

Original Article

Asian Pacific Journal of Tropical Medicine

doi: 10.4103/1995–7645.356993

Impact Factor: 3.041

A cross-sectional study of post-COVID syndrome at a tertiary care center in Turkey

Efraim Guzel¹✉, Oya Baydar Toprak¹, Burak Mete², Yasemin Saygıdeger¹, Bengü Curuk¹, Sedat Kuleci¹¹Cukurova University, Faculty of Medicine, Department of Chest Diseases, Adana, Turkey²Cukurova University, Faculty of Medicine, Department of Public Health, Adana, Turkey

ABSTRACT

Objective: To investigate long-term symptoms after acute COVID-19, the link between symptoms and respiratory function, radiological changes in the post-COVID period, and risk factors for post-COVID syndrome.

Methods: In this cross-sectional study, 123 participants who were admitted within the first 3 months were categorized as group 1, and those who applied after 3 months were categorized as group 2. According to thoracic imaging and pulmonary function tests, patients were split into 3 groups as mild, moderate and severe.

Results: At least one symptom was present in 91.9% and 61.8% in acute and post-COVID period, respectively. Pulmonary function tests were normal in 60 (70.6%) in the first three months, and 30 (78.9%) in 91-days to 1-year period after acute COVID-19 infection. After 3 months, 22.4% of chest X-rays and 7.9% of computerized tomography revealed progression. Patients who developed acute complications (*OR* 9.91, 95% *CI* 1.93-50.87), had 2 or more symptoms at admission (*OR* 7.73, 95% *CI* 2.56-23.33), had 1% to 14% CT involvement (*OR* 3.05, 95% *CI* 1.06-8.79), or had 50% or more CT involvement (*OR* 14.68, 95% *CI* 1.24-172.55) had a higher risk of developing post-COVID syndrome.

Conclusions: COVID-19 symptoms can last for long time. Severity of symptoms, acute complications, and the extent of radiological involvement may all contribute to elevated risk of post-COVID syndrome. As a result, patients with COVID-19 should be checked for long-term clinical difficulties on regular basis.

KEYWORDS: Post-COVID syndrome; COVID-19; Symptoms; Pulmonary function tests; Risk factors

1. Introduction

As the COVID-19 pandemic enters its third year, the World Health Organization reported that more than 610 million individuals have been infected with the virus, with more than 6.5 million deaths[1]. COVID-19 is typically asymptomatic or advances with modest illness symptoms in the acute stage, but it may potentially evolve to severe forms which can lead almost to death in a group of patients. Furthermore, survivors have been seen to have persisting symptoms of various organs and systems which can linger for weeks or months[2]. Post-COVID Syndrome (PCS) has been defined as signs and symptoms that develop during or after an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by an alternative diagnosis; it usually presents with

Significance

It is still unclear how severely SARS-CoV-2 affects certain organs and systems, what symptoms remain in the post-COVID period, and what additional variables are at play. This study shows that COVID-19 symptoms can last frequently for a long time, and risk may rise due to symptom load, acute complications, and significant radiological involvement. Clinical issues that have persisted after COVID-19 should be monitored carefully.

✉To whom correspondence may be addressed. E-mail: efraimguzel@gmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

©2022 Asian Pacific Journal of Tropical Medicine Produced by Wolters Kluwer-Medknow.

How to cite this article: Guzel E, Toprak OB, Mete B, Saygıdeger Y, Curuk B, Kuleci S. A cross-sectional study of post-COVID syndrome at a tertiary care center in Turkey. Asian Pac J Trop Med 2022; 15(9): 410-417.

Article history: Received 6 July 2022

Revision 22 September 2022

Accepted 25 September 2022

Available online 30 September 2022

clusters of symptoms, often overlapping, which can fluctuate and change over time and can affect any system in the body; PCS might be considered before 12 weeks while the possibility of an alternative underlying disease is also being assessed[3].

Dyspnea is known to be the most often reported respiratory symptom after COVID-19. The frequency of persistent dyspnea varied from 5%-81% in hospitalized patients and 14% in non-hospitalized patients, according to studies reporting respiratory symptoms after 1 to 12 months following COVID-19[4-11]. Cough is less prevalent, although it can last for weeks or months after SARS-CoV-2 infection and has been observed in a wide range (2%-42%) of patients[5,7-9,12]. While numerous researches have effectively documented the symptoms of the post-COVID period, data on the incidence of these symptoms is reported in a wide range. Uncertainties regarding when the respiratory dysfunction may develop in which patients, when the resulting impairment will improve, or the predisposing factors of this dysfunction still continue. The goal of this study was to determine the long-term symptoms that may arise as a result of the COVID-19, to assess the relationship between these symptoms and pulmonary functions, and to identify the risk factors for post-COVID symptoms in patients who had an acute COVID-19 either at home or in the hospital at least four weeks after recovery.

2. Subjects and methods

2.1. Ethical approval and participants consent statement

This is a cross-sectional study that was approved by the local institutional ethics committee of Cukurova University, Adana, Turkey (approval No. 117/2021). An informed consent statement was required to be assigned by the participants. All procedures performed in the study involving human participants were in accordance with the ethical standards of the hospital, national research committee and the 1964 Helsinki declaration.

2.2. Study design and participants

This cross-sectional study was conducted at Cukurova University Faculty of Medicine Balcali Hospital, Department of Chest Diseases between December 2020 and May 2021. A total of 123 individuals who had COVID-19 and followed-up either at home or in the hospital participated the study at least after four weeks of acute infection. The patients were separated into two groups:

Group 1: the participants in long-COVID first three months;

Group 2: the participants in post-COVID period after three months to 1 year of acute infection.

The severity of COVID-19 disease has been assessed in the literature using several parameters[4,13]. This study categorized the diseases severity as:

Mild disease: less than 25% uptake on thorax computed tomography (CT) and outpatients;

Moderate disease: 25%-49% CT involvement or hospitalized or with low flow oxygen support and not admitted to the intensive care unit;

Severe disease: more than 50% CT involvement or high flow oxygen support or treatment in the intensive care unit.

2.3. Variables and measurement

The data collection forms were used to record sociodemographic characteristics, previous history of post-COVID symptoms, momentary history and physical examination signs, previous and novel laboratory and radiographic findings, medical therapies employed during the acute infection and in post-COVID period. Extensive biochemical tests including routine complete blood count, C-reactive protein, procalcitonin, ferritin, liver and kidney function tests were documented. According to the Charlson Comorbidity Risk Index, the participant's comorbidities were classified as "0 points low, 1-2 points moderate, 3-4 points high, and 5 points and above very high risk"[14].

Thorax CT/high resolution computed tomography was performed in all patients in the radiological evaluation. Major CT images have been described in international standard terminology defined by the Fleischner Society dictionary and in the peer-reviewed literature on viral pneumonia using terms such as ground glass opacity, crazy pavement pattern, and consolidation[5,16]. A semi-quantitative scoring system was used to quantitatively predict the pulmonary involvement of all these abnormalities based on the area of interest[17]. Lung involvements were evaluated over 6 lobes by considering the lingula as a separate lobe and 0=no involvement, 1=1%-24% involvement, 2=25%-49% involvement, 3=50%-75% involvement and 4 \geq 75% involvement classified[17]. Image analysis was evaluated by expert radiologists in our institution using the institutional digital database system (HBYS Mergentech PACS, version v3.22.03.1-20220314).

Pulmonary function tests (PFTs) were performed in accordance with the American Thoracic Society (ATS) guideline with a calibrated Sensor Medics V-Max 20 Spirometer (Jaeger MS-PFT Analyzer Unit, Viasys Healthcare GmbH, Höchberg, Germany). Basal forced expiratory volume 1 second (FEV₁) and forced vital capacity (FVC) measurements were made according to the ATS guideline. Total lung capacity was measured with helium dilution technique (Jaeger MS-PFT Analyser Unit) and Transfer Factor for Carbon Monoxide was measured with a single breath method. It is measured by a single breath technique where 10% helium and 0.3% carbon monoxide are rapidly inspired, held for 10 seconds

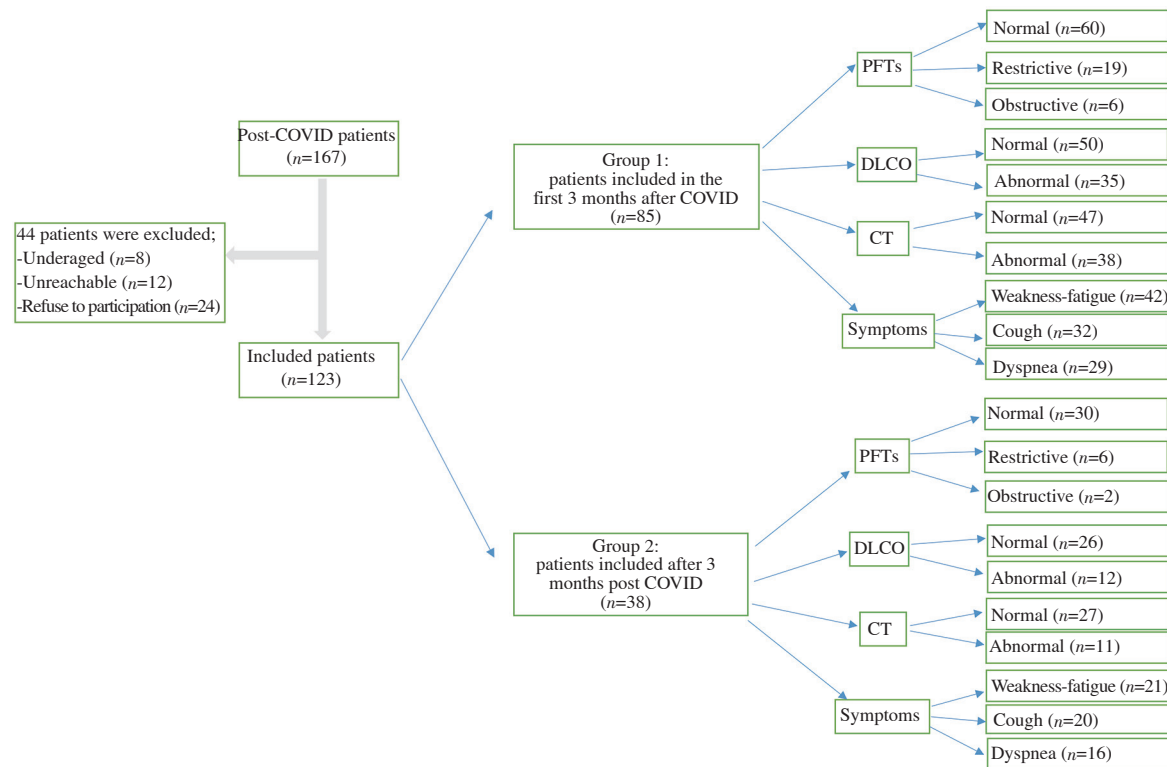


Figure 1. Registration and follow-up of post-COVID patients in the first three months and after three months.

and then expired with the measurement of the remaining carbon monoxide[18]. Test results are presented as percentage of predicted values. The results of pulmonary function tests are interpreted based upon the ATS/ European Respiratory Society recommendations[19].

The experimental model of our study, in which we show the PFTs, symptoms and radiological features of 2 groups who applied to the outpatient clinic early and late in the post-COVID period, in a single picture, is explained in detail in Figure 1.

2.4. Outcomes

Primary outcome:

- To determine the incidence of post-COVID syndrome and post-COVID pulmonary symptom frequencies;
- To identify the risk factors in post-COVID syndrome.

Secondary outcomes:

- To clearly document the incidence and characteristics of radiologic and pulmonary functional abnormalities in both the first three months and after three months of acute infection;
- To identify the long-term radiologic sequela of COVID-19.

2.5. Data analysis

SPSS22 program was used in the analysis of the data. Kolmogorov Smirnov test was used as the normal distribution test. *T* test, Mann Whitney *U* test, One Way ANOVA test, Kruskal Wallis test, *Chi*-square test were used in the analysis. Binary logistic regression test, Cox regression test were used in the analysis. A value of $P < 0.05$ was considered statistically significant.

3. Results

The mean age of 123 participants in the post-COVID period was (54.8 ± 13.8) years (range: 21-84). The mean time of admission to the outpatient clinic was (75.4 ± 46.1) days (range: 24-330). A total of 85 (69.1%) patients admitted to outpatient clinic visit in the first three months after acute infection. There was at least one additional disease in 54 (63.5%) of our patients admitted within the first 3 months after acute COVID-19 (group 1) and in 30 (78.9%) of the patients admitted after the 3rd month (group 2). The most common comorbidities observed in group 1 patients were hypertension (29.4%), chronic lung diseases (21.2%), diabetes mellitus (DM) (15.3%) and cardiovascular diseases (15.3%). The most common comorbidities in group 2 patients were chronic lung diseases (34.2%), hypertension (23.7%), DM (18.4%) and neuropsychiatric diseases (18.4%), respectively. At least one symptom was present in 91.9% ($n=110$) of the patients during the acute disease and 61.8% ($n=76$) in the post-COVID period. The most common symptoms were weakness-fatigue ($n=63$, 51.2%), loss of taste/smell ($n=25$, 20.3%), myalgia ($n=24$, 19.5%), others ($n=22$, 17.9%) whereas the most common respiratory symptoms were cough ($n=52$, 42.3%), dyspnea ($n=45$, 36.6%) and chest pain ($n=5$, 4.1%) consequently. At least one symptom was present in 78 (91.8%) of our group 1 patients and 35 (92.1%) of our group 2 patients. The most common symptoms observed in both group 1 and group 2 patients were fatigue-fatigue, cough and dyspnea, respectively. Comorbidities and

symptoms by groups are listed in Table 2. DM ($n=2$), HT ($n=1$), respiratory failure ($n=2$), pulmonary embolism ($n=1$), organized pneumonia ($n=2$), pulmonary nodule ($n=1$), and neuropsychiatric disease ($n=1$) were among the new diagnosed diseases after COVID-19. Thirty-five (28.5%) of the participants used systemic corticosteroid (1 mg/kg/day methyl prednisolone) during the acute illness. The detailed data of sociodemographic characteristics and symptom distribution of the participants are given in Table 1.

Table 1. Sociodemographic and clinical characteristics.

Variables	n (%)
Sex	
Female	69 (56.1)
Male	54 (43.9)
Age (years)	
21-45	27 (22.0)
46-64	67 (54.5)
≥65	29 (23.6)
Body mass index	
<30	75 (61.0)
≥30	48 (39.0)
The severity of acute infection	
Mild	66 (53.7)
Moderate	39 (31.7)
Severe	18 (14.6)
Total	123 (100.0)

Of the 123 participants in the study, 25 (20.3%) had restrictive, 8 (6.5%) had obstructive type of respiratory dysfunction, and 47 (38.2%) had a decrease in the diffusing capacity of the lung for carbon monoxide (DLCO). In the first three months, PFTs were normal in 60 (70.6%), restrictive in 19 (22.4%) and obstructive in 6 (7.1%) of the participants. In the 91 days to one-year period, PFTs were normal in 30 (78.9%), restrictive in 6 (15.8%) and obstructive in 2 (5.3%) of the participants. The FEV₁(L) and DLCO (%) in the first three months after acute infection were found to be statistically significantly lower ($P=0.027$ and $P=0.025$, respectively) than later periods. When the PFTs in post-COVID era were examined according to the severity of the acute illness, it was discovered that there was a statistically significant difference between the post-COVID period FVC (% pred), FVC (L), and FEV₁/FVC values; in the post-COVID period, severe patients had lower FVC (% pred) and FVC (L) compared to mild and moderate patients, while FEV₁/FVC was higher (Table 3).

The radiologic features were normal in 42.4% and 55.3% of Chest X-Ray and computerized tomography respectively in the first three months. After three months, 22.4% of chest X-rays and 7.9% of computerized tomography revealed progression. Of

Table 2. Comorbidities and symptoms by time of admission to the outpatient clinic.

Comorbidities/symptoms	Group 1 (in the first three months, $n=85$)		Group 2 (>90 days, $n=38$)		P
	(+) (%)	(-) (%)	(+) (%)	(-) (%)	
At least one comorbidities	54 (63.5)	31 (36.5)	30 (78.9)	8 (21.1)	0.066
Diabetes mellitus	13 (15.3)	72 (84.7)	7 (18.4)	31 (81.6)	0.424
Hypertension	25 (29.4)	60 (70.6)	9 (23.7)	29 (76.3)	0.335
Cardiovascular diseases	13 (15.3)	72 (84.7)	3 (7.9)	35 (92.1)	0.204
Chronic lung diseases	18 (21.2)	67 (78.8)	13 (34.2)	25 (65.8)	0.096
Malignant diseases	7 (8.2)	78 (91.8)	5 (13.2)	33 (86.8)	0.293
Neuropsychiatric diseases	6 (7.1)	79 (92.9)	7 (18.4)	31 (81.6)	0.061
Chronic kidney disease	5 (5.9)	80 (94.1)	1 (2.6)	37 (97.4)	0.396
At least one symptom	78 (91.8)	7 (8.2)	35 (92.1)	3 (7.9)	0.628
Dyspnea	29 (34.1)	56 (65.9)	16 (42.1)	22 (57.9)	0.258
Cough	32 (37.6)	53 (62.4)	20 (52.6)	18 (47.4)	0.088
Weakness-fatigue	42 (49.4)	43 (50.6)	21 (55.3)	17 (44.7)	0.343
Loss of taste/smell	14 (16.5)	71 (83.5)	11 (28.9)	27 (71.1)	0.091
Myalgia	15 (17.6)	70 (82.4)	10 (26.3)	28 (73.3)	0.193
Others	17 (20.0)	68 (80.0)	5 (13.2)	33 (86.8)	0.259

Table 3. Pulmonary function tests according to admission time and disease severity (%).

Tests	Outpatient clinics visit			Severity of acute COVID-19			P
	In the first three months ($n=85$)	>90 days ($n=38$)	P	Mild ($n=66$)	Moderate ($n=39$)	Severe ($n=18$)	
FEV ₁ L	2.43±0.86	2.75±0.82	0.027*	2.62±0.84	2.48±0.89	2.29±0.82	0.256
FEV ₁	93.01±22.48	97.98±19.24	0.120	97.00±20.95	94.48±18.86	85.69±27.58	0.144
FVCL	3.03±1.08	3.28±0.90	0.116	3.29±1.02	3.01±1.01	2.64±0.98	0.046*
FVC	94.91±23.42	99.57±20.18	0.145	101.61±20.78	94.96±19.09	80.06±27.76	0.001*
FEV ₁ /FVC	80.77±8.29	82.57±6.93	0.115	79.65±7.95	80.99±6.45	88.21±7.29	<0.001*
DLCO	78.89±13.34	83.22±11.51	0.025*	81.65±12.01	80.76±10.02	73.72±19.12	0.180

Data are expressed as mean±SD. * $P<0.05$. FEV₁: Post-bronchodilator forced expiratory volume in one second; FVC: Forced vital capacity; DLCO: Transfer factor of the lung for carbon monoxide.

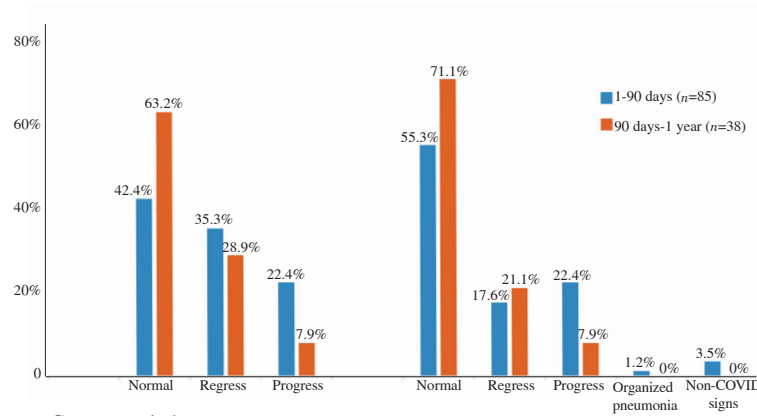


Figure 2. Radiologic features in post-COVID period.

Table 4. Logistic regression analysis for post-COVID symptoms.

Variables	B	P	OR	95% CI
Age (<i>vs.</i> 21-45 years)				
46-64	0.636	0.316	1.88	0.54-6.56
≥65	0.380	0.632	1.46	0.30-6.91
Sex (<i>vs.</i> female)	-0.098	0.863	0.90	0.29-2.76
Outpatient visit (<i>vs.</i> the first trimester)	0.840	0.146	2.31	0.74-7.18
Symptoms (<i>vs.</i> symptom count>2)	2.046	<0.001*	7.73	2.56-23.33
Systemic steroid in acute infection (<i>vs.</i> none)	-0.568	0.438	0.56	0.13-2.37
Severity of acute infection (<i>vs.</i> mild)				
Moderate	-0.713	0.417	0.49	0.08-2.73
Severe	0.014	0.990	1.01	0.11-8.77
Acute complications (<i>vs.</i> none)	2.294	0.006*	9.91	1.93-50.87
Oxygen supply requirement in acute infection (<i>vs.</i> none)	-0.077	0.924	0.92	0.19-4.50
CT signs in acute infection (<i>vs.</i> no involvement, %)				
1%-49%	1.118	0.038*	3.05	1.06-8.79
>50%	2.687	0.033*	14.68	1.24-172.55
PFT (<i>vs.</i> normal)				
Restrictive	-0.522	0.493	0.59	0.13-2.64
Obstructive	-1.151	0.261	0.31	0.04-2.35
DLCO (<i>vs.</i> normal)	0.451	0.466	1.57	0.46-5.28
Charlson comorbidity index	-0.115	0.761	0.89	0.42-1.86
Constant	0.872	0.187	2.39	

* $P < 0.05$.

the patients in group 1 with progression observed in thoracic CT, ground glass opacity was detected in 8 (9.4%), consolidation in 6 (7.1%), fibrosis in 5 (5.9%) and organized pneumonia in 1 (1.2%). Mosaic attenuation was observed in 2 patients (2.3%) in whom non-COVID-19 findings were detected, and cavitation was observed in 1 (1.2%). Fibrosis was detected in 3 (7.9%) patients in group 2 with progression on thorax CT. The detailed data about radiologic features is presented in Figure 2.

The model developed to predict post-COVID syndrome is significant (Omnibus test $P < 0.001$), with an accuracy rate of 80.5 percent and a Nagelkerke R square value of 45%. Patients who developed acute complications (severe pneumonia, acute respiratory distress syndrome, irregularity of blood sugar level due to the use of corticosteroids, etc.) (OR 9.91, 95% CI 1.93-50.87), had 2 or more symptoms at the time of admission (OR 7.73, 95% CI 2.56-23.33), had 1% to 14% CT involvement (OR 3.05, 95% CI 1.06-8.79), or

had 50% or more CT involvement (OR 14.68, 95% CI 1.24-172.55) had a higher risk of developing post-COVID syndrome, among the variables included in the model (Table 4).

4. Discussion

The study revealed that nearly 90% of patients during the acute illness and 60% during post-COVID period had at least one symptom according to their own notifications. The most common symptoms were fatigue/weakness, cough and dyspnea. Pulmonary function tests were significantly deteriorated in patients with chronic airway diseases, systemic steroid need in acute illness, and moderate-severe illness in acute infection phase. Those who had two or more symptoms at the time of their first hospital admission, as well as those who experienced complications such as severe pneumonia, acute respiratory distress syndrome, or blood sugar

dysregulation during the acute illness phase, were shown to have a higher risk of PCS. Furthermore, patients with 1%-49% CT involvement at the time of admission had a 3 times higher chance of PCS, while those with 50% or more had a 14.6 times higher risk.

In a meta-analysis with 14-118 days of follow-up, the most common symptoms were fatigue (58%), headache (44%), attention deficit (27%), hair loss (25%), and shortness of breath (24%)[20]. A cohort study conducted from January to May 2020 with a mean follow-up of 186 days found that fatigue, muscle weakness (63%), sleep difficulties (26%) and anxiety or depression (23%) were the most common disorders[21]. In a multicenter study of patients in the first wave of the pandemic in Spain, participants were evaluated an average of seven months after hospital discharge, and only 18.6% found that they were completely free of any post-COVID symptoms, and the most common symptoms were fatigue (60.8%), hair loss (26.3%) and shortness of breath (23.5%)[22]. At the end of a one-year follow-up of the same group, the prevalence of cough, chest pain, dyspnea, and fatigue were 2.5%, 6.5%, 23.3%, and 61.2%, respectively[23]. The reported disparity in long-term COVID symptom prevalence rates can be explained by the different methodologies used, as greater prevalence with active inquiry than with passive inquiry. As is typically noted in the literature, the frequency of symptoms continues to decrease as the duration of post-COVID follow-up is prolonged. The overall symptom frequency in our findings was consistent with the literature, but unlike many other studies, the frequency of cough and dyspnea were higher than selected studies. This was thought to be due to the inclusion of both inpatients and outpatients in the study, and thus patients of different severity.

A few limited studies evaluating respiratory function in MERS-CoV and SARS-CoV-1 pandemics reported deterioration in exercise capacity and DLCO in SARS-CoV-1 survivors with a follow-up period of 6 months to 15 years, suggesting that there may be damage to the intra-alveolar diffusion pathway[24-26]. According to a two-year follow-up research, 52% of SARS-CoV-1 survivors exhibited chronic impaired diffusion function and reduced exercise capacity[27]. In another multicenter study, which included 145 patients who recovered from acute COVID-19 infection, and systematically evaluated cardiopulmonary injury by following the 60th and 100th day; decreased static and/or dynamic lung volumes or impaired lung functions reflected by impaired DLCO were found in 42% and 36% of cases, respectively[28]. One hundred days after being diagnosed with COVID-19, 22% of patients had decreased FVC and/or FEV₁, 11% had decreased TLC, and 21% of all patients had impaired DLCO[28]. In our study, compatible with literature, as predicted, FEV₁ and DLCO improved after three months compared to the first three months. In a review including seven studies evaluating the respiratory functions of post-COVID patients, diffusion capacity deterioration, restrictive pattern and obstructive pattern were 39%, 15% and 7%, respectively[29] and our results

were coherent.

The decrease in diffusion capacity, which is directly related to the severity of the acute disease, is the most frequently reported physiological disorder after acute COVID-19[5,21,30]. It has been observed that other respiratory function test parameters may also be impaired in the post-COVID period in those who have had a severe or severe acute disease process[21,31,32]. In another retrospective study examining hospitalized COVID-19 cases, a very high prevalence of diffusion capacity deterioration (66%) was detected especially in those with severe disease who were more likely to develop pulmonary fibrosis, and those with high levels of inflammatory markers such as C-reactive protein and interleukin-6 [33]. In our study, we found a significant decrease in FVC and an increase in FEV₁/FVC in the post-COVID-19 period, in line with the literature, especially in severe COVID-19 patients. This was thought to be due to the preservation of FEV₁ values despite the significant decrease in FVC values as a result of widespread lung involvement and sequelae in severe COVID-19 patients.

In a review of the post-acute COVID-19 syndrome, those who were severely ill during acute COVID-19 and/or required intensive unit care, the elderly, those with multiple organ comorbidities and/or active cancer, those after transplantation, and those with a high symptom burden during acute infection phase were more susceptible to the development of PCS[32]. In a prospective and longitudinal study, it was reported that male sex, advanced age, presence of multiple symptoms, diarrhea, anosmia, and baseline IgG titers between 1.2 and 4 may be risk factors for a PCS after 7 months[11]. In another study, it was reported that the risk of developing PCS is high in people with advanced age, obesity and a history of pulmonary disease[34]. Patients with more than two symptoms at the time of admission, those with acute complications, and those with CT involvement all had a higher risk of PCS, according to our research. To the best of our knowledge, this is the first data indicating the increased risk according to the involvement in radiological examination at the time of acute infection.

In a thorough 6-month follow-up analysis, around 50% of the 353 patients who had lung computed tomography had at least one abnormality; the most frequent were ground-glass opacities and irregular lines, and 1% had thickening of the interlobular septum[35]. Risk factors for the development of interstitial lung disease, such as ICU follow-up, invasive MV support, and bacterial superinfections, have been observed in a study looking at post-COVID pulmonary sequelae[36]. Regardless of the underlying cause, 70% of acute respiratory distress syndrome patients who recover have abnormal imaging results at 6 months, and in some situations, they may also develop sequelae such fibrosis and pulmonary hypertension[37]. Some authors asserted that after a three-month follow-up, a higher incidence of fibrosis was connected to prior coronavirus-related epidemic illnesses, such as the Middle East respiratory syndrome and the severe acute respiratory syndrome, in 33% and 38% of

patients, respectively[38]. Our results were also consistent with the literature. Approximately 45% of patients in the early post-COVID period had at least 1 abnormality on thoracic CT. While the most common abnormality was ground glass opacity, we found the rate of post-COVID fibrosis to be 5.9% in group 1 patients and 7.9% in group 2 patients.

This was a single-center, cross-sectional study with lack of active surveillance so the conclusions do not represent the entire population. There is a requirement for data verification in trials with a high number of participants, and prospective periodical follow-up.

SARS-CoV-2 infects a wide variety of tissues and has multi-organ and multi-system effects. Long-COVID, on the other hand, has no recognized genesis or biological foundation. Meanwhile, the prevalence, type, and related factors of such post-acute symptoms remain unclear. Long-COVID's burden must be quantified at the population level in order to assess its impact on the healthcare system and allocate resources properly. In addition, it would not be correct to completely associate the symptoms and clinical findings after acute COVID-19 with PCS. These cases should definitely be evaluated in multidisciplinary councils established on this subject and all other causes should be excluded. Long-term symptoms must be contextualized, and risk factors must be definitively identified in order to enhance the management of such cases.

Conflict of interest statement

The authors declare that they have no potential conflict of interest including any financial, personal or other relationships with other people or organizations that could inappropriately influence or be perceived to influence the presented work.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

EG, OBT, BM, SK have made significant contributions to the working concept and design. EG, OBT, YS, BC, SK contributed to the data's collection, analysis, and interpretation. EG, OBT, BM, YS, BC, SK have written the piece or significantly edited it, accepted the submitted version, and agreed to be held personally liable for their contributions. They have also promised to ensure that any concerns regarding the truthfulness or integrity of any portion of the work are resolved. All authors read and approved the final version of the manuscript.

References

- [1] World Health Organization. *Coronavirus disease (COVID-19) pandemic*. [Online]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. [Accessed on 21 September 2022].
- [2] Centers for Disease Control and Prevention. *Long COVID or post-COVID conditions*. [Online]. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html>. [Accessed on 24 May 2022].
- [3] National Institute for Health and Care Excellence. *COVID-19 rapid guideline: Managing the longterm effects of COVID-19*. [Online]. Available from: <https://www.nice.org.uk/guidance/ng188/resources/covid19-rapid-guideline-managing-the-longterm-effects-of-covid19-pdf-51035515742>. [Accessed on 24 May 2022].
- [4] Wu X, Liu X, Zhou Y, Yu H, Li R, Zhan Q, et al. 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: A prospective study. *Lancet Respir Med* 2021; **9**(7): 747-754.
- [5] Zhao YM, Shang YM, Song WB, Li QQ, Xie H, Xu QF, et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine* 2020; **25**: 100463.
- [6] De Lorenzo R, Conte C, Lanzani C, Benedetti F, Roveri L, Mazza MG, et al. Residual clinical damage after COVID-19: A retrospective and prospective observational cohort study. *PLoS One* 2020; **15**: e0239570.
- [7] Jacobs LG, Gourna PE, Lesky-Di BD, Nyirenda T, Friedman T, Gupta A, et al. Persistence of symptoms and quality of life at 35 days after hospitalization for COVID-19 infection. *PLoS One* 2020; **15**: e0243882.
- [8] Ghosn J, Piroth L, Epaulard O, Le Turnier P, Mentré F, Bachelet D, et al. Persistent COVID-19 symptoms are highly prevalent 6 months after hospitalization: Results from a large prospective cohort. *Clin Microbiol Infect* 2021; **27**: 1041.e1-1041.e4.
- [9] Morin L, Savale L, Pham T, Colle R, Figueiredo S, Harrois A, et al. Four-month clinical status of a cohort of patients after hospitalization for COVID-19. *JAMA* 2021; **325**(15): 1525-1534.
- [10] Bellan M, Soddu D, Balbo PE, Baricich A, Zeppego P, Avanzi GC, et al. Respiratory and psychophysical sequelae among patients with COVID-19 four months after hospital discharge. *JAMA Netw Open* 2021; **4**: e2036142.
- [11] Augustin M, Schommers P, Stecher M, Dewald F, Gieselmann L, Gruell H, et al. Post-COVID syndrome in non-hospitalised patients with COVID-19: A longitudinal prospective cohort study. *Lancet Reg Health Eur* 2021; **6**: 100122.
- [12] González J, Benítez ID, Carmona P, Santistevé S, Monge A, Moncusí-Moix A, et al. Pulmonary function and radiologic features in survivors of critical COVID-19: A 3-month prospective cohort. *Chest* 2021; **160**: 187-198.
- [13] Munker D, Veit T, Barton J, Mertsch P, Mümmeler C, Osterman A, et al. Pulmonary function impairment of asymptomatic and persistently

- symptomatic patients 4 months after COVID-19 according to disease severity. *Infection* 2022; **50**(1): 157-168.
- [14]Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis* 1987; **40**(5): 373-383.
- [15]Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. *Radiographics* 2018; **38**(3): 719-739.
- [16]Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: Glossary of terms for thoracic imaging. *Radiology* 2008; **246**(3): 697-722.
- [17]Chang YC, Yu CJ, Chang SC, Galvin JR, Liu HM, Hsiao CH, et al. Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome: Evaluation with thin-section CT. *Radiology* 2005; **236**(3): 1067-1075.
- [18]Ranu H, Wilde M, Madden B. Pulmonary function tests. *Ulster Med J* 2011; **80**(2): 84-90.
- [19]Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, et al. Standardization of spirometry 2019 update. *Am J Respir Crit Care Med* 2019; **200**(8): e70-e88.
- [20]Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo P, Cuapio A, et al. More than 50 long-term effects of COVID-19: A systematic review and meta-analysis. *medRxiv* 2021. doi: 10.1101/2021.01.27.21250617.
- [21]Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: A cohort study. *Lancet* 2021; **397**(10270): 220-232.
- [22]Fernández-de-Las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, Rodríguez-Jiménez J, Palacios-Ceña M, Velasco-Arribas M, et al. Long-term post-COVID symptoms and associated risk factors in previously hospitalized patients: A multicenter study. *J Infect* 2021; **83**(2): 237-279.
- [23]Fernández-de-Las-Peñas C, Guijarro C, Plaza-Canteli S, Hernández-Barrera V, Torres-Macho J. Prevalence of post-COVID-19 cough one year after sars-cov-2 infection: A multicenter study. *Lung* 2021; **199**(3): 249-253.
- [24]Ngai JC, Ko FW, Ng SS, To KW, Tong M, Hui DS. The long-term impact of severe acute respiratory syndrome on pulmonary function, exercise capacity and health status. *Respirology* 2010; **15**(3): 543-550.
- [25]Su MC, Hsieh YT, Wang YH, Lin AS, Chung YH, Lin MC. Exercise capacity and pulmonary function in hospital workers recovered from severe acute respiratory syndrome. *Respiration* 2007; **74**(5): 511-516.
- [26]Liu YX, Ye YP, Zhang P, Chen J, Ye H, He YH, et al. Changes in pulmonary function in SARS patients during the three-year convalescent period. *Zhongguo Wei Zhong Bing Ji Jiu Yi Xue* 2007; **19**(9): 536-538.
- [27]Hui DS, Joynt GM, Wong KT, Gomersall CD, Li TS, Antonio G, et al. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. *Thorax* 2005; **60**(5): 401-409.
- [28]Sonnweber T, Sahanic S, Pizzini A, Luger A, Schwabl C, Sonnweber B, et al. Cardiopulmonary recovery after COVID-19: An observational prospective multicentre trial. *Eur Respir J* 2021; **57**(4): 2003481.
- [29]Torres-Castro R, Vasconcello-Castillo L, Alsina-Restoy X, Solis-Navarro L, Burgos F, Puppo H, et al. Respiratory function in patients post-infection by COVID-19: A systematic review and meta-analysis. *Pulmonology* 2021; **27**(4): 328-337.
- [30]Huang Y, Tan C, Wu J, Chen M, Wang Z, Luo L, et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. *Respir Res* 2020; **21**(1): 163.
- [31]Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. *Nat Med* 2021; **27**(4): 601-615.
- [32]Montani D, Savale L, Noel N, Meyrignac O, Colle R, Gasnier M, et al. Post-acute COVID-19 syndrome. *Eur Respir Rev* 2022; **31**(163): 210185.
- [33]Yu M, Liu Y, Xu D, Zhang R, Lan L, Xu H. Prediction of the development of pulmonary fibrosis using serial thin-section CT and clinical features in patients discharged after treatment for COVID-19 pneumonia. *Korean J Radiol* 2020; **21**: 746-755.
- [34]Halpin S, O'Connor R, Sivan M. Long COVID and chronic COVID syndromes. *J Med Virol* 2021; **93**(3): 1242-1243.
- [35]Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: A cohort study. *Lancet* 2021; **397**(10270): 220-232.
- [36]Esendagli D, Yilmaz A, Akçay Ş, Özlü T. Post-COVID syndrome: Pulmonary complications. *Turk J Med Sci* 2021; **51**(SI-1): 3359-3371.
- [37]Sheard S, Rao P, Devaraj A. Imaging of acute respiratory distress syndrome. *Respir Care* 2012; **57**(4): 607-612.
- [38]Das KM, Lee EY, Singh R, Enani MA, Al Dossari K, Van Gorkom K, et al. Follow-up chest radiographic findings in patients with MERS-CoV after recovery. *Indian J Radiol Imag* 2017; **27**(3): 342-349.

Publisher's note

The Publisher of the *Journal* remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.