JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pendemic

Correlation of the severity of the clinical presentation of SARS-CoV-2 pneumonia with respiratory function parameters in the post-COVID period

Slobodan Belic[1,2 #], Andjelka Ivanovic[1], Aleksandra Todorovic[1], Nikola Maric[1], Sandra Milic[3], Jovan Perić[4], Mihailo Stjepanović[1,2], Snjezana Krajisnik[1], Ivana Milosevic[2,5], Jelena Jankovic[1,2 #]

[1] *Clinic for Pulmonology, University Clinical Center of Serbia, Belgrade, Serbia*
[2] *Faculty of Medicine, University of Belgrade, Belgrade, Serbia*
[3] *Klinik Güssing, Güssing, Austria*
[4] *Center for Anesthesiology and Resuscitation, University Clinical Center of Serbia, Belgrade, Serbia*
[5] *Clinic for Infectious and Tropical Diseases, University Clinical Center of Serbia, Belgrade, Serbia*

# Authors contributed equally to this work.

Abstract

Introduction: Since COVID-19 first surfaced in 2019, it has seriously threatened public health. The most prevalent symptoms are respiratory ones. This study aimed to present the correlation between the severity of the clinical presentation of the disease and the results of respiratory function tests conducted within 6 months after hospital discharge.

Methodology: This retrospective study included 99 patients with confirmed SARS-CoV-2 virus infection. Of all patients 24.2% had accentuated bronchovascular pattern, 9.1% had unilateral, and 29.3% had bilateral pneumonia. In comparison, 35.4% patients had diffuse changes, which were described as acute respiratory distress syndrome (ARDS) on computed tomography (CT).

Results: Patients with unilateral, bilateral pneumonia or diffuse lung damage had significantly lower forced vital capacity (FVC) values. They were treated with non-invasive mechanical ventilation (NIV) or invasive mechanical ventilation (MV) and had lower FVC values (0.039). A negative, weak correlation existed between CT findings during the infection and Diffusing capacity for carbon monoxide (DLCO) measured after the infection (0.003). A negative, weak correlation was found between oxygen therapy, the use of NIV, and MV findings during the infection with DLCO. A negative correlation was noted between leukocyte values during the infection and forced expiratory volume in the first second (FEV1) and FVC after the infection.

Conclusions: Patients with COVID-19 infection who need oxygen support and MV continue to suffer from loss of respiratory function after the resolution of COVID-19 infection. These findings highlight the negative predictive value of pulmonary tests in the long-term follow-up for the development of PC-ILD as well as decreased pulmonary capacity.

Key words: Post-covid; lung function test; DLCO; SARS-COV2; pneumonia.

J Infect Dev Ctries 2024; 18(9):1347-1352. doi:10.3855/jidc.19471

(Received 29 October 2023 – Accepted 15 December 2023)

Introduction

COVID-19 is an acute systemic infectious disease caused by the SARS-CoV-2 coronavirus. [1]. The disease, first described in December 2019 in Wuhan, China, has led to a global pandemic that continues to persist. This disease has significant consequences on global mortality, as well as socio-economic repercussions [2]. The presentation of the disease varies from asymptomatic or mild symptoms to severe clinical forms with a fatal outcome [3]. In approximately 80% of cases, the virus leads to symptoms of the upper respiratory tract, resulting in a mild form that can be managed with symptomatic therapy. In the remaining 20% of cases, a significantly more severe form of the disease occurs, leading to a systemic inflammatory response with a cytokine storm, followed by fibrosis [4]. Over 15% of hospitalized patients with COVID-19 infection develop acute respiratory distress syndrome (ARDS) [5]. In addition to epidemiological data, clinical characteristics, and laboratory findings, radiological diagnostics plays an invaluable role in early recognition, triage, and prognostic assessment. These methods can also be used in the evaluation of therapy and the monitoring of COVID-19 patients [6]. Among the imaging methods for visualizing structural changes, the literature describes the sensitivity of MSCT (multi-slice computed tomography) in screening for SARS-CoV-2 as high as 98% [7].

Lung parenchymal damage during COVID-19 infection in clinical studies correlates with a reduction in lung function several months after acute infection. Evidence regarding lung function tests post-discharge in COVID-19-treated patients is described in retrospective studies with small sample sizes. In patients with a severe clinical presentation, there is a reduction in forced vital capacity (FVC), diffusing capacity for carbon monoxide (DLCO), total lung capacity (TLC), six-minute walk test, and impaired respiratory muscle strength, thus respiratory rehabilitation [8,9]. Numerous studies have shown that lung function parameters partially improved in post-discharge lung function tests. However, a certain degree of restrictive alterations persisted [8]. In comparison to patients who did not have a severe clinical presentation, patients with severe forms of the disease showed a higher frequency of deviations in DLCO values, a decrease in TLC, as well as a reduction in the distance covered in the 6-minute walk test [10]. All of these factors have a consequential impact on the quality of life of these patients and their daily activities.

Long COVID or post-COVID is a disorder characterized by the persistence of COVID-19 symptoms after 3 months of infection and affects millions of people globally. The most common long-lasting symptoms are dyspnea, chest pain, fatigue, tachycardia, “brain fog”, anxiety, and depression [11]. The most supported theory is an autoimmune process. “Post-COVID-19 Interstitial Lung Disease” (PC-ILD) is a disorder characterized by fibrotic-like signs at chest CT-scan associated with pulmonary function test abnormalities [12]. We need more clinical trials to evaluate the efficacy of treatment for long-term COVID and sequelae.

This study aimed to evaluate the long-term consequences of severe COVID patients by comparing respiratory function test results with the severity of clinical presentation or need for applying oxygen\MV support.

Methodology

Clinical Methodology

This retrospective study was conducted at the Clinic for Pulmonology of the University Clinical Center of Serbia during the year 2021. The study included 99 patients with previously confirmed SARS-CoV-2 virus infection. Sociodemographic information, clinical characteristics (need for oxygen therapy, NIMV or MV), chest imaging methods, and laboratory analyses (complete blood count, D-dimer, lactate dehydrogenase, C-reactive protein, ferritin) were obtained from the patients' medical history. After recovery, during follow-up outpatient visits in the 6 months following the infection, lung function tests were conducted. Lung function parameters were measured through spirometry and the diffusion capacity for carbon monoxide (CO) in accordance with the guidelines of the American Thoracic Society/European Respiratory Society ATS/ERS) (13). Spirometry measurements included forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and their ratio FEV1/FVC. Lung diffusion capacity (DLCO) and the coefficient of diffusion (KCO) were measured using a lung carbon monoxide transfer factor measurement apparatus. (Master Screen Diff) [13,14].

Statistical Methodology

This study used both descriptive and analytical statistical methods. Descriptive statistics were calculated for basic demographic and clinical characteristics. Normal distribution was tested using graphical and mathematical methods. Continuous variables were presented as mean with standard deviation or median and percentiles, depending on the data distribution. Nominal data were presented as absolute and relative numbers. To compare statistically significant differences between the study groups, the χ^2 test (or Fisher's test) for nominal data was used. The significance level was set at 0.05. Statistical analysis was performed using the IBM SPSS software package 21. (Chicago).

Results

The average age of the patients was 60.0 ± 12.4 years, with the youngest patient being 31 years old and the oldest 83 years old. Approximately two-thirds of the patients were male (58.6%). Only two patients had no radiographic structural changes on the chest CT scan. Of all patients-24 (24.2%) had accentuated bronchovascular patterns, 9 (9.1%) had unilateral, and 29 patients (29.3%) had bilateral pneumonia, while 35 (35.4%) patients had diffuse changes, which were described as ARDS on CT scan.

Three-quarters of the patients were on oxygen therapy, with half using an oxygen mask, 16 using a high-flow nasal cannula (HFNC), 9 on NIV, and one patient was intubated and on MV. Two-thirds of the patients had white blood cell counts within the reference range, 12% had decreased values, and 19% had elevated values. One-third of the patients had lymphocyte counts within the reference range, while decreased values were observed in two-thirds of the patients. CRP values were elevated in 96% of the

patients. More than 80% of the patients had elevated Lactate dehydrogenase (LDH) values. Ferritin was elevated in two-thirds of the patients. D-dimer was elevated in three-quarters of the patients Up to 6 months after the infection, the lung function of the patients was analyzed, and the results are shown in Table 1. The FVC of 17 patients and the FEV1 value of 16 patients were below the LLN values.

The correlation between FVC after a COVID-19 infection and the clinical presentation during the COVID-19 infection was examined, and the results are shown in Table 2. A negative, weak correlation existed between CT findings during the infection and FVC measured after the infection. Patients with unilateral or bilateral pneumonia or diffuse lung damage had significantly lower FVC values. A negative, weak, statistically significant correlation was observed between oxygen therapy during the infection and FVC measured after the infection. Patients who used NIV or MV had lower FVC values. A negative correlation was noted between leukocyte values during the infection and FVC after the infection. Patients with higher leukocyte values had significantly lower FVC values. There was no statistically significant association between lymphocyte values and CRP during the infection with FVC values after the infection. A weak, negative correlation existed between LDH and ferritin during the infection with FVC after the infection. Patients with higher LDH and ferritin values had significantly lower FVC values. D-dimer was not significantly associated with FVC.

The correlation between FEV1 after a COVID-19 infection and the clinical presentation during the COVID-19 infection was examined, and the results are shown in Table 2. A negative, weak correlation existed between CT findings during the infection and FEV1 measured after the infection. Patients with unilateral or bilateral pneumonia or diffuse lung damage had significantly lower FEV1 values. There was no significant association between FEV1 and oxygen therapy. A negative correlation was noted between leukocyte values during the infection and FEV1 after the infection. Patients with higher leukocyte values had significantly lower FEV1 values. There was no statistically significant association between lymphocyte values, CRP, LDH, ferritin, or D-dimer during the infection with FEV1 values after the infection.

Table 1. Distribution of patients based on lung function parameters.

	n (%)
FVC	
Restriction	17 (17.2)
Normal Value	82 (82.8)
FEV1	
Obstruction	16 (16.2)
Normal Value	83 (83.8)
DLCOc	
Impaired Diffusion	75 (75.8)
Normal Value	24 (24.2)
KCOc	
Impaired Diffusion	53 (53.5)
Normal Value	46 (46.5)

The correlation between DLCOc after a COVID-19 infection and the clinical presentation during the COVID-19 infection was examined, and the results are shown in Table 2. A negative, weak correlation existed between CT findings during the infection and DLCOc measured after the infection. Patients with unilateral or bilateral pneumonia or diffuse lung damage had significantly lower DLCOc values. A negative, weak correlation was found between oxygen therapy, the use of NIV, and MV findings during the infection with DLCOc measured after the infection. There was no statistically significant association between leukocyte, lymphocyte, CRP, LDH, ferritin, or D-dimer values during the infection with DLCOc values after the infection.

The correlation between KCOc after a COVID-19 infection and the clinical presentation during the COVID-19 infection was examined, and the results are shown in Table 2. There was no significant association between CT findings and oxygen therapy during the COVID infection with KCOc measured after the infection. There was no statistically significant association between leukocyte, lymphocyte, CRP,

Table 2. Association of FVC, FEV1, DLCOc and KCOc after COVID infection with the clinical presentation during the COVID infection.

	FVC		FEV1		DLCOc		KCOc	
	r	p	r	p	r	p	r	p
CT	-.295**	0.003	-.219*	0.03	-.293**	0.003	-0.124	0.22
O_2	-.223*	0.026	-0.144	0.154	-.235*	0.019	-0.116	0.251
NIMV/MV	-.209*	0.039			-.203*	0.024		
Leukocytes	-.205*	0.042	-.248*	0.013	-0.165	0.104	0.047	0.644
#Lymphocytes	-0.01	0.923	0.053	0.601	0.026	0.802	0.115	0.257
CRP	-0.117	0.25	-0.154	0.127	0.009	0.926	0.091	0.372
LDH	-.202*	0.045	-0.189	0.061	-0.18	0.074	-0.06	0.558
Ferritin	-.227*	0.024	-0.171	0.09	-0.183	0.069	-0.01	0.918
D Dimer	-0.149	0.142	-0.182	0.071	-0.16	0.114	-0.035	0.732

LDH, ferritin, or D-dimer values during the infection with KCOc values after the infection.

Discussion

In the early months of the pandemic, scientific literature focused on studying the transmission mechanisms, virus detection tests, diverse clinical presentation, and the search for suitable therapeutic options. It soon became clear that attention needed to be paid to the long-term consequences of this disease in the post-COVID period. The first studies, which included the monitoring of patients after discharge following treatment for the infection and conducted lung function tests at various time intervals, emerged a few months after the start of the pandemic. This had an impact on the treatment approach and the use of pulmonary rehabilitation. In this study we have shown respiratory dysfunction in COVID-19 patients after up to 6 months of discharge from the clinic.

About two-thirds of the patients in our study group were male. These data are in line with findings in the global literature [15]. Male individuals are more frequently affected compared to females, with a gender ratio ranging from 1.6 to 1 up to 2.8 to 1 in favor of males. Various social and behavioral factors (alcohol consumption, smoking history, profession) as well as comorbidities could explain the worse outcomes in males compared to females globally [16]. The most common comorbidities in our study group were cardiovascular, respiratory, or endocrinological conditions. At least one comorbidity was present in 87% of the patients, which is expected given the average age of the patients (78% of patients were older than 50 years).

Three-quarters of our patients were on oxygen therapy (via mask or HF) regardless of the extent of structural changes, with only nine requiring NIV, and one patient was on mechanical ventilation. Our results confirm that high oxygen flow rates via a mask or HFNC, as well as the use of the prone position, reduce the need for intubation and the use of NIV. Tascon *et al.* compared the effects of HF oxygen therapy via nasal cannula with conventional oxygen therapy via a mask in terms of the need for endotracheal intubation and the duration of clinical recovery in patients with severe COVID-19. In their conclusion, the authors stated that the use of HF oxygen therapy in patients with a severe clinical presentation significantly reduced the need for mechanical ventilation and had a favorable impact on the duration of clinical recovery for patients [17]. These findings align with the data from our study.

A negative, weak, statistically significant correlation existed between oxygen therapy (mask or HFNC) during the infection and FVC measured after the infection. Patients who used NIV or mechanical ventilation had significantly lower FVC values. These results are correlated with CT findings of extensive structural changes, diffuse or bilateral, as well as elevated leukocyte values. Leukocytosis was associated with a more severe clinical presentation and CT findings of diffuse and bilateral changes, likely resulting in impairment of the subjects' vital capacity. The persistence of fibrotic changes after a COVID infection could explain the lower FVC values [18]. Recovery from pneumonia takes around 3–6 months in patients with severe COVID-19 pneumonia [19,20]. So, if we want to detect the structural damage or functional abnormalities caused by COVID-19, the 6-month period after the recoveries is best. Lower FVC values, or restriction, can be a consequence of the development of fibrous tissue during the healing process. Low values of FEV1 (in patients with obstructive ventilation disorder or mixed disorder with a predominance of obstruction) can be a consequence of bronchial mucosa inflammation due to the virus or the appearance of traction bronchiectasis. The development of restrictive lung disease and reduced diffusion capacity during the post-COVID period is due to fibrosis [18]. However, we still cannot provide a comprehensive assessment of the mechanisms behind persistent sequelae [21]. In COVID infection, lung injuries such as edema, bronchial inflammation and cytokines, and abnormal surfactant function, can cause deterioration in gas diffusion due to prolonged MV, and these changes may decrease the functional capacity [22]. The study by Afsin *et al.*, conducted 12 weeks after a COVID infection, demonstrated that patients with a severe form of bilateral pneumonia who required mechanical ventilation had significantly lower values of FEV1, FVC, and DLCO [23]. Our data are in line with the literature, as a negative correlation has been demonstrated between CT findings during the infection and FVC, FEV1, and DLCOc measured after the infection. Patients with unilateral, bilateral pneumonia, or diffuse lung damage had significantly lower DLCOc values. Sirayder *et al.* concluded that respiratory function, functional capacity, quality of life, and fatigue in patients with severe COVID-19 infection were impaired even 6 months after discharge from the intensive care unit, which can be explained by fibrosis during the recovery process from acute infection [19]. We did not find a correlation between mechanical ventilation (invasive) and the development of post-

COVID abnormalities, probably because of the small number of patients treated with such respiratory support.

Vascular inflammation and coagulation disorders can be seen in older patients with comorbidities [24]. This is why we investigated the correlation of D-dimer with lung function tests, and we did not find a statistically significant association between this marker and lung function parameters [25]. Ferritin was elevated in two-thirds of the patients, and we only found a statistical association with lower FVC values. It is believed that hyperferritinemia, caused by excessive inflammation in the context of infection, is associated with admission to intensive care units and high mortality, allowing the identification of high-risk patients. These are the patients who had severe forms of COVID pneumonia, bilateral changes or ARDS, and consequently had restrictions during the follow-up period [26].

Biomarkers such as CRP and lactate dehydrogenase (LDH) values are associated with inflammation and inflammation-associated cellular lung damage [27]. An important finding in our study was that LDH as strong inflammatory marker, was associated with FVC, but not with FEV1, DLCO, or KCO. LDH indicated that inflammation in the lung affects respiratory capacity.

Our study has some limitations. First, only one center was included. Second, lack of baseline pulmonary tests and findings of chest CT scans performed before COVID-19 pneumonia. Third, a small number of patients were on mechanical ventilation.

Conclusions

In an ongoing epidemic, early identification of patients at risk of serious consequences after contracting COVID-19 is of great importance. The data from our study indicate the need for careful monitoring of lung function tests in patients treated for COVID-19 infection, to plan respiratory rehabilitation, introduce timely therapy, and organize healthcare systems effectively. Our results showed that patients with COVID-19 infection who need oxygen support and MV continue to suffer from loss of respiratory function after the resolution of COVID-19 infection. These findings highlight the negative predictive value of pulmonary tests in the long-term follow-up for the development of post COVID-ILD and decreased pulmonary capacity.

References

1. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses (2020) The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 5: 536-544. doi: 10.1038/s41564-020-0695-z.
2. WHO (2023) Coronavirus COVID-19 Global Cases. Available: https://data.who.int/dashboards/covid19/cases?n=c Accessed: 20 March 2020.
3. Center for Disease Control and Prevention (2019) Symptoms of COVID-19. Available from: https://www.cdc.gov/covid/signs-symptoms/?CDC_AAref_Val=https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html Accessed: 26 June 2024.
4. Wu Z, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 323: 1239-1242. doi: 10.1001/jama.2020.2648. PMID: 32091533.
5. Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, Aaron JG, Claassen J, Rabbani LE, Hastie J, Hochman BR, Salazar-Schicchi J, Yip NH, Brodie D, O'Donnell MR (2020) Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet 395: 1763-1770. doi: 10.1016/S0140-6736(20)31189-2.
6. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A (2020) Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 215: 87-93. doi: 10.2214/AJR.20.23034.
7. Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, Ji W (2020) Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology 296: E115-E117. doi: 10.1148/radiol.2020200432.
8. Fumagalli A, Misuraca C, Bianchi A, Borsa N, Limonta S, Maggiolini S, Bonardi DR, Corsonello A, Di Rosa M, Soraci L, Lattanzio F, Colombo D (2021) Pulmonary function in patients surviving to COVID-19 pneumonia. Infection 49: 153-157. doi: 10.1007/s15010-020-01474-9.
9. Zhao YM, Shang YM, Song WB, Li QQ, Xie H, Xu QF, Jia JL, Li LM, Mao HL, Zhou XM, Luo H, Gao YF, Xu AG (2020) Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. EClinicalMedicine 25: 100463. doi: 10.1016/j.eclinm.2020.100463.
10. Huang Y, Tan C, Wu J, Chen M, Wang Z, Luo L, Zhou X, Liu X, Huang X, Yuan S, Chen C, Gao F, Huang J, Shan H, Liu J (2020) Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. Respir Res 21: 163. doi: 10.1186/s12931-020-01429-6.
11. Raman B, Bluemke DA, Lüscher TF, Neubauer S (2022) Long COVID: post-acute sequelae of COVID-19 with a cardiovascular focus. Eur Heart J 43:1157-1172. doi: 10.1093/eurheartj/ehac031.
12. Sanna A, Pellegrino D, Messina E, Siena LM, Baccolini V, D'Antoni L, Landini N, Baiocchi P, Villari P, Catalano C, Panebianco V, Palange P (2023) The role of pulmonary function testing and lung imaging in the long-term follow-up of patients with COVID-19 pneumonia. Respiration 102: 287-295. doi: 10.1159/000529441.

13. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, Kaminsky DA, McCarthy K, McCormack MC, Oropez CE, Rosenfeld M, Stanojevic S, Swanney MP, Thompson BR (2019) Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement. Am J Respir Crit Care Med 200: e70-e88. doi: 10.1164/rccm.201908-1590ST.
14. Graham BL, Brusasco V, Burgos F, Cooper BG, Jensen R, Kendrick A, MacIntyre NR, Thompson BR, Wanger J (2017) ERS/ATS standards for single-breath carbon monoxide uptake in the lung. Eur Respir J 49: 1600016. doi: 10.1183/13993003.00016-2016.
15. Taslem Mourosi J, Anwar S, Hosen MJ (2022) The sex and gender dimensions of COVID-19: A narrative review of the potential underlying factors. Infect Genet Evol 103: 105338. doi: 10.1016/j.meegid.2022.105338.
16. Budimir Mršić D, Perković-Tabak L, Ćavar M, Luetić A, Petričević M, Dolić K (2021) Pulmonary embolism associated with COVID-19 occurs in predominantly elderly patients with comorbidities: a single center retrospective study. Gerontol Geriatr Med 7: 23337214211017398. doi: 10.1177/23337214211017398.
17. Ospina-Tascón GA, Calderón-Tapia LE, García AF, Zarama V, Gómez-Álvarez F, Álvarez-Saa T, Pardo-Otálvaro S, Bautista-Rincón DF, Vargas MP, Aldana-Díaz JL, Marulanda Á, Gutiérrez A, Varón J, Gómez M, Ochoa ME, Escobar E, Umaña M, Díez J, Tobón GJ, Albornoz LL, Celemín Flórez CA, Ruiz GO, Cáceres EL, Reyes LF, Damiani LP, Cavalcanti AB, HiFLo-Covid Investigators (2021)) Effect of high-flow oxygen therapy vs conventional oxygen therapy on invasive mechanical ventilation and clinical recovery in patients with severe COVID-19: a randomized clinical trial. JAMA 326: 2161-2171. doi: 10.1001/jama.2021.20714.
18. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, Kang L, Guo L, Liu M, Zhou X, Luo J, Huang Z, Tu S, Zhao Y, Chen L, Xu D, Li Y, Li C, Peng L, Li Y, Xie W, Cui D, Shang L, Fan G, Xu J, Wang G, Wang Y, Zhong J, Wang C, Wang J, Zhang D, Cao B (2023) 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 401: e21-e33. doi: 10.1016/S0140-6736(23)00810-3.
19. Sirayder U, Inal-Ince D, Kepenek-Varol B, Acik C (2022) Long-term characteristics of severe COVID-19: respiratory function, functional capacity, and quality of life. Int J Environ Res Public Health 19: 6304. doi: 10.3390/ijerph19106304.
20. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, Li Y, Cao Y, Gu J, Wu H, Shi H (2021) Six-month follow-up chest CT findings after severe COVID-19 pneumonia. Radiology 299: E177-E186. doi: 10.1148/radiol.2021203153.
21. Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, Vilaró J (2021) Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. Pulmonology 27: 328-337. doi: 10.1016/j.pulmoe.2020.10.013.
22. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, Liu S, Zhao P, Liu H, Zhu L, Tai Y, Bai C, Gao T, Song J, Xia P, Dong J, Zhao J, Wang FS (2020) Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 8: 420-422. doi: 10.1016/S2213-2600(20)30076-X.
23. Afsin DE, Kerget B (2022) Evaluation of the relationship between CRP/albumin ratio and pulmonary function parameters in patients with post-acute COVID-19. Clin Lab 68. doi: 10.7754/Clin.Lab.2021.211102.
24. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z, Chen X, Chen S, Yu K, Huang Z, Hu B (2020) D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care 8:49. doi: 10.1186/s40560-020-00466-z.
25. Kernan KF, Carcillo JA (2017) Hyperferritinemia and inflammation. Int Immunol 29: 401-409. doi: 10.1093/intimm/dxx031.
26. Carcillo JA, Sward K, Halstead ES, Telford R, Jimenez-Bacardi A, Shakoory B, Simon D, Hall M, Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network Investigators (2017) A systemic inflammation mortality risk assessment contingency table for severe sepsis. Pediatr Crit Care Med 18: 143-150. doi: 10.1097/PCC.0000000000001029.
27. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G (2020) Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med 58:1021-1028. doi: 10.1515/cclm-2020-0369.

Corresponding author

Jelena Jankovic MD
Head of Emergency department, Clinic for Pulmonology, University Clinical Center of Serbia
Belgrade
Adress Koste Todorovic 26, 11000 Belgrade, Serbia
Tel: +381641772448
E mail: jjelena1984@gmail.com

Conflict of interests: No conflict of interests is declared.