in the Seattle region - case series. *N Engl J Med*. 2020;382 (21):2012–2022. doi:10.1056/NEJMoa2004500
16. Oudit GY, Kassiri Z, Jiang C, et al. SARS coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. *Eur J Clin Invest*. 2009;39(7):618–625. doi:10.1111/j.1365-2362.2009.02153.x
17. Ding Y, He L, Zhang Q, et al. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. *J Pathol*. 2004;203(2):622–630. doi:10.1002/path.1560
18. Yashavantha Rao HC, Jayabaskaran C. The emergence of a novel coronavirus (SARS-CoV-2) disease and their neuroinvasive propensity may affect in COVID-19 patients. *J Med Virol*. 2020;92(7):786–790. doi:10.1002/jmv.25918
19. Natoli S, Oliveira V, Calabresi P, Maia LF, Pisani A. Does SARS-Cov-2 invade the brain? Translational lessons from animal models. *Eur J Neurol*. 2020;27(9):1764–1773. doi:10.1111/ene.14277
20. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol*. 2020;92(6):552–555. doi:10.1002/jmv.25728
21. Das G, Mukherjee N, Ghosh S. Neurological Insights of COVID-19 Pandemic. *ACS Chem Neurosci*. 2020;11(9):1206–1209. doi:10.1021/acschemneuro.0c00201
22. Wu Y, Xu X, Chen Z, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020;87:18–22. doi:10.1016/j.bbi.2020.03.031
23. Berger JR. COVID-19 and the nervous system. *J Neurovirol*. 2020;26(2):143–148. doi:10.1007/s13365-020-00840-5
24. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: a Literature Review. *J Clin Neurosci*. 2020;77:8–12. doi:10.1016/j.jocn.2020.05.017
25. Schmidt G, Malik M, Barthel P, et al. Heart-rate turbulence after ventricular premature beats as a predictor of mortality after acute myocardial infarction. *Lancet*. 1999;353(9162):1390–1396. doi:10.1016/S0140-6736(98)08428-1
26. Segerson NM, Wasmund SL, Abedin M, et al. Heart rate turbulence parameters correlate with post-premature ventricular contraction changes in muscle sympathetic activity. *Hear Rhythm*. 2007;4(3):284–289. doi:10.1016/j.hrthm.2006.10.020
27. Berkowitsch A, Zareba W, Neumann T, et al. Risk stratification using heart rate turbulence and ventricular arrhythmia in MADIT II: usefulness and limitations of a 10-minute holter recording. *Ann Noninvasive Electrocardiol*. 2004;9(3):270–279. doi:10.1111/j.1542-474X.2004.93600.x
28. Zuern CS, Barthel P, Bauer A. Heart rate turbulence as risk-predictor after myocardial infarction. *Front Physiol*. 2011;2:99. doi:10.3389/fphys.2011.00099
29. Wichterle D, Melenovsky V, Simek J, Malik J, Malik M. Hemodynamics and autonomic control of heart rate turbulence. *J Cardiovasc Electrophysiol*. 2006;17(3):286–291. doi:10.1111/j.1540-8167.2005.00330.x
30. Markides V, Schilling RJ. Atrial fibrillation: classification, pathophysiology, mechanisms and drug treatment. *Heart*. 2003;89(8):939–943. doi:10.1136/heart.89.8.939
31. Liu L, Nattel S. Differing sympathetic and vagal effects on atrial fibrillation in dogs: role of refractoriness heterogeneity. *Am J Physiol*. 1997;273:805–816 doi:10.1152/ajpheart.1997.273.2.H805
32. Geddes LA, Hinds M, Babbs CF, et al. Maintenance of atrial fibrillation in anesthetized and unanesthetized sheep using cholinergic drive. *Pacing Clin Electrophysiol*. 1996;19(2):165–175. doi:10.1111/j.1540-8159.1996.tb03308.x

33. Iwasaki M, Yuasa F, Yuyama R, et al. Correla-tion of heart rate turbulence with sympathovagal balance in patients with acute myocardial infarction. *Clin Exp Hypertens*. 2005;27(2–3):251–257. doi:10.1081/CEH-48872
34. Nikki N. Long covid: how to define it and how to manage it. *BMJ*. 2020;370:m3489. doi:10.1136/bmj.m3489
35. Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of Long-COVID: analysis of COVID cases and their symptoms collected by the covid symptoms study app. *medRxiv*. 2020. doi:10.1101/2020.10.19.20214494
36. Davis HE, Assaf GS, McCorkell L, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClin Med*. 2021;38:101019. doi:10.1016/j.eclinm.2021.101019
37. Ingul CB, Grimsmo J, Mecinaj A, et al. Cardiac dysfunction and arrhythmias 3 months after hospitalization for COVID-19. *J Am Heart Assoc*. 2022;11(3):e023473. doi:10.1161/JAHA.121.023473
38. Spinoni EG, Mennuni M, Rognoni A, et al. Contribution of atrial fibrillation to in-hospital mortality in patients with COVID-19. *Circ Arrhythm Electrophysiol*. 2021;14(2):e009375. doi:10.1161/CIRCEP.120.009375
39. Gawałko M, Kapłon-Cieślicka A, Hohl M, Dobrev D, Linz D. COVID-19 associated atrial fibrillation: incidence, putative mechanisms and potential clinical implications. *Int J Cardiol Heart Vasc*. 2020;30:100631. doi:10.1016/j.ijcha.2020.100631
40. Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):1–8. doi:10.1001/jamacardio.2020.1017
41. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet*. 2023;401 (10393):e21–e33. doi:10.1016/S0140-6736(23)00810-3
42. Yılmaz M, Mirzaoğlu Ç. Retrospective cohort study: severe COVID-19 leads to permanent blunted heart rate turbulence. *Diagnostics*. 2025;15 (5):621. doi:10.3390/diagnostics15050621
43. Taş S, Taş Ü. Effects of COVID-19 on the autonomic cardiovascular system: heart rate variability and turbulence in recovered patients. *Tex Heart Inst J*. 2023;50(4):e227952. doi:10.14503/THIJ-22-7952
44. Huang B, Yan H, Hu L, et al. The contribution of psychological distress to resting palpitations in patients who recovered from severe COVID-19. *Int J Gen Med*. 2021;14:9371–9378. doi:10.2147/IJGM.S334715
45. Keshtkar A, Bahrami B. Relationship between COVID-19 anxiety and hypochondriasis in retirees aged 60 to 70 years in Shiraz. *J Environ Treat Tech*. 2021;9(4):737–740. doi:10.47277/JETT/9(4)739
46. Kasi LS, Moorthy B. A case report on care-seeking type illness anxiety disorder after COVID-19 infection. *Case Rep Psychiatry*. 2023;2023:3003499. doi:10.1155/2023/3003499
47. Kumar A, Cohen C. Post-COVID-19 panic disorder in older adults: two case reports. *Am J Geriatric Psychiatry*. 2021;29(4):58–59. doi:10.1016/j.jagp.2021.01.050
48. Javelot H, Weiner L. Panic and pandemic: narrative review of the literatüre on the links and risks of panic disorder as a consequence of the SARS-CoV-2 pandemic. *Encephale*. 2021;47(1):38–42. doi:10.1016/j.encep.2020.08.001