

INCIDENCE OF PERI-ARREST ARRHYTHMIAS ASSOCIATED WITH COVID-19

UČESTALOST PERIARESTNIH ARITMIJA TOKOM PANDEMIJE COVID-19

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Abstract

Introduction. The COVID-19 pandemic has profoundly impacted all aspects of life, with increasing evidence highlighting its severe extrapulmonary effects. Notably, it has been implicated in the development of peri-arrest arrhythmias in patients with pre-existing cardiovascular conditions, underscoring the need for further investigation. The study aimed to evaluate the impact of the COVID-19 pandemic on the incidence of peri-arrest arrhythmias among hospitalized patients at the Institute of Cardiovascular Diseases of Vojvodina, all of whom had underlying cardiac pathology. **Material and Methods.** A retrospective observational study was conducted on patients hospitalized at the Institute from March 2018 to January 2022 for cardiovascular diseases. Risk factors, including hyperlipidemia, alcohol consumption, smoking, diabetes, and hypertension, were analyzed. **Results.** The findings revealed a significant increase in peri-arrest arrhythmias, particularly tachyarrhythmias, during the COVID-19 pandemic. Hypertension (80.6%) and hyperlipidemia (54.6%) were highly prevalent among the study population. In COVID-19-positive patients, tachyarrhythmias occurred were more frequent (31%) compared to the pre-pandemic period (11.4%), whereas the incidence of bradyarrhythmias remained unchanged. A strong association between arrhythmias and acute myocardial infarction was also observed in COVID-19-positive patients. **Conclusion.** The study confirms that the COVID-19 pandemic contributed to a heightened incidence of peri-arrest arrhythmias in hospitalized cardiac patients. **Key words:** Arrhythmias, Cardiac; COVID-19; Risk Factors; Cardiovascular Diseases; Myocardial Infarction; Tachycardia; Bradycardia

Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic has introduced significant changes in medical practice, including a potential increase in peri-arrest arrhythmias. The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), responsible for the pandemic, has infected over 776 million people worldwide. While primarily affecting the respiratory system, it also exerts substantial extrapulmonary effects, particularly on the cardiovascular system [1, 2]. This impact is likely attributed to the ability of SARS-

Sažetak

Uvod. Pandemija COVID-19 značajno je uticala na sve aspekte života, a sve više dokaza ukazuje na ozbiljne vanplućne posledice. Posebno se ističe njen doprinos razvoju periarestnih aritmija kod pacijenata sa primarnim kardiovaskularnim oboljenjima, što zahteva dalje istraživanje. Cilj istraživanja bio je da se proceni uticaj pandemije COVID-19 na učestalost periarestnih aritmija kod hospitalno lečenih pacijenata u Institutu za kardiovaskularne bolesti Vojvodine, koji su imali primarno kardiološko oboljenje. **Materijal i metode.** Sprovedena je retrospektivna opservaciona studija na pacijentima hospitalizovanim u Institutu od marta 2018. do januara 2022. godine zbog kardiovaskularne patologije. Analizirani su faktori rizika kao što su hiperlipidemija, konzumacija alkohola, pušenje, dijabetes i hipertenzija. **Rezultati.** Studija je pokazala značajan porast periarestnih aritmija, posebno tahiaritmija, tokom pandemije COVID-19. Utvrđen je visok procenat hipertenzije (80,6%) i hiperlipidemije (54,6%). U COVID-19 pozitivnoj grupi tahiaritmije su se javljale češće (31%) nego u periodu pre pandemije (11,4%), dok je učestalost bradiaritmija ostala nepromenjena. Takođe, utvrđena je značajna povezanost između aritmija i akutnog infarkta miokarda kod COVID-19 pozitivnih pacijenata. **Zaključak.** Rezultati istraživanja potvrđuju uticaj pandemije COVID-19 na povećanu učestalost periarestnih aritmija kod hospitalizovanih pacijenata sa kardiološkim oboljenjima. **Ključne reči:** aritmije; COVID-19; faktori rizika; kardiovaskularne bolesti; infarkt miokarda; tahikardija; bradikardija

CoV-2 to exploit the angiotensin-converting enzyme 2 (ACE2) receptor, which is abundantly expressed in key organs, in combination with the systemic hyper-inflammatory response triggered by the infection [3].

Gojković et al. report that COVID-19 can induce both direct and indirect cardiovascular complications. Direct infection of cardiomyocytes, pericytes, and fibroblasts leads to myocardial injury with cardiotoxic effects, while hypoxia, microvascular damage of coronary blood vessels, endothelial cell infection, and widespread inflammation further exacerbate cardiovascular dysfunction [4].

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Abbreviations

COVID-19	– Coronavirus Disease 2019
SARS-CoV-2	– Severe Acute Respiratory Syndrome Coronavirus 2
ACE 2 receptors	– angiotensin-converting enzyme 2 receptors
ARDS	– Acute Respiratory Distress Syndrome
ICVDV	– Institute of Cardiovascular Diseases of Vojvodina
PCR	– polymerase chain reaction

Peri-arrest arrhythmias, defined as cardiac rhythm disturbances occurring immediately before or after cardiac arrest, and are classified into bradyarrhythmias and tachyarrhythmias [5].

Bradyarrhythmias (heart rate <50 bpm) may remain asymptomatic until they become critical, manifesting as altered consciousness, dyspnea, chest pain, hypotension, and oliguria [6]. Tachyarrhythmias (heart rate >100 bpm) are categorized based on their origin (supraventricular or ventricular) and QRS complex morphology (narrow and wide) [7, 8].

The progression of COVID-19 occurs in multiple phases, including the viral phase, the secondary replication phase, and culminating in severe stage marked by multisystem failure due to excessive cytokine release [9, 10]. Inflammatory cytokines, such as interleukin-6, can disrupt cardiac potassium and calcium channels, contributing to arrhythmogenesis [11]. Moreover, acute respiratory insufficiency and Acute Respiratory Distress Syndrome (ARDS), resulting from COVID-19-associated pulmonary infiltration, exacerbate hypoxia, further increasing the risk of arrhythmias [12].

Direct myocardial injury in COVID-19 patients is evidenced by markers such as NT-proBNP, cardiac troponin I, and high-sensitivity C-reactive protein, all of which are associated with an increased risk of arrhythmias. Additionally, electrolyte imbalance and early treatments such as hydroxychloroquine and azithromycin may further predispose patients to arrhythmic events by inhibiting potassium channels, thereby prolonging cardiac action potential and increasing risk of torsades de pointes [13, 14].

Early reports from Wuhan indicated that 44% of intensive care unit patients experienced arrhythmias, raising concerns about the between COVID-19 and peri-arrest arrhythmias.

This study aims to assess the impact of the COVID-19 pandemic on the prevalence of peri-arrest arrhythmias among patients hospitalized at the Institute of Cardiovascular Diseases of Vojvodina (ICVDV) following emergency admission, all of whom had pre-existing cardiovascular conditions.

Hypotheses

1. The prevalence of peri-arrest arrhythmias is higher among COVID-19-positive patients with pre-

existing cardiovascular disease compared to similar patients hospitalized before the pandemic.

2. Cardiovascular risk factors, including hyperlipidemia, excessive alcohol consumption, smoking, diabetes, and hypertension, are associated with an increased prevalence of peri-arrest arrhythmias in COVID-19 positive patients.

3. Tachyarrhythmias occur more frequently than bradyarrhythmias in COVID-19 positive patients.

4. Myocardial infarction diagnosed alongside peri-arrest arrhythmias is more common in COVID-19-positive patients than in those with myocardial infarction before the pandemic.

5. Peri-arrest arrhythmias in COVID-19-positive patients are attributable to SARS-CoV-2 infection rather than to acute myocardial infarction, which is a known cause of peri-arrest arrhythmias.

Material and Methods

This observational cohort study included 602 patients hospitalized at the ICVDV due to primary cardiovascular conditions following emergency admission between March 2018 and January 2022. Patient data were retrieved from the ICVDV information system.

The dataset included demographic information and cardiovascular risk factors such as alcohol consumption, smoking, hyperlipidemia, hypertension, diabetes mellitus, and the presence of a diagnosed myocardial infarction. Additionally, data on positive polymerase chain reaction (PCR) test results were collected for the experimental group.

Patients were categorized into two groups based on PCR test results:

– Experimental group consisting of 313 patients with a positive PCR test, hospitalized with a primary cardiovascular condition following emergency admission between March 15, 2020 and January 15, 2022.

– Control group comprising 289 randomly selected patients hospitalized with a primary cardiovascular condition following emergency admission before the COVID-19 pandemic, between March 15, 2018 and March 1, 2020. This group was included to minimize the potential misclassification due to false-positive PCR results, as some patients were diagnosed positive only after multiple tests.

Descriptive statistical measures, including mean, standard deviation, median, frequencies, and percentages, were applied. Comparisons of mean values between the two groups were conducted using the t-test for independent samples. Associations between categorical variables were assessed using the chi-square test for contingency tables or Fisher's exact test, where appropriate. Results were presented in both tabular and

graphical formats. A p-value of < 0.05 was considered statistically significant. Data analysis was performed using SPSS 17 statistical software.

Results

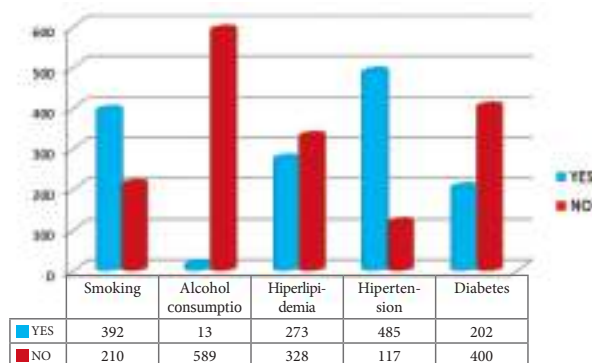
The study included 602 emergency-hospitalized patients with primary cardiac pathology, of whom 346 (59.1%) were men and 246 (40.9%) were women. The mean age was 68.24 ± 11.99 years, with no statistically significant difference between genders. Demographic characteristics and cardiovascular risk factors, including smoking, alcohol consumption, hyperlipidemia, hypertension, and diabetes mellitus, are presented in **Graph 1**.

In regard to the risk factors, 34.9% of patients were smokers, 2.2% reported consuming alcohol, 54.6% had hyperlipidemia, 80.6% had hypertension, 33.6% had diabetes mellitus, 48.3% had a history of myocardial infarction, and 24.4% had pneumonia.

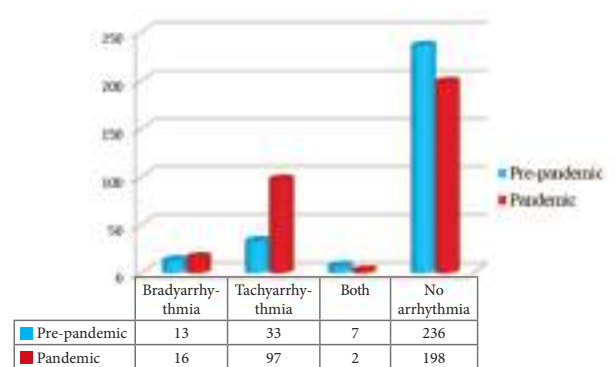
Peri-arrest arrhythmias were classified into bradyarrhythmias and tachyarrhythmias. Tachyarrhythmias were observed in 32.7% of patients, with atrial fibrillation (18.8%) and ventricular tachycardia (4.7%) being the most common. Bradyarrhythmias occurred in 7.2%, with third-degree AV block (4.2%) being the most frequent.

Patients were divided into two groups: pre-pandemic and COVID-19-positive. Tachyarrhythmias were significantly more frequent in COVID-19-positive patients (31%) compared to the pre-pandemic group (11.4%). Bradyarrhythmias showed similar prevalence in both groups, as shown in **Graph 2**.

A significant association was found between arrhythmia and COVID-19 status ($p < 0.0005$). The portion of patients without arrhythmias declined from 81.7% pre-pandemic to 63.3% during the pandemic. Bradyarrhythmias occurred in 4.5% pre-pandemic vs. 5.1% after the pandemic. Tachyarrhyth-

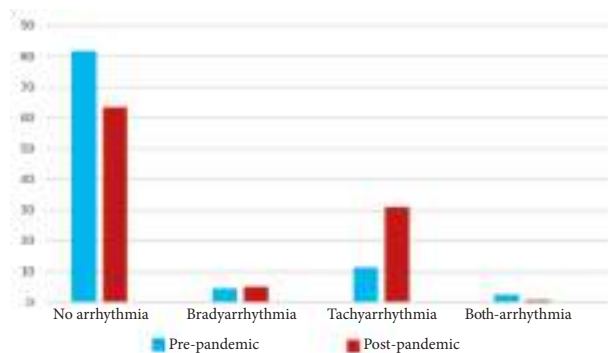


Graph 1. Overview of risk factors for the development of cardiovascular diseases



Graph 2. Overview of incidence of peri-arrest arrhythmias in PCR-positive vs. PCR-negative patients

mias increased from 11.4% pre-pandemic to 31% during the pandemic. The portion of patients with both bradyarrhythmias and tachyarrhythmias decreased from 2.4% pre-pandemic to 0.6% during the pandemic, as shown in **Graph 3**.



Graph 3. Arrhythmia prevalence trend pre- and during pandemic

A significant association was found between arrhythmias and AMI in COVID-19-positive patients ($p=0.004$): 53% of patients with AMI had no arrhythmias, 43.8% had bradyarrhythmias, 32% had tachyarrhythmias, and 0% had both bradyarrhythmia and tachyarrhythmia. These findings suggest that the increased incidence of arrhythmias during the pandemic was primarily due to COVID-19 infection rather than myocardial infarction.

The results highlight a significant impact of COVID-19 on the incidence of peri-arrest arrhythmias, particularly tachyarrhythmias. Additionally, hypertension and pneumonia emerged as key risk factors in this patient population.

Discussion

Cardiac arrhythmias are a well-documented cardiovascular complication in patients with COVID-19. In a study of 138 COVID-19 patients, heart palpita-

tions were reported in 7.3% of cases [15]. In a retrospective study from Wuhan, China, found that 16.7% of hospitalized patients experienced cardiac arrhythmias, with a higher incidence in those in intensive care unit (ICU) patients (44.4%) compared to non-ICU patients (6.9%) [16, 17]. However, specific types of arrhythmias were not detailed.

Our study compared the incidence of peri-arrest arrhythmias before (March 2018 – March 2020) and during the pandemic (March 2020 – January 2022). The findings confirm a higher prevalence of peri-arrest arrhythmias during the pandemic. In another study, 16.7% of patients experienced arrhythmias, with a higher occurrence in ICU patients (44.4%) compared to non-ICU patients (6.9%) [18]. Guo et al. reported that 5.9% of patients developed sustained ventricular tachycardia or fibrillation [19].

Recent studies have investigated the types of arrhythmias associated with COVID-19 patients in the U.S.A. In a study of 393 patients in New York, 7.1% experienced atrial arrhythmias, while 0.3% had ventricular arrhythmias [20]. Critically ill patients had a higher incidence of arrhythmias, with 16.5% of ICU patients presenting with atrial arrhythmias [21]. Our study also confirmed that atrial fibrillation was the most frequent peri-arrest arrhythmia among critically ill patients.

Diverse arrhythmic manifestations have been observed in COVID-19 patients, including transient third-degree AV block, transient atrioventricular block, and pulmonary artery hypertension as part of ARDS [22, 23]. Tachyarrhythmias such as atrial fibrillation, atrial flutter, supraventricular tachycardias, and ventricular arrhythmias have also been reported [24]. Additionally, cases of multifocal ventricular tachycardia following ST-segment elevation and atrial flutter with second-degree AV block have been documented [16, 25, 26].

Atrial arrhythmias appear more frequent in COVID-19 patients compared to the general population, often occurring without a prior history of cardiac surgery, ablation, cardioversion, or antiarrhythmic drug use. A study from Columbia University during the pandemic peak in New York found that 31% of COVID-19 patients had atrial arrhythmias, although only 13% had a prior history of the condition [27]. The etiology involves ACE2 receptor alternations, inflammation, direct viral endothelial damage, and metabolic disturbances.

Atrial fibrillation is associated with worse outcomes in patients with acute respiratory illnesses, including ARDS and severe pneumonia. Increased mortality has been observed in patients with new-onset atrial fibrillation, particularly those requiring mechanical ventilation, where the incidence was 17.7% compared to 1.9% in non-ventilated patients. Moreover, some medications used for COVID-19 may contribute to QT interval prolongation, increasing the risk of torsades de pointes.

Conclusion

This study assessed the impact of the COVID-19 pandemic on the prevalence of peri-arrest arrhythmias in patients hospitalized at the Institute of Cardiovascular Diseases of Vojvodina following emergency admission. All patients had pre-existing primary cardiovascular conditions. Among cardiovascular risk factors, hypertension emerged as a significant contributor to the increased incidence of peri-arrest arrhythmias in COVID-19 patients. Moreover, our results suggest that peri-arrest arrhythmias in COVID-19-positive patients were primarily attributable to the coronavirus rather than acute myocardial infarction, a well-established cause of such arrhythmias.

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