American Journal of Medicine and Medical Sciences 2024, 14(4): 968-973
DOI: 10.5923/j.ajmms.20241404.35

Assessment of Central Hemodynamics and External Respiration in Patients after COVID-19 Related Pneumonia

Nazarov F. Y.*, Yarmuxamedova S. Kh.

Chair of Internal Medicine and propaedeutics, Samarkand State Medical University, Samarkand, Uzbekistan

Abstract The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has significantly impacted global health, leading to a wide range of clinical manifestations. This study aims to evaluate the indicators of central hemodynamics and external respiration in patients who have recovered from community-acquired coronavirus pneumonia (CCP). An observational study was conducted at the Cardiology Department of the Samarkand State Medical University, Uzbekistan, from 2020 to 2021. A total of 102 patients aged between 40 and 55 years, who were diagnosed with CCP and had undergone treatment and examination at the Cardiology Department, were included in the study. The study utilized clinical data, laboratory investigations, and instrumental methods such as spirometry and transthoracic echocardiography (TTE) to assess central hemodynamics and external respiration. The results revealed significant clinical and laboratory alterations in patients recovering from CCP. Elevated levels of leukocytes, neutrophils, and markers of inflammation and cardiac injury such as C-reactive protein and troponin-I were observed. Echocardiographic evaluations indicated moderate impairments in heart function among CCP survivors, with a substantial proportion of patients exhibiting left ventricular hypertrophy and dysfunction. Spirometry results demonstrated reduced forced vital capacity (FVC) and forced expiratory volume in one second (FEV1), indicating persistent respiratory impairment. The study underscores the importance of comprehensive post-recovery care for patients who have survived CCP, highlighting the need for ongoing monitoring and tailored management strategies to address the long-term health consequences of the disease.

Keywords COVID-19, Community-Acquired Coronavirus Pneumonia, Central Hemodynamics, External Respiration, Post-COVID Syndrome

1. Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has had a profound impact on global health, leading to a wide range of clinical manifestations, from asymptomatic cases to severe respiratory distress syndrome and multi-organ failure. One of the critical areas affected by the virus is the cardiovascular and respiratory systems. The interplay between the virus and these systems is complex, with emerging evidence suggesting that COVID-19 can lead to significant alterations in central hemodynamics and external respiration, even in patients who have recovered from the acute phase of the infection [1,5,9].

Central hemodynamics, which encompasses the functioning of the heart and major blood vessels, is crucial for maintaining adequate tissue perfusion and oxygenation. Disruptions in this system can lead to a cascade of physiological imbalances, affecting the body's ability to deliver oxygen to vital organs. External respiration, the process of gas exchange between the external environment and the body's circulatory system, is equally vital. Impairments in this process can compromise oxygen uptake and carbon dioxide elimination, leading to hypoxemia and hypercapnia [2,4,12,16-18].

The long-term consequences of COVID-19 on central hemodynamics and external respiration are still being unraveled. There is growing concern that patients who have recovered from the acute phase of the infection may continue to experience cardiovascular and respiratory complications, a condition often referred to as "post-COVID-19 syndrome" or "long COVID." These complications can manifest as persistent symptoms such as dyspnea, chest pain, and fatigue, which can significantly impact the quality of life and increase the risk of long-term morbidity [3-7,12,19].

COVID-19 primarily affects the respiratory system, targeting the lungs and airways. The virus enters host cells

* Corresponding author:
therapy.ssmu@gmail.com (Nazarov F. Y.)
Received: Mar. 22, 2024; Accepted: Apr. 7, 2024; Published: Apr. 11, 2024
Published online at http://journal.sapub.org/ajmms

via the angiotensin-converting enzyme 2 (ACE2) receptor, which is highly expressed in the respiratory tract. This viral entry can lead to a range of respiratory complications, including pneumonia, acute respiratory distress syndrome (ARDS), and respiratory failure [10-14].

The pathophysiology of COVID-19 respiratory involvement involves a cascade of events, starting with viral replication in respiratory epithelial cells, leading to an inflammatory response characterized by cytokine release (cytokine storm), immune cell infiltration, and tissue damage. This inflammatory cascade can result in alveolar damage, impaired gas exchange, and respiratory dysfunction [4-9].

Clinical manifestations of COVID-19 respiratory involvement vary widely, from mild symptoms such as cough and shortness of breath to severe respiratory distress requiring mechanical ventilation. The severity of respiratory complications often correlates with patient age, comorbidities, and immune response [13-17].

A critical aspect of COVID-19 pathology is the cytokine response triggered by the viral infection. Cytokines are small proteins released by cells, particularly immune cells, that play a crucial role in cell signaling and the regulation of immune responses. In the context of COVID-19, the virus-induced activation of the immune system can lead to an excessive release of cytokines, a phenomenon known as a "cytokine storm." [12,17,19]

The cytokine storm is characterized by elevated levels of various cytokines, including interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF-α), and others. This hyperactive immune response can contribute to the severity of the disease by causing widespread inflammation, tissue damage, and multi-organ dysfunction [12,15,17].

In this context, our study aims to evaluate the indicators of central hemodynamics and external respiration in patients who have recovered from community-acquired coronavirus pneumonia. By examining these parameters, we seek to understand the extent of residual cardiovascular and respiratory dysfunction in this population and to identify potential risk factors associated with adverse outcomes. Such insights are crucial for guiding the clinical management of post-COVID-19 patients and for developing targeted rehabilitation strategies to mitigate the long-term effects of the disease.

2. Materials and Methods

This observational study was conducted at the Cardiology Department of the Samarkand State Medical University, Uzbekistan, from 2020 to 2021. The study aimed to evaluate the central hemodynamics and external respiration parameters in patients who had recovered from community-acquired coronavirus pneumonia (CCP).

A total of 102 patients aged between 40 and 55 years, who were diagnosed with CCP and had undergone treatment and examination at the Cardiology Department, were included in the study. The inclusion criteria were as follows: age between 40 and 55 years, diagnosis of community-acquired coronavirus pneumonia. Patients with a history of chronic cardiovascular or respiratory diseases were excluded from the study.

Clinical data, including demographic information, medical history, and physical examination findings, were collected using standardized forms. Laboratory investigations comprised a complete blood count, biochemical analysis, and assessment of hormone levels (testosterone, cortisol, estradiol, prolactin) and pro-inflammatory cytokines (IL-6 and IL-8) in serum. Instrumental methods included spirometry for evaluating external respiration and transthoracic echocardiography (TTE) along with Doppler imaging for assessing central hemodynamics.

Central hemodynamics were evaluated using TTE and Doppler imaging, focusing on parameters such as cardiac output, ejection fraction, and blood flow velocities. External respiration was assessed through spirometry, measuring parameters such as forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio.

Data were analyzed using descriptive statistics, including means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Comparative analyses were performed using t-tests for continuous variables and chi-square tests for categorical variables. A p-value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS software (version 26.0).

The study protocol was approved by the Institutional Review Board of the Samarkand State Medical University. All participants provided informed consent before enrollment in the study. The study was conducted in accordance with the Declaration of Helsinki and ethical guidelines for human research.

To ensure the accuracy and reliability of the data, all measurements were performed by trained and experienced medical personnel. The equipment used for clinical and laboratory measurements was regularly calibrated and maintained according to the manufacturer's guidelines.

3. Results

The analysis of the anamnestic data revealed that 88 (86.3%) patients with community-acquired pneumonia (CCP) had no preceding pathologies. Chronic bronchitis was the FEF common pathology among the patients in the main group, reported in the history of 5.9% of the patients, with no signs of recurrence in the last 2 years. Additionally, three patients (2.9%) had chronic pyelonephritis prior to hospitalization for CCP, also without significant signs of the disease in the last 2 years.

Significant changes were observed in the peripheral blood indicators of the main group patients. Upon admission, patients who had undergone CCP exhibited a significant increase in the levels of leukocytes (14.3±6.4 $\times 10^9$/L), neutrophils (10.3±5.1$\times 10^9$/L), lymphocytopenia

(1.01±0.4 $\times 10^9$/L), and a slight decrease in platelet count (204.4±75.9 $\times 10^9$/L). The mean blood glucose level was significantly higher in patients who had undergone CCP (7.6±1.8 mmol/L). Additionally, the average indicators of creatinine (131±26.4 μmol/L), urea (8.6±3.7 mmol/L), and lactate dehydrogenase (667.1±162.5 U/L) significantly exceeded the normal values in the main group patients.

The analysis of the inflammation marker C-reactive protein (CRP) showed that in patients who had undergone CCP, this indicator significantly exceeded the values of healthy individuals (140.3±98.7 mg/L compared to 3.5±12.3 mg/L). The main group patients also exhibited an increase in the cardiac injury marker troponin-I (0.36±0.47 ng/L), an increase in the average value of the fibrin fragment molecule - D-dimer (3.1±1.1 mg/L), and fibrinogen (588.3± 161.7 mg/dL).

Table 1. Prevalence of comorbidities

	Main group n =102 n (%)	Comparison group n =42 n (%)	Control group n =92 n (%)
Without pathologies	88 (86.3%)	13(30.9%)*	79 (85.9%)
Bronchitis	6 (5.9%)	17(18.5%)*	7 (7.6%)
Pyelonephritis	3 (2.9%)	12(28.6%)*	1 (1.1%)
Stomach ulcer	3 (2.9%)	5(11.9%)	0 (0.0%)
Chronic gastritis	1 (0.98%)	6(14.3%)	0 (0.0%)
Diabetes mellitus	0 (0.0%)	15(35.7%)	0 (0.0%)

Table 2. Echocardiographic characteristics of patients survived CCP

Options	Main group n =102 (M ± m)/ n (%)	Comparison group n =42 (M ± m)/ n (%)	Control group n =92 (M ± m)/n (%)	p-value
LVEF (%)	55.2 ± 9.1	65.8 ± 7.2	67.4 ± 6.4	p1=0.26 p2<0.01
LVEF <50%, n (%)	16 (15.7%)	1(2.4%)	0 (0.0%)	NA NA
LVEDV, ml	132.1±37.2	83.1 ± 17.5	78.9±21.2	p1<0.01 p2<0.01
LVESV, ml	57.4±13.6	36.7 ± 9.4	32.0 ± 8.2	p1<0.01 p2<0.01
LAVI, ml/m2	44.8±7.6	24.8 ± 7.1	22.6± 6.3	p1<0.01 p2<0.01
LAVI >34 ml/m2, n (%)	24 (23.5%)	2(4.8%)	0 (0.0%)	NA NA
LV hypertrophy, n (%)	29 (28.4%)	6(14.3%)	16 (17.4%)	p1<0.01 p2<0.01
TAPSE, mm	19.1±4.6	23.6 ± 2.3	23.3±3.8	p1<0.01 p2<0.01
RV dysfunction, n (%)	48 (47.1%)	2(4.8%)	1 (1.1%)	p1<0.01 p2<0.01
Dilatation of the pancreas, n (%)	46 (45.1%)	5(11.9%)	3 (3.2%)	p1<0.01 p2<0.01
E/A ratio	0.7±0.41	0.95 ±0.35	0.98±0.44	p1=0.62 p2=0.72
Septal e ', cm/s	6.6±1.8	8.8 ±1.7	9.1±1.9	p1=0.55 p2=0.67
Lateral e ', cm/s	9.4±3.6	10.6 ± 3.1	10.8±3.0	p1=0.10 p2=0.14
C septal-lateral ratio E/e	9.3±4.7	7.2 ±1.8	7.3±1.5	p1=0.22 p2=0.24
Aortic stenosis > 1, n (%)	3 (2.9%)	0 (0.0%)	0 (0.0%)	NA NA

LVEF - left ventricular ejection fraction. LV - left ventricle. LVEDV - LV end-diastolic volume. LAVI - left atrial volume index, TAPSE - tricuspid valve annulus systolic excursion. RV - right ventricle.

Echocardiographic studies were conducted for all patients in the main and control groups. The echocardiography parameters at rest in the main group patients indicated moderate heart function impairments. The mean left ventricular ejection fraction (LVEF) value was slightly reduced (55.2±9.1%) compared to the control group. Left ventricular dysfunction (LVEF<50%) was registered in 16 (15.7%) patients of the main group. The end-diastolic volume of the left ventricle (LVEDV) in patients who had undergone CCP was significantly larger than that in the comparison and control groups (132.1±37.2 compared to 83.1±17.5 and 78.9±21.2, respectively). Hypertrophy of the left ventricle was established in 87 (85.3%) patients of the main group compared to 6 (14.3%) in the comparison group and 6 (17.4%) in the control group (table 2).

Spirometry was performed without complications in all patients of the study groups. A comparative assessment of the respiratory system indicators in patients after CCP, the comparison group, and the control group revealed statistically significant changes in the respiratory system parameters of patients who had undergone CCP and non-viral etiology pneumonia compared to the indicators of healthy individuals. The forced vital capacity (FVC) in the main group and the comparison group was 87.12±13.1% and 89.8±12.2%, respectively, which significantly differed from the indicator of healthy individuals - 98.7±4.9% (p<0.001).

The analysis of cortisol, testosterone, prolactin, and estradiol levels in the blood of patients who had undergone CCP at admission and after therapy showed hormonal imbalances compared to the control group. In particular, in the main group, there was an increase in the levels of cortisol, prolactin, estradiol, and a decrease in testosterone in both men and women.

The study of cytokines IL-6 and IL-8 in predicting the effectiveness of recovery after CCP revealed significant changes. Upon admission, the mean level of interleukin-6 (IL-6) in the main group was 29.4±19.3 pg/mL, which was three times higher than the average indicators of the comparison group (8.9±4.5 pg/mL, p<0.001) and five times higher than the average level of IL-6 in healthy individuals in the control group (6.9±2.1 pg/mL, p<0.001). More than 70% of the patients in the main group (n=72) had pathologically high levels of IL-6 in the serum. Similarly, the average level of interleukin-8 (IL-8) in the main group was 32.5±8.7 pg/mL, which was 1.75 times higher than in the comparison group and 2.5 times higher than the average level of IL-8 in healthy individuals of the control group (13.2±3.4 pg/mL, p<0.001).

Table 3. Comparative results of spirometry in patients survived CCP

	Main group n =102 (M ± m)/ n (%)	Comparison group n =42 (M ± m)/ n (%)	Control group n =92 (M ± m) / n (%)	p-value
FVC%	87.12 ± 13.1	8 6.4 ± 1 4.7	98.7 ± 4.9	p1>0.05 p2<0.001
FVC <80%, n (%)	12 (11.8%)	7(16.7%)	0 (0%)	p1>0.05 p2=NA
FEV_1%	83.2 ± 13.7	81.9 ± 9.6	97.2 ± 5.1	p1>0.05 p2<0.05
FEV_1 <80%, n (%)	15(14.7)	6(14.3%)	2 (2.2%)	p1>0.05 p2<0.05
FEV_1 / FVC%	76.2± 6.44	7 9.2 ± 6.44	84.2 ± 4.1	p1>0.05 p2<0.01
FEV_1 / FVC <70%, n (%)	19(18.6%)	7(16.7%)	0(0%)	p1>0.05 p2=NA
$FEF_{25\%}$	93.4±7.1	9 1.8 ± 8.4	100.4±4.3	p1>0.05 p2<0.01
FEF_{25} <65%, n (%)	12(11.8%)	7(16.7%)	0(0%)	p1>0.05 p2=NA
$FEF_{50\%}$	93.13±15.3	9 1.0 ± 8.6	105.6±8.1	p1>0.05 p2<0.05
FEF_{50} <65%, n (%)	13(12.7%)	5(11.9%)	0(0%)	p1>0.05 p2=NA
$FEF_{75\%}$	89.8 ±12.2	8 8.6 ± 9.5	102.8±7.3	p1>0.05 p2<0.01
FEF_{75} <65%, n (%)	7 (6.9%)	1(2.4%)	2 (2.2%)	p1>0.05 p2>0.05

Further analysis revealed that patients with higher levels of IL-6 (>7 pg/mL) exhibited more severe systemic inflammation and cardiac injury, as indicated by higher levels of CRP, troponin-I, D-dimer, and fibrinogen compared to those with lower levels of IL-6 (<7 pg/mL). The echocardiographic findings also showed a significant association between higher IL-6 levels and impaired cardiac function, particularly left ventricular ejection fraction (LVEF), with a greater prevalence of left ventricular dysfunction in patients with IL-6 levels above 7 pg/mL.

Pulmonary Function:

In terms of pulmonary function, patients with higher IL-6 levels showed significantly reduced diffusing capacity for carbon monoxide (DLCO), indicating impaired gas exchange efficiency in the lungs. This was consistent with the overall trend of reduced respiratory function parameters like FVC and forced expiratory volume in one second (FEV1) among CCP survivors, compared to the healthy control group (table 3).

The results underscore the persistent impact of CCP on both cardiovascular and pulmonary systems, with significant alterations in hemodynamic parameters, increased levels of inflammatory and cardiac injury biomarkers, and compromised respiratory function. The findings highlight the necessity for ongoing monitoring and tailored management strategies for patients recovering from CCP to address these long-term health consequences.

4. Conclusions

Our study reveals significant clinical and laboratory alterations in patients recovering from community-acquired coronavirus pneumonia (CCP). The majority of these patients had no preceding pathologies, with chronic bronchitis being the most commonly reported condition. Laboratory findings showed elevated levels of leukocytes, neutrophils, and markers of inflammation and cardiac injury, such as C-reactive protein and troponin-I. Echocardiographic evaluations indicate moderate impairments in heart function among CCP survivors, with a substantial proportion of patients exhibiting left ventricular hypertrophy and dysfunction. This underscores the potential long-term cardiovascular effects of CCP.

Spirometry results demonstrate reduced forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) in patients post-CCP, indicating persistent respiratory impairment. These findings highlight the need for continued respiratory assessment and rehabilitation in these individuals. Our analysis suggests a hormonal imbalance in CCP survivors, characterized by elevated levels of cortisol and prolactin and reduced testosterone levels, which may have implications for long-term health and recovery.

Elevated levels of interleukins IL-6 and IL-8 in CCP survivors point to a sustained inflammatory response, which may contribute to the ongoing symptoms and complications observed in these patients. The results of this study underscore the importance of comprehensive post-recovery care for patients who have survived CCP. Healthcare providers should be vigilant for cardiovascular and respiratory complications and consider hormonal and inflammatory markers in the long-term management of these individuals. Further studies are needed to elucidate the mechanisms underlying the persistent effects of CCP on cardiovascular and respiratory systems and to develop targeted interventions to address these long-term consequences.

Table 4. Comparative results of the analysis of hormonal parameters of patients survived CCP

		Norm	Main group n =102 (M ± m)	Comparison group n =42 (M ± m)/ n (%)	Control group n =92 (M ± m)	p-value
Cortisol (nmol/l)	F	200-700	652.4±128.2	431.7 ± 97.8	2 7 8.5±46.3	p1<0.001 p2<0.001
	M	200-700	6 16.8 ±1 02.5	318 ± 77.1	19 8.8 ± 37.0	p1<0.001 p2<0.001
Testosterone (nmol/l)	F	<4.0	1.1±0.21	1.9 ± 0.21	2.4±0.40	p2<0.001 p2<0.001
	M	8.3- 30.2	6.16 ±1.2	16.1 ± 3.1	17.2 ± 4.2	p<0.001 p2<0.001
Prolactin , (µg/l)	F	1.1-13.0	15.3 ± 4.1	8.8 ± 2.8	6.3 ±1.1	p<0.001 p2<0.001
	M	1.0-9.2	11.6 ± 3.8	6.9 ± 2.1	4.7 ±1.2	p<0.001 p2<0.001
Estradiol (pg/ml)	F	7 2 -24 6	76.4 ±9. 8	88.7 ±9. 5	106 ±11.3	p<0.001 p2<0.001
	M	0 -56	41.2 ±7.2	32.8 ± 6.4	28.5 ±5. 8	p<0.01 p2<0.001

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