EVALUATION OF CARDIAC COMPLICATIONS IN THE POST-ACUTE PHASE OF COVID-19 PATIENTS

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Abstract

Introduction. Cardiovascular complications linked to SARS-CoV-2 infection are both frequent and varied, contributing to elevated mortality during the acute phase and significant morbidity in the chronic phase, thereby impacting quality of life and overall health outcomes.

Objective. To assess the incidence and type of post-acute cardiac complications in patients with and without COVID-19.

Materials and Methods. This is a retrospective study involving 201 patients admitted to the Cardiology Diseases Service at UHC "Mother Teresa" in Tirana, Albania, during the period January– April 2021. For each patient, data were collected onCOVID-19status, comorbidities and previous cardiovascular events. The study describes post-acute cardiac complications: myocardial infarction (MI), arrhythmia, right ventricular dysfunction, pericardial effusion, and Takotsubo cardiomyopathy.

Results. The study included 201 patients, of whom 77 (38.3%) were female and 124 (61.7%) were male. The average age of the patients was 64.1 (±10.6) years, ranging from 32 to 91 years. Most patients, 116 (57.7%) of them, had COVID-19 (p=0.028). A significant association was found between COVID-19 and comorbidities such as hypertension (p=0.001), diabetes (p=0.035) and previous cardiovascular events (p=0.025). The incidence of post-acute cardiac complications in COVID-19 patients was 56 (48.3%).

Conclusions. Understanding the interaction between cardiovascular diseases and COVID-19 is essential for several critical reasons, including diagnosis, clinical management, and improving patient outcomes.

Keywords: COVID-19, post-acute cardiac complications

VLERËSIMI I KOMPLIKACIONEVE KARDIAKE POST-AKUTE NË PACIENTËT ME COVID-19

Abstrakt

Hyrje: Komplikimet kardiovaskulare të lidhura me infeksionin SARS-CoV-2 janë të zakonshme dhe të shumëllojshme, duke çuar në vdekshmëri të lartë në fazën akute dhe sëmundshmëri të lartë në fazën kronike, duke ndikuar në cilësinë e jetës dhe rezultatet shëndetësore të një individi.

Objektivi: Të vlerësojë incidencën dhe llojin e komplikimeve kardiake pas akute te pacientët me dhe pa COVID-19.

Materialet dhe Metodat: Ky është një studim retrospektiv që përfshin 201 pacientë të shtruar në Shërbimin e Sëmundjeve Kardiologjike në QSUT "Nënë Tereza" në Tiranë, Shqipëri, gjatë periudhës janar-prill 2021. Për çdo pacient janë mbledhur të dhëna për statusin e COVID-19. Komorbiditetet dhe ngjarjet e mëparshme kardiovaskulare. Studimi përshkruan komplikimet kardiake post-akute: infarkt miokardi (MI), aritmi, mosfunksionim të ventrikulit të djathtë, efuzion

perikardial dhe kardiomiopati Takotsubo.
Rezultatet: Në studim janë përfshirë 201 pacientë, nga të cilët 77 (38.3%) ishin femra dhe 124 (61.7%) meshkuj. Mosha mesatare e pacientëve ishte 64.1 (±10.6) vjeç, duke filluar nga 32 deri në 91 vjeç. Shumica e pacientëve, 116 (57.7%) prej tyre, kishin COVID-19 (p=0.028). U gjet një lidhje e rëndësishme midis COVID-19 dhe sëmundjeve shoqëruese si hipertensioni (p=0.001), diabeti (p=0.035) dhe ngjarjet e mëparshme kardiovaskulare (p=0.025). Incidenca e komplikimeve kardiake post-akute në pacientët me COVID-19 ishte 56 (48.3%).
Përfundime: Kuptimi i ndërveprimit midis sëmundjeve kardiovaskulare dhe COVID-19 është thelbësor për disa arsye kritike, duke përfshirë diagnostikimin, menaxhimin klinik dhe përmirësimin e rezultateve të pacientit.

Fjalë kyçe: COVID-19, komplikacioneve kardiake post-akute

Introduction

The COVID-19 pandemic is a growing public health concern globally, with case reports continuing to rise. As our understanding of COVID-19 continues to grow, there has been considerable discussion related to the acute effects of the virus on the cardiovascular system, including myocarditis, pericarditis, and acute complications such as myocardial infarction and arrhythmias (1,2). These factors not only contribute to grave outcomes of acute infections but have also been linked to post-acute outcomes. The term post-acute is defined as a phase that extends from the time of resolution of symptoms of an acute illness to a prolonged phase of symptoms, after which it may take up to 12 or even 24 weeks for symptoms to resolve (3). Around 27% of individuals with a confirmed case of COVID-19 have symptoms of the infection that have lasted for more than 12 weeks. Symptoms of acute and post-acute cardiac complications found in individuals with COVID-19 may range from asymptomatic to death due to cardiac arrest arising from a malignant arrhythmia. Acute cardiac complications are defined as an evidenced acute change in cardiac function and structure such as cardiac dysfunction with myocarditis, myocardial infarction, or arrhythmias observed during the initial infection of COVID-19 (4,5). Although the exact prevalence of such cardiac complications is unknown, they are known to occur but are rare. Post-acute cardiac complications are defined as evidence of loss of cardiac function when compared to pre-COVID imaging or recurrence of symptoms beyond the acute phase of COVID-19 infection (6-8). Mechanisms that explain the development and persistence of such symptoms likely relate to ongoing inflammation and/or disarray that interrupt the function of the cardiomyocytes or the sympathetic nervous system innervation (9-12)). Quite disturbing is the observation that older patients or people with chronic diseases such as diabetes or high blood pressure were most likely included in the criteria for the samples of survivors under study. At these ages, with these professional post-acute problems, an important component of rehabilitation occurs before their visit.

As such, we have argued that the follow-up for these patients emphasizes that the treatment of cardiac complications, such as inflammation, remains a necessary aspect of the assessments provided following discharge for COVID-19 survivors (13). There is growing recognition of the need to study post-acute complications, especially as they have a significant impact on public health and healthcare resources. Increasing research in this area could help with developing targeted rehabilitation programs, improving quality of life for patients, and creating guidelines for long-term management (14). In this study, the incidence and type of post-acute cardiac complications in Covid-19 and non-COVID-19 patients were evaluated.

Materials and Methods

This is a retrospective descriptive study involving 201 adult patients admitted to the cardiology

Service at UHC "Mother Teresa" in Tirana, Albania, during the interval period between January and April 2021. For each patient, data were collected on COVID-19status, comorbidities and previous CV events. The study aims to describe the incidence of post-acute cardiac complications: myocardial infarction (MI), arrhythmia, right ventricular dysfunction, pericardial effusion, and Takotsubo cardiomyopathy in patients with and without history of COVID-19infection. Post acute cardiac complications were diagnosed based on established criteria from the European Society of Cardiology (ESC) guidelines, ensuring standardized and consistent evaluation of conditions such as myocardial infarction, myocarditis, arrhythmias, and heart failure (15-20).

Statistical Analysis

Data analysis was performed using IBM SPSS Statistical Software version 25.0. Continuous variables are reported as mean and standard deviation (SD), and categorical variables are summarized as frequencies and percentages. The chi-square test was used to compare categorical variables, with statistical significance defined as a p-value of ≤0.05.

Results

The study included 201 patients, of whom 77 (38.3%) were female and 124 (61.7%) were male. The average age of the patients was 64.1 (±10.6) years, ranging from 32 to 91 years. The average age of the COVID-19 patients was 65.4 ± 10.6 years, while the average age of the non-COVID-19 patients was 60.1 ± 9.7 years. In the age group ≤50 years, there were 23 (11.4%) patients, in the age group 51-70 years there were 121 (60.2%) patients, while in the age group >70 years there were 57 (28.4%).

Table 1. Sociodemographic and clinical characteristics of the patients

Variables	**Total (n=201)**	**COVID-19(n=116)**	**Non- COVID-19 (n=85**
	n (%)	n (%)	n (%)
Sex			
Female	77 (38.3)	44 (37.9)	33 (38.8)
Male	124 (61.7)	72 (62.1)	52 (61.2)
Age M (SD)	64.1 (10.6)	65.4 (10.6	60.1 (9.7)
Age group			
≤50	23 (11.4)	11 (9.5)	12 (14.1)
51-70	121 (60.2)	68 (58.6)	53 (62.4)
>70	57 (28.4)	37 (31.9)	20 (23.5)
Underlying conditions			
Hypertension	155 (77.1)	87 (75.0)	68 (80.0)
Diabetes	60 (29.9)	32 (27.6)	28 (32.9)
Previous CV events	62 (30.8)	36 (31.0)	26 (30.6)
Stroke	3 (1.4)	1 (0.9)	2 (2.4)
Venous or arterial thrombosis	2 (1.0)	2. (1.7)	-
Respiratory illness	11 (5.4)	8 (6.9)	3 (3.5)
Malignancy	1 (0.5)	1 (0.9)	-
Chronic hepatic illness	1 (0.5)	-	1 (1.2)
Chronic renal illness	9 (4.4)	7 (6.0)	2 (1.4)

Out of 201 cases, 116 patients (58%) had history of recent COVID-19infection. Hypertension (HTA) was the more common comorbidity (77.1%), followed by diabetes (29.9%), previous CV events (30.8%), stroke (1.4%), venous or arterial thrombosis (1%), respiratory disease (5.4%), malignancy (0.5%), chronic liver disease (0.5%), and chronic kidney disease (4.4%). A total of 70 (34.8%) patients manifested post-acute cardiac complications. Among the post-acute cardiac complications, myocardial infarction (MI)was reported in 29 patients(14.4%), followed by arrhythmia in 14 patients (7%), right ventricular dysfunction and pericardial effusion in 7 patients (3.5%) each, and Takotsubo cardiomyopathy in 1 (0.5%) patient.

No significant difference was found between two groups of patients regarding the rate of underlying conditions. The incidence of post-acute cardiac complications in COVID-19 patients 56 (48.3%) is significantly higher as compared to patients without COVID-19,14 cases (16.5%) ($p<0.001$). The following table, shows the incidence of cardiac complications in patients regarding the Covid-19 status (Table 2).

No significant difference between two groups was found regarding the incidence of MI (15.5% vs 12.9%) ($p=0.608$) whereas the incidence of arrhythmia ($p<0.001$) right ventricular dysfunction (7, 6%) ($p=0.021$), and pericardial effusion (7, 6%) ($p=0.021$)was significantly higher among patients confirmed with COVID-19. Takotsubo cardiomyopathy was found in one (0.9%) COVID-19 patient ($p=0.392$), only.

Table 2. Incidence of post-acute complications according to the status of Covid-19

Post-acute complications	**COVID-19(n=116)**	**Non- COVID-19 (n=85)**	**P**
	n (%)	n (%)	
MI	18 (15.5)	11 (12.9)	0.608
Arrhythmias	23 (19.8)	3 (3.5)	<0.001
Right ventricular dysfunction	7 (6.0)	-	0.021
Pericardial effusion	7 (6.0)	-	0.021
Takotsubo cardiomyopathy	1 (0.9)	-	0.392

The incidence of all post-acute cardiac complications was higher in the period >3 months after infection, ranging from 0.9 to 12.1% (table 3).

Table 3. Incidence of complications from the time of infection with COVID-19

Post-acute complications	**< 1 month**	**1 – 3 months**	**> 3 months**	**P**
	n (%)	n (%)	n (%)	
MI	3 (2.6)	4 (3.4)	11 (9.5)	0.042
Arrhythmias	2 (1.7)	7 (6.0)	14 (12.1)	0.165
Right ventricular dysfunction	1 (0.9)	2 (1.7)	4 (3.4)	0.008
Pericardial effusion	1 (0.9)	1 (0.9)	5 (4.3)	0.101
Takotsubocardiomyopathy			1 (0.9)	-

Discussion

A year after the COVID-19 pandemic, we have acquired significant insights into the symptoms, complications, and underlying pathophysiological mechanisms of the disease and its effects on

human health. This includes not only its impact on the respiratory system but also its association with other conditions, such as alterations in the blood and changes affecting the cardiovascular system.

While respiratory illness is the primary clinical feature of COVID-19, the overall disease burden suggests that many patients either have pre-existing cardiovascular conditions or may experience new cardiac dysfunction as the disease progresses.

This study provides an in-depth evaluation of post-acute cardiac complications in COVID-19 patients, demonstrating the significant burden of cardiovascular sequelae even months after the resolution of the acute phase of the infection. Higher Incidence of Post-Acute Cardiac Complications in COVID-19 Patients: The findings reveal that post-acute cardiac complications were significantly more common in patients with a history of COVID-19 infection compared to non-COVID-19 patients (48.3% vs. 16.5%, $p<0.001$). This aligns with growing evidence suggesting that SARS-CoV-2 infection has both direct and indirect effects on cardiac health, potentially mediated by systemic inflammation, endothelial dysfunction, and direct viral invasion of myocardial cells (***21***, 2***2***). The observed increased prevalence of arrhythmias, right ventricular dysfunction, and pericardial effusion in COVID-19 patients underscores the need for targeted cardiac monitoring and intervention strategies during follow-up care (***2***3, ***2***4).

Temporal Trends in Post-Acute Complications: Interestingly, the study found a progressive increase in the incidence of post-acute cardiac complications over time, with the highest rates observed beyond three months after infection. For example, myocardial infarction was reported in 9.5% of patients more than three months post-infection compared to 2.6% within the first month ($p=0.042$). Similarly, arrhythmias and right ventricular dysfunction showed an upward trend over time. These results are consistent with other studies reporting delayed cardiac manifestations, which may result from prolonged inflammation, autoimmunity, or unresolved myocardial injury initiated during the acute phase of COVID-19 (***2***5, ***2***6).

Specific Complications: Mechanisms and Implications

Myocardial Infarction (MI): The comparable rates of MI between COVID-19 and non-COVID-19 groups (15.5% vs. 12.9%, $p=0.608$) suggest that traditional risk factors and comorbidities, such as hypertension and diabetes, may play a dominant role in these patients. However, systemic inflammation and pro-thrombotic states observed in COVID-19 could exacerbate pre-existing cardiovascular risks, potentially leading to MI (27, 28).A meta-analytic study has shown that the rate of myocardial infarction can reach up to 10% in some specific groups of patients with high risk factors, such as those with a previous cardiovascular history (29). These figures show high variability, which is often related to the demographic and medical factors of the patients as well as the different methodologies used in different studies.

Arrhythmias: A significantly higher incidence of arrhythmias was observed in COVID-19 patients (19.8% vs. 3.5%, $p<0.001$). This may result from direct myocardial injury, hypoxia, electrolyte disturbances, or autonomic dysfunction. Persistent arrhythmias in the post-acute phase can contribute to long-term morbidity and require careful management (30). In an international prospective study, ventricular arrhythmia accounted for the reason for echocardiographic assessment in 3% of cases(31).

In contrast, other authors have found arrhythmia complications in 9.3% of patients, mainly represented by atrial fibrillation (32). But figures in 40% and 60% of patients with severe forms of COVID-19 have also been reported in the literature (33,34).

Right Ventricular Dysfunction and Pericardial Effusion: The exclusive presence of these complications in COVID-19 patients ($p=0.021$) highlights the potential for unique pathophysiological effects of the virus, including pulmonary vascular disease, increased right heart

strain, and persistent pericardial inflammation. These findings align with other reports emphasizing the role of right ventricular dysfunction in COVID-19-related morbidity (35, 36).
Takotsubo Cardiomyopathy: Although rare, Takotsubo cardiomyopathy was observed in one COVID-19 patient. The exact mechanism remains unclear, but it may involve stress-related catecholamine surges exacerbated by COVID-19 (37).
In our study, no cases of myocarditis were identified, perhaps due to the smaller number of patients compared to studies with large patient populations in the literature. The incidence is low and very low even in studies with a large patient population and varies from 0.1% to 3% (24). In the literature, it is reported that ventricular dysfunction was detected during echocardiography evaluation in 21% (29) and in 39% of patients (38).

Implications for Clinical Practice

The observed burden of post-acute cardiac complications in COVID-19 survivors highlights the necessity for structured follow-up programs. Cardiac rehabilitation tailored to address arrhythmias, ventricular dysfunction, and inflammatory conditions could improve outcomes. Additionally, early identification of at-risk individuals, particularly older patients or those with pre-existing conditions, is crucial (37).

Conclusion

Post-acute cardiac complications in COVID-19 are an area of intensive study due to the potential long-term impacts of the virus on the cardiovascular system.
This study underscores the significant burden of post-acute cardiac complications in COVID-19 patients, with a marked increase in incidence beyond three months after infection. Understanding the interaction between cardiovascular diseases and COVID-19 is essential for several critical reasons, including diagnosis, clinical management, and improving patient outcomes.
The findings emphasize the importance of long-term cardiac monitoring and the development of rehabilitation programs to address these complications, ultimately improving patient outcomes.

Compliance with Ethics Requirements:

*"*The authors declare no conflict of interest regarding this article"
"All procedures performed in this study were in accordance with the ethical standards of the institutional and/ or national research committee(s) and with the Helsinki Declaration (as revised in 2013), as well as the national law. Informed consent was obtained from the patients included in the study"
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