ORIGINAL ARTICLE

DO LATENT TUBERCULOSIS AND AGE IMPACT THE POST-COVID-19 EXPERIENCE?

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Abstract

Background: There is not enough information about the long-term effects of COVID-19 infection in those who have recovered. According to epidemiological studies, COVID-19 progresses less severely in countries where the Bacillus Calmette-Guerin vaccine is regularly applied than in those where it is not. The purified protein derivative of tuberculin is an indicator of the Bacillus Calmette-Guerin vaccine's protective effectiveness against latent tuberculosis. In our study, we aimed to investigate the relationship between latent tuberculosisand the permanent effects of COVID-19.Our objective was to analyze the long-term relationship between latent tuberculosisand COVID-19.

Materials and Method: We included all clinical, laboratory, and radiological baseline data of patients who were hospitalised for COVID-19 pneumonia between 2020 and 2021 during the pandemic in our study and compared them with data from six months later.

Results: Although there was no statistically significant correlation between purified protein derivative of tuberculin positivity and the long-term effects of COVID-19 ($p = 0.084$), age exhibited a statistically significant relationship with the presence of post-COVID-19 sequelae ($p = 0.004$). Patients with chronic pulmonary disease displayed a significantly greater percentage of symptoms ($p=0.005$).

Conclusion: We could not find any relationship between purified protein derivative of -tuberculin latent tuberculosis infection and long COVID-19 symptoms. We observed sequelae lesions more frequently in the follow-up of elderly patients. Post-COVID-19 symptoms were more common in patients with chronic lung disease. Thus, it is recommended to prioritise radiological and clinical follow-up in elderly patients and those with chronic lung conditions.

Keywords: Post-Acute COVID-19 Syndrome, Latent Tuberculosis, COVID-19, Aged.

INTRODUCTION

According to data from the World Health Organization (WHO), as of July 2023, approximately 697 million patients with SARS-CoV-2 (COVID-19) have been reported. Additionally, seven million people have claimed to have contracted COVID-19(1). The development of vaccines and the influence of herd immunity have significantly mitigated this situation, leading to a substantial reduction in the number of fatalities. However, there is a lack of clear data about the long-term effects of COVID-19 in those who have recovered from infection, and new discussions are emerging concerning the pathologies caused by COVID-19.

Some epidemiological studies conducted during the pandemic have reported that in countries where the Bacillus Calmette-Guerin (BCG) vaccine is routinely administered, the course of COVID-19 infection is less severe, and mortality rates are lower than those in countries where it is not applied (2,3,4). The BCG vaccine enhances the resilience of the human immune system to viruses such as human respiratory syncytial virus (hRSV) and human papillomavirus (HPV) (4). In light of this, in studies conducted in countries where the BCG vaccine is not routinely administered, individuals aged older than 60 years received the BCG vaccine to determine how it impacts COVID-19 infection; nevertheless, its ability to prevent infection has not been conclusively proven (5-6).

Latent tuberculosis is a condition not associated with active tuberculosis; it is characterised by the absence of symptoms, laboratory results, or radiological findings. The diagnosis is made bythe use of a purified protein derivative of tuberculin (PPD) and the interferon gamma release test (QuantiFERON test) (7).

In our country, Türkiye where the BCG vaccine is routinely administered during childhood, tuberculosis is endemic. Hence, the PPD skin test, which serves as an indicator of cellular immunity, is employed for assessing latent tuberculosisand as an indicator of the BCG vaccine.

At the beginning of the pandemic, information regarding the outcomes of surviving patients was limited and a topic of curiosity. As time progressed, patients' follow-up results began to be reported, and the terms 'long COVID' and 'post COVID' started to be used.

The term 'long COVID-19' refers to the persistence of symptoms and complaints following COVID-19 infection (8,9,10). The most common long COVID-19 symptom in the respiratory system is dyspnoea(10,11). Emerging chronic inflammation leads to alveolar damage through the activation of cytokines and reactive oxygen products, resulting in the continuation of symptoms (11,12). In some cases where long COVID-19 was detected, post-COVID pulmonary fibrosis (PCPF) was observed; this condition negatively affected patients' quality of life and respiratory functions in a manner similar to idiopathic pulmonary fibrosis. Thus, even though the pandemic has ended, it is important to identify these patients and determine the factors leading to PCPF to guide treatment approaches.

Our main goal was to perform symptom, radiological, and biochemical evaluations of individuals who needed to be hospitalised due to COVID-19 infection to establish the duration of symptoms and persistence of the disease. Second, we investigated the relationship between PPD (LTBI), an indicator of the protective effect of the BCG vaccine, and the long-term and lasting effects of COVID-19after six months.

MATERIALS AND METHOD

This study was approved by the Clinical Research Ethics Committee of the Yedikule Chest Diseases and Thoracic Surgery Training Research Hospital at Health Education University (No: 2021-69/May 2021). This study was planned as a longitudinal cohort study.

Our study included patients admitted to the chest disease service due to COVID-19 pneumonia who were aged 18 to 85 years old between March 25, 2020 and February 16, 2021. Six months after discharge, these patients were contacted by phone and invited for follow-up visits. A total of 282 surviving patients were contacted by phone, and 92 agreed to take part in the study by participating in the follow-up visit.

Our patients consisted of those who tested positive for COVID-19 by PCR or who were likely infected with SARS-CoV-2 (those who were clinically or radiologically diagnosed with COVID-19 pneumonia despite receiving negative test results). Our study included both probable and confirmed cases of SARS-CoV-2 infection according to the WHO's classification (13).

The inclusion criteria were patients over the age of 18 who were admitted to our hospital with a definite or probable diagnosis of COVID-19 and who agreed to participate in a check-up and signed a voluntary consent form after 6 months.

We excluded the following patients from the study: those with active tuberculosis; those who had been in contact with a person diagnosed with activetuberculosis; those who had active tuberculosis in the past; those using immunosuppressant medication for any reason; and those who did not agree to participate in the study and did not come when called by phone.

Routine verification of COVID-19 cases in our country requires real-time reverse transcription, which involves specific detection of viral RNA by a Nucleic Asid Amplification Tests(NAAT) such as polymerase chain reaction (rRT-PCR) detection of viral sequences and, when necessary, by nucleic acid sequence analysis.

High-resolution computed tomography (HRCT) was performed on the patients during hospitalisation and at their 6-month follow-up. Radiological images were evaluated by two radiologists. HRCT images were recorded as reticular, honeycomb, fibrotic focus, and interseptal thickening ground glass.

Bronchiectasis, chronic obstructive pulmonary disease (COPD), and asthma were recorded as chronic lung diseases.

All patients received the BCG vaccine in accordance with the national vaccination programme.During the period of our study, the COVID-19 vaccination programme had not been initiated in our country. As a result, patients included in the study had not been vaccinated.

The PPD-tuberculin skin test is an indicator of BCG vaccination and latent tuberculosis. Hence, this method was applied to all volunteers in our study to explore the connection between the BCG vaccine and post-COVID-19 sequelae.The QuantiFERON test was not administered.

The PPD antigen, used for the tuberculin skin test, was administered by intracutaneous injection of 0.1 mL of a solution equivalent to 5 tuberculin units with a 27-gauge needle into the 2/3 upper inner part of the left forearm, after which the induration formed within 48 to 72 hours was measured with a ruler, and the results were recorded in millimetres (mm). The results were evaluated according to the National Tuberculosis Diagnosis and Treatment Guidelines (7). The indicator diameter was evaluated and recorded by chest disease specialists. Furthermore, all patients were examined for BCG vaccine scars on their left shoulders.

The initial 24-hour symptoms of patients upon admission to the hospital, their physical examination findings, oxygen saturation levels, biochemical parameters (glucose, urea creatine, C-reactive protein, hemogram, fibrinogen, D-dimer, ferritin,Aspartate aminotransferase(AST), Alanine Transaminase (ALT), Lactate dehiydrogenase(LDH), gama – glutamyl transferase(GGT), Na, K, protein, albumin), and radiological features (ground-glass, consolidation, focal, multifocal involvement, bilateral, unilateral involvement) were recorded in our database.

All patients who attended the 6-month follow-up visit were re-evaluated by chest disease specialists. Their symptoms were scrutinised, physical examinations were performed, and oxygen saturation, radiological, and biochemical evaluations were conducted. During the follow-up visit, radiological findings—including ground-glass opacities, consolidation, focal, multifocal, bilateral, and unilateral involvement as well as increased reticular density increase, fibrosis, tractional bronchiectasis, and honeycomb formation—were assessed.

Statistical analysis

We used SPSS 23.0 for Windows to performstatistical analysis. We present descriptive statistics as numbers and percentages for categorical variables and means, standard deviations, and as minima and maxima for scale variables. We made two independent patient group comparisons using Student's t-test. We made comparisons of patient conditions at the time of hospitalisation and at the time of the control using paired t-tests. We performed comparisons of ratios in independent and dependent groups with Pearson's chi-square test and McNemar's test, respectively.To examine the relationships, we employed Pearson's correlation. We determined the cut-off points using receiver operating characteristic (ROC) curves and tested them using the log-rank test of equality. The significance level, alpha, is accepted as $p<0.05$.

RESULTS

(1) Patients' conditions at the time of hospitalisation

Characteristics of the patient group are summarized in Table 1.

The study included a total of 92 patients (n=92), 39 of whom were female (42.4%) and 53 of whom were male (57.6%). Their average age was 51.97 years (ranging from 30 to 72 years). While 69% (n=75) tested positive for SARS-CoV-2 by PCR, 31% (n=17) were given negative test results.

The most common comorbidity among the patients was hypertension (30%), followed by diabetes mellitus (18%) and chronic obstructive pulmonary disease (COPD) (16%). The percentage of patients without comorbidities was 28.8% (n=27). The most common symptoms observed in patients during hospitalisation were cough and dyspnoea, reported as 67.4% and 69.6%, respectively (see Table 1).

The patients had the following average laboratory values at the time of hospitalisation: ferritin: 372.64±389.12, fibrinogen: 510.75±160.44, D-dimer: 1.65±4.37, CRP: 69.25±64.38, averageplatelet count: 250.38±123.83, lymphocyte count: 1.68±1.03, and neutrophil-to-lymphocyte ratio: 4.82±4.63 (Table 1).

The patients had an average oxygen saturation (SaO2) of 94.95%, ranging from 84% to 98%. Among the patients, 58.7% received oxygen support through a nasal cannula, while 5.7% required oxygen, delivered via an Ambu bag or reservoir mask (Table 1).

Among the 92 patients, 73 had HRCT images taken during hospitalisation. The remaining 19 were evaluated using chest radiography.

Among the patients who underwent chest HRCT imaging, ground-glass opacity was observed in 95.9%, while consolidation was detected in 47.9%. Multifocal and bilateral involvement was observed in 90.4% of patients (Table 1).

While hospitalised, 2 patients experienced pulmonary embolism, and pulmonary embolism worsened in 5 (5.5%) of them, necessitating immunosuppressive treatment. All other patients were treated with the current medications specified in the Ministry of Health's COVID-19 treatment guidelines (Table 1).

The patients' hospital stays ranged from a minimum of 1 day to a maximum of 30, with an average of 7 days. Among the patients, 4.3% (n=4)

required intensive care during their hospitalisation, while 7.6% were discharged with oxygen concentrator support (Table 1).

(2) Information on the patients' conditions at the follow-up visits (six months later)

During the follow-up visits, 42.4% of patients experienced dyspnoea, while 8.7% had cough. On the lung CT scans obtained during these visits, sequelae were observed in 50% of the patients (n=41). The most common sequela lesion was an increase in ground-glass opacity (28.3%, n=26), followed by fibrotic lesions (23.9%, n=22) and increased reticulation (20.7%, n=19). A total of 78% of the lesions (n=32) were bilateral or multifocal (Table 2).

(3) Changes in patients' conditions from the time of hospitalisation to the follow-up visits

During the follow-up visits, patients' average oxygen saturation (SaO2) was 96.98%±3.02%. Among the 7 patients who were given oxygen

Table 1. Demographical and clinical characteristics of the patient group

		Mean±SD	Min-Max
Age		51.97±10.22	30-72
		N	%
Gender	Female	39	42.4
	Male	53	57.6
Symptoms	Cough	62	67.4
	Dyspnea	64	69.6
	Fever	38	41.3
	Loss of smell	18	19.6
	Fatigue	60	65.2
Comorbid diseases	Hypertension	30	32.6
	Chronic pulmonary disease	16	17.4
	Chronic heart failure	12	13.0
	Coronary artery disease	11	12.0
	Chronic renal failure	0	0.0
	Malignity	2	2.2
	Diabetes	18	19.6
	Asthma	7	7.6
PCR	Positive	75	81.5
	Negative	17	18.5
PPD	Positive	32	34.8
	Negative	57	62.0
	Missing information	3	3.3
BCG	Yes	77	83.7
	No	12	13.0
	Missing information	3	3.3

Table 1. *continued...*

Test results at the time of hospitalization			
	Valid n	**Mean±SD**	**Min-Max**
WBC	92	8.27±3.15	2.86-17.77
HGB	91	13.25±1.60	10.0-19.2
MCV	92	82.88±5.14	57.0-93.0
PLT	92	250.38±123.83	75-1018
Lymphocyte	92	1.68±1.03	0.38-8.01
Neutrophil/Lymphocyte ratio	86	4.82±4.63	0.43-29.79
Glucose	92	129.93±39.96	78-273
Urea	92	28.66±13.12	12-116
Creatine	92	0.83±0.25	0.49-2.01
TGL	17	136.53±76.29	54-318
Total Cholesterol	19	163.95±43.64	69-230
LDH	57	330.51±166.59	31-1150
Ferritin	87	372.64±389.12	6.0-2000.0
ALT	92	41.47±43.19	7-369
AST	92	40.58±24.15	11-154
Sedimentation	31	47.65±25.75	4-104
CRP	92	69.25±64.38	0.3-252.0
D-dimer	87	1.65±4.37	0.12-36.48
Fibrinogen	84	510.75±160.44	191-983
Procalcitonin	89	0.14±0.42	0.01-3.52
SpO2	92	94.95±3.59	84-98

WBC: white blood cell, HGB: haemoglobin, MCV: mean corpuscular volume, PLT: platelet, TGL: triglycerides, LDH: lactate dehydrogenase, ALT: alanine transaminase, AST: aspartate transaminase, CRP: C-Reactive protein, SpO2: oxygen saturation

Summary of hospitalization process			
		N	**%**
Treatment	Enoksaparin Sodyum	88	95.7
	Faviravir	69	75.0
	Plaquenil	35	38.0
	Antibiotic	83	90.2
	Prednol	31	33.7
	Tocilizumab	1	1.1
	Pulsesteroid(metilprenizolon)	1	3.3
Oxygen support	Nasal cannula	54	58.7
	Ambureservoir	6	6.5
	Highflow	5	5.4
Problems arisen	Cardiac involvement	0	0.0
	Pulmonary embolism	2	2.2
	Clinical deterioration	5	5.4

Table 1. *continued...*

Findings of Chest X-ray and CT at the time of hospitalization			
		N	%
Chest X-ray (92 valid patients)	Yes	72	78.3
	No	20	21.7
CT (73 valid patients)	Ground glass opacity	70	95.9
	Consolidation	35	47.9
	Focal	5	6.8
	Multifocal	66	90.4
	Right	70	95.9
	Left	65	90.3
	Bilateral	66	90.4

Summary of discharge conditions			
		N	%
ICU	Yes	4	4.3
	No	88	95.7
Oxygen concentrator	Yes	7	7.6
	No	85	92.4
		Median	Min – Max
Length of hospitalization stay (LoS)		7 days	1 day – 30 days

Table 2. CT Findings and symptoms at control

		N	%
Symptoms	Cough	8	8.7
	Dyspnoea	39	42.4
	Fever	3	3.3
CT (91 valid patients)	Unifocal	11	12
	Multifocal	32	34.8
	Right	37	40.2
	Left	37	40.2
	Bilateral	32	34.8
	Reticular	19	20.7
	Honeycombing	1	1.1
	Fibrotic	22	23.9
	Interseptal thickening	6	6.5
	Ground-glass opacity	26	28.3
Oxygen concentrator (90 valid patients)	Yes	3	3.3

concentrators during discharge for oxygen therapy at home, only 1 still required oxygen. The average ferritin level, assessed during the follow-up visits, was 85.41±73.9, the D-dimer level was 0.34±0.38, and the CRP level was 3.93±5.12 (Table 3).

(4) Observations of PPD

During the follow-up visits, the tuberculin skin test (PPD) was conducted, and 34.8% of the patients (n=32) tested positive (Table 4). According to the independent t-test results, patients with a positive PPD had a longer hospitalisation than PPD-negative patients ($p<0.001$). According to Pearson's chi-square test, fever symptoms were more common in PPD-positive patients during hospitalisation ($\chi 2$ (1) =4.43, p=0.035). Apart from these findings, there was no statistically significant relationship between PPD positivity and other parameters during the hospitalisation of COVID-19 patients.

(5) Symptoms at the follow-up visits

At the follow-up visits, 32 patients still had at least one of the symptoms (cough, dyspnoea, or fever). We further analysed these 32 patients. For the next part, all the remaining symptoms were observed for different patient groups. Only significant results were recorded. Patients with chronic pulmonary disease had a significantly greater percentage of symptoms, especially dyspnoea, at follow-up (p=0.013 for symptoms, p=0.005 for dyspnoea) (Table 5).

Table 3. Test results for the control

	Valid n	Mean±SD	Min–Max
Glucose	91	115.81±40.75	11-323
Urea	91	22.78±14.99	0.50-80
Creatine	91	8.49±14.68	0.47-69
TGL	89	173.18±124.78	40-1129
Total cholesterol	89	194.73±40.14	93-289
LDH	90	218.40±78.78	38-579
Ferritin	86	85.41±73.91	0.90-391
ALT	91	23.74±21.06	9-181
AST	91	23.51±20.46	11-200
Sedimentation	36	15.44±15.83	2-62
CRP	89	3.93±5.12	0.19-31.80
D-dimer	85	0.34±0.38	0.01-2.58
Procalcitonin	91	0.04±0.02	0.003-0.14
ALB	86	44.66±5.71	0.80-52
Protein	2	42±7.1	37-47
SpO2	91	96.98±3.02	76-99

Table 4. Information on patient PPD results

PPD	Positive	32	34.8
	Negative	57	62.0
	Missing information	3	3.3

Table 5. Relationship between sequelae and demographic characteristics and Relationship with consolidation on CT and having sequelae at control

		P
Age		0.004
Sex		0.202
Symptoms	Cough	0.085
	Dyspnoea	0.972
	Fever	0.974
	Loss of smell	0.934
	Fatigue	0.588
Comorbid diseases	Hypertension	0.781
	Chronic pulmonary disease	0.734
	Chronic heart failure	0.126
	Coronary artery disease	0.109
	Malignity	0.912
	Diabetes	0.372
	Asthma	0.544
PCR		0.934
PPD		0.084

		CT_Sequelae		Total	p
		No	Yes		
CT_consolidation	No	27	11	38	
	Yes	15	20	35	
Total		42	31	73	0.015

Patients with dyspnoea and cough comprised a significantly greater percentage of patients with fibrotic sequelae at follow-up (p=0.007 and p=0.009, respectively). Likewise, patients with dyspnoea and cough at the time of hospitalisation comprised a significantly greater share of patients with interseptal thickening at follow-up (p=0.041 and p=0.001, respectively). Moreover, patients with cough at the time of hospitalisation comprised a significantly greater number of patients with GGOs at follow-up (p=0.028).

(6) Observations of having sequelae after the disease

The results of the independent samples t-tests suggest a significant difference (p=0.004) in the ages of the patients who had sequelae after the disease compared with those who did not have sequelae. The patients who had sequelae were older than the patients who did not.

The following tables provide all the information on the CT and subsequent conditions of the patients (Table 5).

The outcomes of Pearson's chi-square test imply a significant relationship between having consolidation of CT and having a sequela at the follow-up visit (Table 5).

DISCUSSION

We aimed to examine the course of COVID-19 infection in the presence of latent tuberculosisand its results in the post-infection period. We did not detect a relationship between PPD positivity and post-COVID-19 symptoms or radiological residual lesions. However, symptoms such as dyspnoea and cough were more common in patients with chronic lung disease (COPD, asthma, bronchiectasis, etc.) and in patients with radiological sequelae in the lung(s). Furthermore, post-COVID sequelae lesions were more common in elderly patients.

We included patients who were hospitalised due to severe pneumonia without intensive care admission; 57% were male and 43% were female, with an average age of 51.97 years. Although the sex distribution of our patients was like that in other studies, the average age was lower (14,15,16,17,18).

Our comorbidity rate was 71.2%. In other reports in the literature, the most common comorbidity rate was hypertension (30%), followed by that of diabetes mellitus (18%) and COPD (16%) (14,15,16,17,18).

At the 6-month follow-up visit, the most common persistent symptom was dyspnoea (42.9%). Various studies have reported persistent dyspnoea after COVID-19, ranging from 10.5% to 20% (15,16,17,18,19). Furthermore, these studies indicate a greater prevalence of persistent dyspnoea in hospitalised patients (15,16,17,18,19). In our study, like the study by Munblit et al., we identified a relationship between the presence of persistent symptoms and dyspnoea and the presence of chronic lung disease (18). Additionally, dyspnoea and cough were correlated with the detection of sequelae lesions at the follow-up visits in the thorax CT scans of our patients. Indeed, 50% of our patients had radiological sequelae in their thorax CT scans. The most common sequelae were an increase in ground-glass opacity (28.3%), followed by fibrotic foci (23.9%) and reticular findings (20.7%). Furthermore, 95% of residual lesions were bilateral and multifocal. Blanco JR et al. did not detect any imaging findings in 48% of patients via tomography after 45 days, which is quite early compared to our study (16). So et al. reported a percentage of 55.7% in their meta-analytic study examining follow-up CT scans taken at different time intervals (19). However, in the study of Balbi M et al., who investigated hospitalised patients, like our study, the rate of sequelae was 81% at the follow-up CT scans taken after an average of 105 days (20).

According to our study, we believe that the high rate of sequelae they detected is because CT control was performed at an earlier period. Like the results of Balbi et al., in our study, the occurrence of tomography sequelae was associated with age, while it did not show any correlation with comorbidity (20).

Epidemiological studies have reported that COVID-19 mortality is lower in countries with a high tuberculosis incidence where the BCG vaccine is routinely administered than in countries with a lower tuberculosis prevalence where it is not (2,3,4). This situation has necessitated the investigation of the potential impact of the BCG vaccine and latent tuberculosisinfection (LTBI) on the clinical course of COVID-19. Therefore, our study is significant because it explores the effect of LTBI on the persistence and sequelae of the disease during long-term follow-up of COVID-19 patients. We did not come across a study in the literature from this perspective. Nevertheless, in our study, we did not identify a statistically significant relationship between persistent PPD positivity and post-COVID-19 symptoms or lung sequelae.

Gao et al. conducted a meta-analysis of 2,383 COVID-19 patients and reported that COVID-19 infection appeared to be twice as severe in patients

with LTBI, but these patients did not have a significantly greater risk of mortality. However, there were inconsistencies in the clinical severity criteria of the studies included in their meta-analysis, and these studies focused on acute-stage COVID-19 patients (21). Mariotti et al. revealed that patients with LTBI experienced significantly greater rates of orotracheal intubation and mortality than did those without LTBI (22).In our study, we observed that the hospital stay was longer among patients with LTBI, and fever symptoms were more common in these patients. However, we did not detect significant relationships for the other parameters.

Erdem et al., from our country, found no significant relationship between QuantiFERON positivity and the clinical severity or mortality of acute-stage COVID-19 (23).

The limiting factors of our study are that it was not planned in a controlled prospective manner and that possible COVID-19 patients were included. The absence of a control group not receiving the BCG vaccine in our study could be considered a limitation. Due to the lack of routine implementation of the BCG vaccine in our country and its status as an endemic region for tuberculosis, it is challenging to identify unvaccinated patients. Furthermore, while PPD testing makes the most significant contribution to the detection of latent tuberculosis by demonstrating cellular immunity, clinical decisions are still limited by inconclusive findings such as uncertain contact and minimal radiological sequelae.During the early days of the pandemic, COVID-19 cases were frequently hospitalized and isolated. The cases in this study therefore consist of patients with mild and moderate pneumonia and include 6-month follow-up of these cases.Cases who survived intensive care couldn't be regularly followed up at the outpatient clinic level due to the difficult times they experienced afterwards. A limiting factor in our study is that cases with severe pneumonia who were even later admitted to intensive care were not included. Nevertheless, our study is significant for demonstrating the presence of sequelae findings even in mild cases.Our main objective was to determine the status of patients in our country's hospitals where the BCG vaccine is routinely administered. Nonetheless, our study—which is the first to investigate the relationship between latent tuberculosis and post-COVID-19 symptoms—may provide guidance for future research.

CONCLUSION

In conclusion, we did not detect a relationship between symptom persistence and the presence of radiological sequelae in post-COVID-19 patients with LTBI, who were followed up with due to PPD positivity and not having been intubated. Patients who were determined to have chronic lung disease and radiological fibrotic sequelae lesions during hospitalisation exhibited a significantly greater persistence of symptoms.Furthermore, the likelihood of residual radiological sequelae was greater in older patients.

The high incidence of idiopathic pulmonary fibrosis, a progressive pulmonary disease, in the elderly group indicates that age predisposes individuals to fibrotic mechanisms.We believe the inflammation caused by COVID-19 triggers these fibrotic mechanisms more in the elderly. Therefore, vaccinating the elderly population and implementing preventive measures are crucial to prevent the development of potential fibrotic sequelae. Besides, these cases should be followed up radiologically and clinically. Our study emphasizes the need to develop vaccines against new COVID mutations and other viral infections, as well as treatments to prevent the fibrotic process.

Declaration of authenticity about the figures: All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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