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PULMONARY FUNCTION TEST RESULTS AND RADIOLOGICAL FINDINGS 90-120 DAYS AFTER COVID-19 PNEUMONIA: A SINGLE-CENTER RETROSPECTIVE STUDY

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A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Survivors of Coronavirus Disease 2019 (COVID-19) pneumonia may have permanent loss of lung function and radiological sequelae. There is a need for markers that predict patients for whom follow-up is required.

Aim of the study: To identify the risk factors associated with post-COVID-19 radiological and functional findings.

Material and methods: This is a single-center retrospective study performed in a university hospital. We obtained the data from all hospitalized patients with COVID-19 pneumonia. We included those who underwent pulmonary function tests (PFT) and chest computerized tomography (CT) 90-120 days later. We analyzed initial and peak laboratory results (C-reactive protein (CRP), d-dimer, ferritin, and fibrinogen), and the length of hospital and intensive care unit (ICU) stay. We examined the relationship between baseline data and radiological findings and PFT.

Results: Fifty-six patients were included in this study. Of these, 31 (55.4%) were women. The mean age of the patients was 55.05±13.29 years. The mean peak ferritin, fibrinogen, d-dimer, and CRP values recorded during hospitalization follow-up were 285.56±339.82, 518.59±186.93, 1.99±5.69, and 98.94±80.77, respectively. The mean length of hospital and ICU stay were 10.21±8.01 and 8.38±8.90 days, respectively. In 18 (32.1%) patients, we observed a restrictive pattern on PFT, and 22 (39.3%) patients had an abnormal diffusion test. In 21 (37.5%) patients we observed ground glass opacities and in 4 (7.1%) patients reticulation was seen on their chest CT. A multivariate logistic regression analysis revealed that the first visit and peak fibrinogen values were significantly associated with abnormal PFT ($p=0.049$, $R2=0.272$), while ferritin and CRP levels at the first visit and peak levels were significantly associated with an abnormality on chest CT ($p<0.001$, $p=0.05$, respectively).

Conclusions: High initial and peak ferritin, fibrinogen, and CRP levels were associated with persistent radiological findings on chest CT and abnormal PFT at 90–120 days follow-up after COVID-19 pneumonia.

KEYWORDS: COVID-19, pneumonia, pulmonary function test, chest computerized tomography

Background

There is a growing number of patients surviving Coronavirus Disease 2019 (COVID-19) who continue to struggle with symptoms of the disease long after clinically testing negative for the disease. On the other side, there are some patients with no symptoms but that have permanent radiological findings and lung function loss. All these were evaluated under the umbrella called a post-viral syndrome. Our previous experience with acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) suggest that the effects of coronavirus infections can last for many years. We hypothesize that similar changes in radiological findings and pulmonary function tests (PFT) may occur in patients with COVID-19. As expected, the early analysis showed a high rate of abnormal lung function and fibrotic remodeling on computerized tomography (CT), particularly in survivors of severe SARS-CoV-2-associated pneumonia. We also observed some patients with post-COVID-19 syndrome despite having non-severe COVID-19 pneumonia.

Many studies have revealed that the overall quality of life is reduced and functional losses can occur in some patients while other studies showed conflicting results on medium-term recovery [1,2]. The optimal time for obtaining a baseline radiologic test is not clear either. The British Thoracic Society (BTS) guidelines recommend a baseline chest X-ray 3 months after discharge in patients with COVID-19 pneumonia [3]. However, routine follow-up may not be necessary for all survivors of COVID-19 pneumonia. Moreover, evaluation of the radiological and functional status of all patients is not possible. So we need data to provide an accurate estimation of whom, when, and which evaluations should be performed on survivors of COVID-19. We suppose that the detection of markers that predict patients requiring advanced radiological exams and PFT will save time and money.

Aim of the study

This study aims to investigate the risk factors associated with the persistence of abnormalities on chest CT and PFT.

Material and methods

Sample

This is a single-center, retrospective study conducted at a university hospital. Among patients of our outpatient clinic, we investigated the patients who underwent a thoracic CT and PFT between 90 and 120 days after a COVID-19 PCR-positive result (Figure 1). Patients under 18 years of age or who were treated as an outpatient were excluded from the study. Patients without COVID-19 pneumonia were excluded. Patients with respiratory distress, a respiratory rate ≥30 breaths/minute, an oxygen saturation of less than 93% at rest, an arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygenation (FiO_2) ≤300mmHg, or a lesion progression of >50% within 24 to 48 hours on pulmonary imaging were interpreted as patients with severe pneumonia. The patient's age, gender, comorbidities, symptoms, laboratory tests (lactate dehydrogenase (LDH), C-reactive protein (CRP), d-dimer, ferritin, and fibrinogen) at the time of admission and their peak values during follow-up, medications, intensive care unit (ICU) need, oxygen support, noninvasive ventilation (NIV) support, mechanical ventilation (MV) support, and the length of hospital stay was examined.

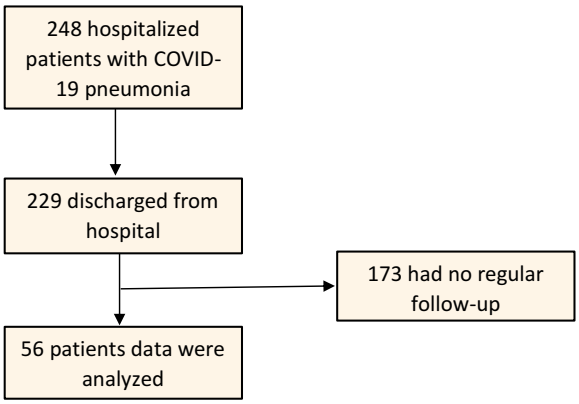

Figure 1. Flowchart of the participants

Pulmonary function tests

All PFT were performed according to the American Thoracic Society (ATS) – European Respiratory Society guidelines [4]. We obtained values for the predicted percent of forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), forced mid-expiratory flow (FEF 25–75%), peak expiratory flow (PEF), and maximal mid-expiratory flow (MMEF). Those below 80% were considered abnormal. Those with a FEV_1/FVC<70% were classified as having an obstructive pattern, while those with a FVC below 80% and a FEV_1/FVC>70% were classified as having a restrictive pattern. Expected values of total lung capacity (TLC), diffusing capacity for carbon monoxide (DLCO), alveolar volume (VA), and DLCO/VA of those who underwent a helium diffusion test were examined. Additionally, desaturation with exertion during a 6-minute walking test was recorded. According to resting fingertip oxygen saturation, a 4%

decrease in SpO_2 during effort or a SpO_2<90 during exertion were interpreted as a desaturation.

Radiological evaluation

The thorax CT scans of the patients included in the study, which were taken simultaneously with PFT, were evaluated by one experienced radiologist. A radiologist evaluated the images for the presence of ground glass opacifications, consolidations, and reticular patterns. CT imaging features were reviewed for the following aspects: presence or absence of lesions, extent, location, distribution of lesions, and the number of involved segments.

Each of the five lung lobes was visually scored (using a semi-quantitative scoring system) based on the involved area from 0 to 4 with a 0 indicating no involvement, a 1 showing<25% involvement, 2 showing 25–49% involvement, 3 showing 50–75% involvement, and 4 having>75% involvement (Literature No). The sum of the individual lobar scores was the total CT scores with a possible range of 0 (minimum) to 25 (maximum). The relationship between radiological findings and PFT was examined.

Ethics

Approval for the study was granted by the Clinical Research Ethics Committee of Akdeniz University Faculty of Medicine (decision no: KAEK-484, dated: 08.07.2020). We also received approval from the Turkish Ministry of Health for the study.

Statistical Analysis

Statistical analyzes were performed using the SPSS (SPSS v.23, IBM, Somers, NY) program and p-values of less than 0.05 were considered statistically significant. The normality of data was determined using Shapiro-Wilk and Kolmogorov-Smirnov tests. For differences and dependencies, categorical data were analyzed using Fisher's Exact Chi-Squared and Yates' Chi-Squared tests while numerical data were analyzed using Independent Samples T-tests. The effects of the parameters on the CT score were analyzed using Univariate or Multivariate Binary Logistic Regression Tests.

Results

Descriptive data

In this study, the radiological and functional results of a total of 56 patients were examined. Of these, 31 (55.4%) were women. The mean age was 55.05±13.29 years, and 17 (34.0%) used to smoke or were still smoking. The mean smoking amount was 19.73±17.65 pack years. The most common comorbidities were diabetes (16 people, 28.6%) and hypertension (16 people, 28.6%). The most common symptom at the time of diagnosis was a cough. The mean peak ferritin, fibrinogen, d-dimer, and CRP values recorded during hospitalization follow-up were 285.56±339.82, 518.59±186.93, 1.99±5.69, and 98.94±80.77, respectively. Twenty (35.7%) patients had severe pneumonia while 36 (64.3%) patients had non-severe pneumonia. In 14 patients (25.0%), steroid treatment was used during the hospitalization. The mean hospitalization length was 10.21±8.01 days. Eight (14.3%) patients needed ICU. The mean length of stay in the ICU was 8.38±8.90 days (Table 1).

Table 1. Patient characteristics

Gender		**n**	**%**
Female		31	55.4
Male		25	44.6
Total		56	
Age (years)			
Mean/Std.Dev.		55.05±13.29	
Smoking		**n**	**%**
Never smoked		33	66.0
Smoking		7	14.0
Ex-smoker		10	20.0
(Packet x Year)			
Mean/Std.Dev.		19.73±17.65	
Comorbidity		**n**	**%**
No comorbidity		28	50.0
Comorbidity		28	50.0
	Diabetes	16	28.6
	Hypertension	16	28.6
Laboratory		**Mean/Std.Dev.**	
Ferritin peak		285.56±339.82	
Fibrinogen peak		518.59±186.93	
D-dimer peak		1.99±5.69	
CRP peak		98.94±80.77	
Clinical		**n**	**%**
Severe pneumonia		20	35.7
Non-severe pneumonia		36	64.3
Hospitalization	Length (Day-Mean/Std.Dev.)	10.21±8.01	
ICU		8	14.3
	Length (Day-Mean/Std.Dev.)	8.38±8.90	
Steroid treatment		14	25.0
	Length (Day-Mean/Std.Dev.)	9.07±5.03	

Values are given in mean and standard deviation or patient count and percentage.

Symptoms, pulmonary function tests, laboratory data, and radiological findings 90 to 120 days after COVID-19 positivity

There were no new symptoms during the 3-month period. The symptoms that were present at the beginning, disappeared in 18 (32.1%) of the patients while symptoms continued in 36 (64.3%) patients. The most common persistent symptoms were dyspnea (19 people, 33.9%) and fatigue (15 people, 26.8%).

Table 2. Clinical, laboratory, pulmonary function test and CT evaluations of the patients

Variations	At beginning	90–120th days
Clinical	**n (%)**	
Symptomatic	**54 (96.4%)**	**36 (64.3%)**
Dyspnea	25 (44.6%)	19 (33.9%)
Cough	37 (66.1%)	7 (12.5%)
Fatigue	27 (48.2%)	15 (26.8%)
Headache	18 (32.1%)	7 (12.5%)
Asymptomatic	2 (3.6%)	20 (37.7%)
Laboratory		
Ferritin ng/ml (Mean/Std.Dev.)	**244.54±304.80**	**70.43±100.86**
150< (n, %)	23 (50.0%)	5 (9.8%)
D-dimer mg/l (Mean/Std.Dev.)	**1.16±3.19**	**0.53±0.46**
0.55< (n, %)	24 (49.0%)	18 (34.0%)
CRP mg/l (Mean/Std.Dev.)	**4.82±5.72**	**0.51±0.84**
0.5< (n, %)	44 (83.0%)	15 (27.8%)
Pulmonary Function Tests	**Mean/Standard Deviation**	
Vital capacity %	**81.65±15.56**	
FEV1 %	**91.92±16.69**	
FVC %	**84.00±15.77**	
FEV1/FVC	**89.59±5.62**	
Obstructive (n, %)	0, %0	
Restrictive (n, %)	18, %32.1	
DLCO %	**78,92±14,65**	
<80% (n, %)	22, %39.3	
CT	**Right Lung**	**Left Lung**
Upper Lobe		
Ground-Glass (n, %)	19 (%48.7)	19 (%48.7)
Reticulation (n, %)	3 (%7.7)	3 (%7.7)
Middle Lob		
Ground-Glass (n, %)	16 (%41.0)	
Reticulation (n, %)	1 (%2.6)	
Lower Lobe		
Ground-Glass (n, %)	21 (%53.8)	20 (%51.3)
Reticulation (n, %)	4 (%10.3)	3 (%7.7)
Total		
Ground-Glass (n, %)	21 (%53.8)	20 (%51.3)
Reticulation (n, %)	4 (%10.3)	3 (%7.7)

Values are given in mean and standard deviation or patient count and percentage.

Ferritin, d-dimer, and CRP values performed at the 3-month follow-up were 70.43±100.86, 0.53±0.46, and 0.51±0.84, respectively. The number of patients who still had higher values was 5 (9.8%), 18 (34.0%), and 15 (27.8%), respectively.

In PFT performed at the 3 months, the mean total vital capacity, FEV_1, FVC, FEV_1/FVC, and DLCO values were 81.65%, 91.92%, 84.00%, 89.59, and 78.92%, respectively. While none of the patients displayed an obstructive pattern of PFT, 18 (32.1%) had a restrictive pattern. Diffusion tests in 22 (39.3%) patients remained low.

The most common pathological finding was ground glass opacities on thorax CT and high-resolution CT (HRCT) images taken at 90-120 days. There were 21 (37.5%) patients with ground glass opacities and 4 (7.1%) with reticulations. The most common radiological abnormalities were in the right lung (52.1%) and lower lobe (35.7%, Table 2).

Univariate/multivariate analysis for abnormal pulmonary function test between 90 and 120 days

The mean FEV_1, FVC, and FEV_1/FVC were 91.92%±16.69, 84.00%±15.77, and 89.59±5.62, respectively. The number of patients with a VC of<80% was 19 (33.9%), with a FEV_1 of<80% was 7 (12.5%), with a FVC of<80% was 18 (32.1%), and with a DLCO of<60% was 3 (5.4%).

A univariate logistic regression analysis revealed that first-visit fibrinogen values had an effect on some of the PFT (VC<80%, FVC<80%, and FEV_1/FVC<80%, p=0.035, R2=0.351). And that aging has an inversely related effect on diffusion capacity (DLCO<60%, p=0.042, R2=0.561).

A multivariate logistic regression analysis revealed that both the first visit and peak fibrinogen values were significantly associated with abnormal PFT (VC<80%, FVC<80%, FEV_1/FVC<80%, p=0.049, R2=0.272).

Univariate/multivariate analysis for CT scores between 90 and 120 days

The mean CT score was 5.11±7.31. While there were no significant differences in patient characteristics and initial symptoms in patients with a CT score equal to or greater than 1 and those with a value of 0. There was a significant difference in BUN, ferritin, fibrinogen, and CRP values at the time of diagnosis. In addition, there was a significant difference in ferritin, fibrinogen, CRP, and LDH peak values, as well as vital capacity, FEV_1, and FVC between patients with a CT score equal to or greater than 1 compared to those

with a 0. While there were no significant differences in hospitalized or ICU-admitted patients with CT scores equal to or greater than 1 and those with a 0. There was a significant difference in steroid treatment (Table 3).

A univariate logistic regression analysis revealed that age (p=0.009, odds ratio 1.101), BUN (p=0.049, odds ratio 1.223), and fibrinogen (p=0.045, odds ratio 1.005) levels during the first visit and ferritin (p=0.026, odds ratio 1.006), D-Dimer (p=0.036, odds ratio 13.310), CRP (p= 0.035, odds ratio 1.011), and LDH (p=0.021, odds ratio 1.016) peak levels were associated with post-COVID-19 radiological finding on chest tomography. A multivariate logistic regression analysis revealed that ferritin and CRP levels at the

Table 3. Patients' clinical, laboratory, pulmonary function test against CT scores

Variations	CT Score		p
	0	1+	
Gender			1.000[a]
Female (n, %)	8 (20.5%)	17 (43.6%)	
Male (n, %)	5 (12.8%)	9 (23.1%)	
Smoking			0.619[a]
Never Smoked (n, %)	9 (23.7%)	17 (44.7%)	
Smoking/Ex-smoker (n, %)	4 (10.5%)	18 (21.1%)	
1st Symptoms			
Pneumonia			0.151[a]
Non-severe (n, %)	11 (28.2%)	15 (38.5%)	
Severe (n, %)	2 (5.1%)	11 (28.2%)	
Dyspnea (n, %)	7 (18.4%)	11 (28.9%)	0.815[b]
Cough (n, %)	10 (26.3%)	15 (39.5%)	0.250[a]
Fatigue (n, %)	7 (18.4%)	13 (34.2%)	1.000[b]
Headache (n, %)	6 (15.8%)	8 (21.1%)	0.305[a]
Laboratory			
BUN 1st Visit (Mean/Std.Dev.)	11.38±3.33	16.25±7.07	**0.007**[c]
Ferritin (Mean/Std.Dev.)			
1st Visit	133.08±95.04	239.23±192.79	**0.037**[c]
Peak	123.49±104.59	324.70±264.32	**0.002**[c]
Fibrinogen (Mean/Std.Dev.)			
1st Visit	299.67±143.07	596.77±174.21	**0.002**[c]
Peak	398.71±98.82	565.81±170.80	**0.026**[c]
d-dimer (Mean/Std.Dev.)			
1st Visit	0.46±0.29	1.82±4.89	0.285[c]
Peak	0.50±0.26	3.60±8.14	0.069[c]
CRP (Mean/Std.Dev.)			
1st Visit	1.95±2.02	6.49±6.97	**0.006**[c]
Peak	60.17±65.85	125.25±87.64	**0.024**[c]
LDH Pik (Mean/Std.Dev.)	243.77±52.16	383.84±147.40	**<0.001**[c]
Pulmonary Function Tests			
Vital capacity% (Mean/Std.Dev.)	88.2±14.13	76.42±16.47	**0.035**[c]
MMEF% (Mean/Std.Dev.)	109.43±28.62	91.81±29.14	0.084[c]
FEV1% (Mean/Std.Dev.)	98.56±14.35	85.87±16.98	**0.033**[c]
FVC% (Mean/Std.Dev.)	90.99±14.18	78.56±16.50	**0.027**[c]
FEV1/FVC (Mean/Std.Dev.)	90.57±3.92	88.71±6.22	0.351[c]
DLCO% (Mean/Std.Dev.)	84.62±16.27	75.67±14.28	0.115[c]
ICU (n, %)	1 (2.6%)	7 (15.8%)	0.221[a]
Steroid Treatment (n, %)	1 (2.6%)	13 (26.3%)	**0.039**[a]

Values are given in mean and standard deviation or patient count and percentage. Statistically significant values marked bold. [a] Fisher's Exact Chi-Squared test; [b] Yates's Chi-Squared test; [c] Independent Samples T-test.

first visit and 3-month follow-up, as well as peak levels, were significantly associated with post-COVID-19 radiological findings on HRCT ($p<0.001$ and $p=0.05$, respectively). Steroid therapy had an inversely proportional and statistically significant relationship to the patient's CT scores (Table 4).

Table 4. Effects of patients' characteristics on CT score

Variations	p	Odds Ratio (%95 C.I.)	R^2
Age	**0.009**[a]	1.101 (1.024–1.184)	0.298
Smoking	0.938[a]	1.059 (0.249–4.500)	0.000
Laboratory			
BUN 1st Visit	**0.050**[a]	1.223 (1.000–1.496)	0.222
Ferritin	<**0.001**[b]		0.450
1st Visit	0.108[a]	1.005 (0.999–1.010)	0.125
Peak	**0.026**[a]	1.006 (1.001–1.011)	0.264
Fibrinogen	0.055[b]		0.230
1st Visit	**0.045**[a]	1.005 (1.000–1.030)	0.635
Peak	0.053[a]	1.010 (1.000–1.020)	0.340
d-dimer	0.339[b]		0.014
1st Visit	0.078[a]	6.875 (0.806–58.658)	0.222
Peak	**0.036**[a]	13.310 (1.179–150.318)	0.375
CRP	**0.050**[b]		0.136
1st Visit	0.071[a]	1.357 (0.974–1.891)	0.248
Peak	0.035[a]	1.011 (1.001–1.021)	0.189
LDH Peak	**0.021**[a]	1.016 (1.002–1.030)	0.394
Steroid treatment	**p**	**Unstd. Reg. Coefficient**	**R^2**
Dose (mg/day) 49.24±25.01	0.006[c]	–0.297±0.80	0.644

[a] Results of Univariate Binary Logistic Regression analysis are given in p, odds ratio (%95 C.I.), Nagelkerke's R2; [b] Results of Multivariate Binary Logistic Regression analysis are given in p, odds ratio (%95 C.I.), Adjusted R2; [c] Results of Linear Regression analysis are given in p, unstandardized regression coefficient and standart error, Adjusted R2. Statistically significant values marked bold.

Discussion

In this study, we found that 64.5% of patients had persistent COVID-19-associated symptoms at 90–120 days. Moreover, 43 (76.8%) patients had persistent radiological findings while 18 (32.1%) had abnormalities in their PFT. Some patients had persistent post-COVID-19 radiological findings or abnormal PFT but no respiratory symptoms. This suggests that the absence of respiratory symptoms cannot predict the resolution of radiological findings or abnormalities on PFT. The high levels of ferritin and CRP at diagnosis, high peak ferritin and CRP levels during the hospitalization, and high levels of ferritin and CRP at 90–120 days were significantly associated with persistent post-COVID-19 radiological findings. Moreover, the values of both the first visit fibrinogen and peak fibrinogen levels were significantly associated with abnormal pulmonary function. So, we suggest performing PFT in patients with elevated ferritin, fibrinogen, and CRP levels at diagnosis, patients with elevated peak levels of ferritin, fibrinogen and CRP during the hospitalization, or high levels of ferritin and CRP at 90–120 days whether they have persistent post-COVID-19 radiological findings on chest CT or any abnormality in PFT. The findings of our study may be a guide to predict which patients will have persistent radiological findings and losses of lung function at 90–120 days after COVID-19 pneumonia.

The loss of lung function may occur following viral pneumonia. Ventilation and blood gas diffusion abnormalities were detected in some patients after viral pneumonia [5]. During the COVID-19 pandemic, some patients had persistent symptoms, radiological findings, and lung function losses after several months [6]. We do not know whose radiological findings will not completely disappear after COVID-19 pneumonia, and who will not fully recover their respiratory functions. It is not known how long it takes for radiological or functional recovery. Moreover, even if some radiological findings persist, we do not know how they will affect the long-term health of patients. Long-term follow-up of these patients is required to understand the long-term clinical effects of the radiological and functional changes associated with COVID-19 that persist after the acute phase of the disease. However, it is not possible to follow up with every patient during the pandemic period. Therefore, it is necessary to identify patients who need long-term follow-up after COVID-19 pneumonia. This can save healthcare providers energy and labor. We think that this study will contribute to the literature regarding these issues.

Post-COVID-19 symptoms may be present weeks or even months later in some patients. It was previously reported that at least one symptom persisted in 84% of patients 60 days after the onset of COVID-19 [7]. Carvalho-Schneider et al. reported a dyspnea frequency of 30.0%, based on self-report at 2 months after noncritical COVID-19 [8]. In another study, dyspnea frequency was 29.0% based on a modified Medical Research Council Dyspnea Scale score of 2 or higher [9]. Post-COVID-19 symptoms can continue for a long time. In this study, we found that some symptoms persisted in 64.3% of patients 90–120 days after COVID-19. Our study showed that the symptoms were not associated with loss of lung function or persistent radiological findings. We have seen that patients without symptoms may also have a loss of lung function or persistent radiological findings. According to our findings, it is not appropriate to consider patients without symptoms during follow-up have no need for further radiological and functional evaluations.

When the radiological course of the disease is monitored during the acute period of COVID-19 pneumonia, the most common tomographic findings are bilateral subpleural ground-glass opacities and consolidation in the lower zones. Focal edema, organizing pneumonia, and diffuse alveolar damage are the underlying causes of these radiological findings [10,11]. Approximately 4–14 days after the onset of symptoms, the tomographic findings may appear as ground glass opacities which later may turn into consolidation by day 9 or begin to gradually disappear by day 14. However, in some patients, ground glass opacities and reticulations can be seen even in early-control tomography scans [12–14]. There are some reports suggesting that the extent of radiological findings and the severity of the disease rather than the pattern on chest CT is more important for radiological sequela [15,16]. It is important to establish a follow-up strategy to determine whether lung fibrosis is developing in patients with COVID-19 pneumonia and to initiate early and appropriate treatments to prevent lung fibrosis in high-risk patients.

Currently, there is no consensus on the frequency and methods of monitoring pulmonary complications that may occur in patients with COVID-19 pneumonia. Most of the patients have radiological improvement during the early period. Complete radiological recovery is expected within 6 months in patients with mild pneumonia without the need for hospitalization, and within 12 months in moderately severe patients who are hospitalized but do not require the ICU. Restrictive lung disease, decreased diffusion capacity, and fibrosis on tomography may develop in patients with severe disease requiring mechanical ventilation. It is recommended to perform a chest CT at 6 and 12 months after discharge to determine whether fibrotic lesions in the lungs have disappeared, partially resolved, remained unchanged, or advanced. It was recommended to perform the chest CT at 24 and 36 months to evaluate the long-term progression in patients with persistent lesions [17].

In our study, we could not perform the initial radiological evaluation of some patients because they had only received chest X-rays or had suboptimal chest CT scans from different healthcare centers. However, in our study, we found that there was a correlation between the levels of CRP, ferritin, and fibrinogen, which were associated with the severity of the disease, persistent radiological findings, and loss of lung function at approximately 3–4 months. There was also an association between steroid use and the persistence of radiological abnormalities. The use of steroids in severe COVID-19 improved clinical outcomes and it was hypothesized that steroids would improve the radiological findings [18]. Our study's results were not as expected in terms of this issue. We assume that the persistence of radiological findings was not secondary to the use of steroids.

Limitations

This study has some limitations. First of all, it is a retrospective study with a small sample size. Secondly, we could not evaluate a baseline chest CT for patients prior to their COVID-19 pneumonia or the findings during the acute phase of COVID-19 pneumonia. So, it is not certain that all the findings on the chest CT were secondary to COVID-19.

Conclusions

In conclusion, we found that symptoms persisted for approximately 3 to 4 months after COVID-19 pneumonia. Some patients had deficits in lung function tests. There were ground glass opacities and reticulations to varying extents in some patients but these findings were resolved. In particular, we found that the loss of lung function and radiological abnormalities were associated with initial high ferritin, fibrinogen, and CRP values. Therefore, we recommend that patients with high ferritin, fibrinogen, and CRP levels during COVID-19 pneumonia, should be followed up regarding lung function and radiological improvement.

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