Long COVID-19 and longer sick leave: longitudinal study of economically active patients

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COVID-19 sick leave is considerably longer than that for any other viral pneumonia. Long-COVID respiratory symptoms such as dyspnoea or chest pain may be associated with longer sick leave, whereas daily exercise may reduce it. https://bit.ly/4fvcbiz

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Abstract

Introduction Sick leave was one of the numerous consequences of the COVID-19 pandemic. Given the relevance of occupational status for any individual, the aim of the study was to evaluate the impact of persistent symptoms after active infection and determine factors associated with longer sick leaves (LSLs).

Methods This observational study focused on economically active patients attending a post-COVID outpatient clinic for persistence of symptoms or radiological alterations after active infection. The LSL temporal cut-off point was defined by the third tertile of total leave days. Median leave time was compared with the optimal sick leave time for any other viral pneumonia, estimated by the local Ministry of Employment. To determine factors associated with LSL, multivariate models were ultilised.

Results A total of 248 patients were included. The median sick leave time for the entire population was 53 days (interquartile range (IQR) 37.0–126.5), global sum of 30 169 days; the median optimal sick leave time was 21.9 days (IQR 19.7–25.9) ($p<0.05$). The third tertile cut-off point for LSL was 83 days and multivariate analysis showed a significant association with dyspnoea (OR 3.26, 95% CI 1.59–6.70, $p=0.0001$), while physical exercise of at least 10 $\text{min}\cdot\text{day}^{-1}$ was significantly associated with shorter sick leave durations (OR 0.45, 95% CI 0.20–0.98, $p=0.04$).

Discussion COVID-19 sick leave was considerably longer than that stipulated for nonsevere acute respiratory syndrome coronavirus 2 viral pneumonia. Long-COVID syndrome, especially dyspnoea, seems to be a very present factor in these patients' inability to work.

Introduction

On 11 March 2020, the World Health Organization declared a global pandemic of a new disease known as coronavirus disease 2019 (COVID-19). It initially led to an exponential rise in cases in China, followed by global spread from December 2019 onward [1, 2]. It was originally considered to be a respiratory disease, as the main organ affected was the lung [3]; however, it is now recognised as a multisystemic disease with various clinical manifestations [1, 4]. Most cases were mild, although about 15% of patients required hospital admission due to the development of respiratory failure, among other organ damage, and up to 5% of patients developed acute respiratory distress syndrome requiring admission to intensive care units (ICUs) [4–6]. These percentages gradually decreased thanks to lower virulence and vaccination.

Despite the high mortality of patients who developed the most severe forms of the disease, many progressively improved until their complete recovery shortly after discharge, while some presented sequelae in one or more organs [7, 8]. This sequelae syndrome has received different names, including post-COVID-19 condition and long-COVID [9, 10]. This condition affects at least 10–30% of people who test positive [11], some having 20 or more different symptoms [12]. In this way, the pandemic has had a health, economic and social impact without recent precedent [13], with returning to work also being affected.

The objective was to evaluate the occupational impact of persistent symptoms after a COVID-19 infection in an economically active population in terms of sick leave time and determine the factors associated with longer sick leave (LSL).

Methodology

A longitudinal study was conducted in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), starting from their first visit to a post-COVID-19 outpatient clinic of a tertiary hospital following hospitalisation or active infection. Enrolment started on 1 July 2020 and ended on 28 September 2021. This outpatient clinic was established in mid-2020 between the first and second waves of the pandemic in Spain, and followed a multidisciplinary protocol leaded by pulmonologists, including visits every 3–6 months according to the patients' characteristics, which included a thorough anamnesis and respiratory functional and/or radiological tests if considered appropriate. This protocol is summarised in figure 1 and is based on those proposed by the British Thoracic Society [14] and the Spanish Society of Pneumology and Thoracic Surgery [15], adapted to our centre resources at the time. For the main objective of our study, follow-up ended when sick leave was terminated. However, most patients continued attending the outpatient clinic until their symptoms were reasonably stable or resolved and no further radiological or functional tests were needed. The inclusion criteria were as follows: 1) over 18 years old; 2) persistent respiratory symptoms after active infection, treated on an outpatient or inpatient basis; and 3) persistent radiological alteration after active infection. The exclusion criteria were 1) retired patients, 2) students and 3) individuals with permanent work disability prior to COVID-19 infection. Patients provided informed consent and the study protocol was approved by the local ethics committee (record 02/2021, 22 February 2021).

The outcome variable was LSL and, to determine its temporal cut-off point, the study population was divided into tertiles. LSL was considered for the third tertile, as it corresponded almost exactly to a 12-week period after hospital discharge or active infection, which was also in line with a cut-off point for long-COVID sequelae [16]. Demographic variables collected included sex assigned at birth, age and body mass index. Medical history and cardiovascular risk factors included high blood pressure, dyslipidaemia, diabetes, asthma, obstructive sleep apnoea, COPD, ischaemic heart disease and heart failure. Regarding hospital admission, the date of admission, date of discharge and ICU admission were recorded. Clinical variables at the time of admission were recorded dichotomously, including the following: dyspnoea,

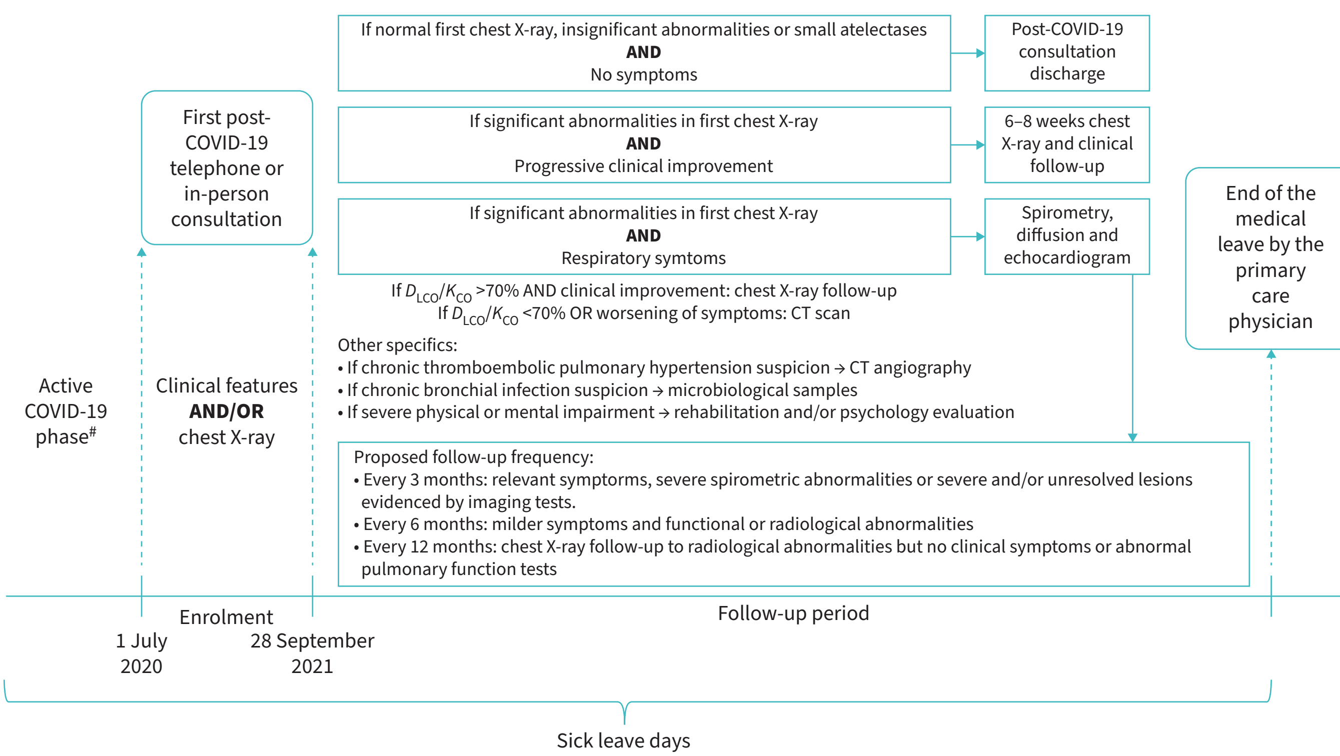

FIGURE 1 Post-COVID-19 outpatient clinic protocol and dates of enrolment, follow-up and study termination. #: With or without hospitalisation. D_{LCO}: diffusing capacity of the lung for carbon monoxide; K_{CO}: transfer coefficient of the lung for carbon monoxide; CT: computed tomography.

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temperature, desaturation by pulse oximetry ⩽93% in patients ⩽50 years and ⩽90% in patients over 50 years. Continuous quantitative analytical variables included neutrophils, lymphocytes, platelets, fibrinogen, D-dimer, alanine aminotransferase, aspartate aminotransferase, bilirubin, lactate dehydrogenase, creatinine, ferritin, C-reactive protein and interleukin-6. Radiological variables included unilateral or bilateral pneumonia. Therapeutic variables included lopinavir/ritonavir, hydroxychloroquine, azithromycin, interferon beta, tocilizumab, anakinra, remdesivir, corticosteroids, antibiotics and type of respiratory support received (conventional oxygen therapy, high-flow therapy with nasal cannula, continuous positive airway pressure, bi-level positive airway pressure and invasive mechanical ventilation). The same analytical variables were also collected at hospital discharge.

From the follow-up, the most commonly described symptoms of long COVID-19, defined as "a condition that occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, generally three months after the initial infection, with symptoms that last at least two months and cannot be explained by an alternative diagnosis" [9, 10], were collected dichotomously in the first evaluation after active infection and/or hospital discharge and included dyspnoea, cough, expectoration, chest pain, asthenia, haemoptysis, orthopnoea, fever, weight loss, mobility alterations, sensory alterations, voice alterations, swallowing alterations, dermatological lesions, hair loss, sleep alterations, cognitive alterations, mood alterations, headaches and arthralgia. With the hypothesis that daily exercise could be associated with a faster recovery, information was also collected dichotomously from those patients who exercised for at least 10 $min \cdot day^{-1}$. Given that the lungs are the most frequently affected organ by COVID-19 and that the sequelae of this disease may include debilitating respiratory symptoms, we consider that physical activity could be a beneficial factor in a potentially chronic respiratory disease.

Date of medical discharge from primary care, which marks the sick leave, was extracted from the common database of the Community of Madrid (HORUS). Optimal sick leave (OSL) time was estimated following the indications of the 4th edition of the *Manual of Optimal Times of Temporary Disability* of the National Social Security Institute of the Spanish Ministry of Employment and Social Security under code J12, corresponding to "Viral pneumonia, not classified elsewhere", with correction factors for age, sex and occupation [17]. Regarding the correction factor for job occupation, all patients were considered in group 15, corresponding to "Unskilled workers in services (except transportation)", which generates a correction factor with more sick leave time. Although time off work begins at the day of hospital admission, sick leave time elapsed from hospital discharge was also estimated in those patients who were admitted. Personal history, as well as the rest of the medical data on admission, follow-up and results of complementary tests, were collected.

Statistical analysis was performed with the STATA 16.1 program (STATACorp LLC, Texas). Qualitative variables are presented as absolute frequencies and percentages, and quantitative variables as means±SD, ranges, medians or interquartile ranges (IQRs) according to their distribution evaluated with the Kolmogorov–Smirnov test. The difference between dichotomous characteristics was analysed with the chi-square test with Fisher's exact correction. Quantitative variables were analysed using the *t*-test for independent samples or the Mann–Whitney U test if the samples were normally distributed or not, respectively. The Wilcoxon test was used to compare the medians of sick leave time following hospital discharge or active infection and the OSL. To determine the association of the independent variables with LSL, a multivariate logistic regression model was developed including variables with a p-value less than 0.20 in the univariate analysis of the sociodemographic variables, medical history and the symptoms referred to in the first post-COVID follow-up, and those variables considered relevant by the investigators. ICU admission was excluded from the model due to its foreseeable influence on the increase in the time of both hospital admission and the added time off work in the recovery phase upon discharge, considered as the component of functional myopathy. The magnitude of association is presented as an odds ratio with its 95% confidence interval. A p-value of less than 0.05 was considered statistically significant.

A subanalysis was performed on the patients included in the study according to the need for hospital admission. Finally, multivariate Bayesian proportional hazard analysis was performed with 12 500 iterations using Markov chain Monte Carlo sampling with default prior distributions to determine the association of factors to time off work. The magnitude of association is presented as a hazard ratio (HR) with its 95% credibility interval.

Results

A total of 248 patients were included, with a mean age of 52.6±10.2 years, of whom 132 were men (53.2%). The patient flowchart is presented in figure 2. The most common cardiovascular risk factors were obesity (98 patients, 39.5%) and high blood pressure (72 patients, 29.0%). A total of 209 patients (84.3%)

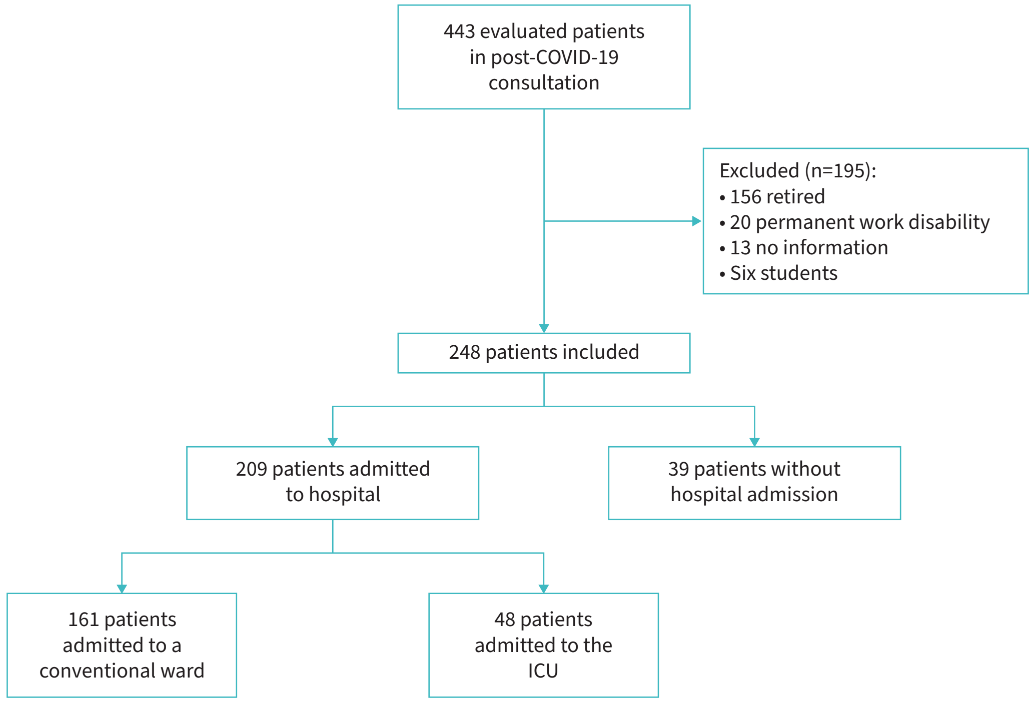

FIGURE 2 Flowchart of patients attended in a post-COVID-19 outpatient clinic. ICU: intensive care unit.

required hospital admission and 48 patients (19.4%) required ICU admission. The median real time off work was 53 days (IQR 37.0–126.5), with a global total of 30 169 days. According to the study groups proposed by tertiles, 84 patients (33.9%) presented LSL of at least 83 days. Table 1 presents the sociodemographic characteristics and medical history of the population depending on the duration of sick leave.

Median OSL time, corrected for sex, age and occupation, was 21.9 days (IQR 19.7–25.9) and the median time off work since hospital discharge or active infection onset for patients not admitted to hospital was 42 days (IQR 27.0–119.8). For hospitalised patients, median sick leave was 51 days since admission (IQR 37.5–130) and 40 days since discharge (IQR 27–127.5), while sick leave for nonadmitted patients was 56 days (IQR 37–113). Statistically significant differences were found when comparing the medians of real

TABLE 1 Sociodemographic characteristics and medical history of patients seen in a post-COVID-19 consultation, according to the temporary duration of their sick leave

Characteristics	Total n=248	First tertile (⩽43 days) n=86	Second tertile (⩾44–82 days) n=78	Third tertile (⩾83 days) n=84	p-value
Age, mean±SD years	52.3±10.3	49.4±11.7	53.0±10.1	54.5±8.2	0.004
Sex, men (%)	132 (53.2)	44 (51.2)	48 (61.5)	40 (47.6)	0.18
Obesity, n (%)	98 (39.5)	31 (36.0)	29 (37.2)	38 (45.2)	0.41
Body mass index, mean±SD kg·m^{-2}	29.0±6.2	28.5±7.1	28.5±5.1	30.0±6.2	0.21
Arterial hypertension, n (%)	72 (29.0)	22 (25.6)	28 (35.9)	22 (26.2)	0.27
Dyslipidaemia, n (%)	57 (23.0)	18 (20.9)	19 (24.4)	20 (23.8)	0.85
Asthma, n (%)	32 (12.9)	12 (14.0)	4 (5.1)	16 (19.0)	0.03
Diabetes, n (%)	26 (10.5)	7 (8.1)	9 (11.5)	10 (11.9)	0.68
Obstructive sleep apnoea, n (%)	16 (6.5)	6 (7.0)	4 (5.1)	6 (7.1)	0.85
Ischaemic heart disease, n (%)	7 (2.8)	3 (3.5)	4 (5.1)	0 (0.0)	0.13
Heart failure, n (%)	3 (1.2)	0 (0.0)	3 (3.8)	0 (0.0)	0.04
COPD, n (%)	5 (2.0)	0 (0.0)	4 (5,1)	1 (1.2)	0.05
Hospitalisation, n (%)	209 (84.3)	74 (86.0)	63 (80.8)	72 (85.7)	0.59
Hospitalisation in intensive care unit, n (%)	48 (19.4)	7 (8.1)	10 (12.8)	31 (36.9)	0.0001

time with OSL (p=0.001), as well as time since hospital discharge or active infection with OSL (p=0.001). No differences were found between the sick leave durations of admitted and nonadmitted patients (Mann–Whitney U test, p=0.98). Figure 3 presents the number of days of sick leave and the frequency of patients.

The median time elapsed until the first assessment in the post-COVID consultation follow-up was 87 days (IQR 49.2–142.0). In this consultation, it was documented that 225 patients (90.7%) had at least one symptom that had lasted for more than 8 weeks after 3 months of active infection, compatible with the definition of long COVID. In this consultation, the average number of symptoms reported was 3.5±2.4 and the most frequent were dyspnoea (144 patients, 58%), asthenia (133 patients, 53.6%), weight loss (109 patients, 44%), sleep disturbances (79 patients, 31.9%) and hair loss (78 patients, 31.5%). Of note, other symptoms such as mood disturbances (43%) or chest pain (41%) were frequent in the LSL tertile group. The rest of the symptoms and their distribution according to the tertiles of time off work are presented in table 2. In the 109 patients who lost weight, a statistically significant difference was observed according to the study groups, such that the third tertile, on LSL, had lost an average of 7.4±6.0 kg, greater than the loss of the first tertile (5.2±3.9 kg) and that of the second (4.6±3.7 kg) (Kruskal–Wallis test, p<0.03).

Multivariate analysis revealed that the factor most associated with LSL was the symptom of dyspnoea reported in the first post-COVID consultation (OR 3.26, 95% CI 1.59–6.70, p=0.0001). On the other hand, physical exercise of at least 10 min·day^{-1} was significantly associated with shorter sick leave (OR 0.45, 95% CI 0.20–0.98, p=0.04) (table 3). The mean time spent exercising for the entire study population was 40.4±38.6 min.

Subgroup analysis

In the subgroup of 209 patients requiring hospital admission, a statistically significant association was found between age (p=0.004), asthma (p=0.04), duration of hospitalisation (p=0.0001) and LSL. Table 4 presents the characteristics and medical history of these patients. No laboratory results at the time of hospital admission were significantly associated with LSL, whereas severe respiratory failure and bilateral pneumonia were (supplementary table 1). When the symptoms reported in the first consultation after admission were analysed, except for cough, hair loss, sleep and voice disturbances, the same results of the association of factors with LSL were replicated in the entire study group (supplementary table 2). Therapeutic features such as high-flow nasal cannula or tocilizumab were significantly associated with LSL (supplementary table 3).

Proportionally, more women and more patients who reported the symptom of dyspnoea were observed in the subgroup of patients who did not have to be admitted (supplementary table 4). Finally, the Bayesian multivariate analysis determined the probability that younger age, obesity, asthma, symptoms of dyspnoea and asthenia reported in the first post-COVID evaluation were associated with LSL (table 5).

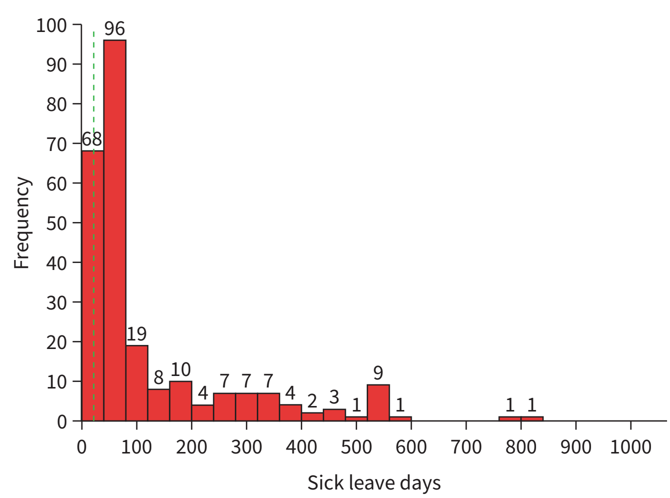

FIGURE 3 Frequency of post-COVID-19 patients and their sick leave days. The green dotted line shows the optimal sick leave time stipulated by the local Ministry of Employment in the worst-case scenario for viral pneumonia.

TABLE 2 Symptoms reported by patients seen for the first time in a post-COVID-19 consultation, after hospital discharge or active infection

Symptoms and characteristics	Total n=248	First tertile (⩽43 days) n=86	Second tertile (⩾44–82 days) n=78	Third tertile (⩾83 days) n=84	p-value
Dyspnoea, n (%)	144 (58.1)	35 (40.7)	41 (52.6)	68 (81.0)	0.0001
Cough, n (%)	43 (17.3)	11 (12.8)	10 (12.8)	22 (26.2)	0.03
Expectoration, n (%)	27 (10.9)	7 (8.1)	7 (9.0)	13 (15.5)	0.25
Haemoptysis, n (%)	1 (0.4)	0 (0.0)	0 (0.0)	1 (1.2)	0.38
Chest pain, n (%)	61 (24.7)	14 (16.3)	13 (16.7)	34 (41.0)	0.0001
Orthopnoea, n (%)	10 (4.0)	3 (3.5)	1 (1.3)	6 (7.1)	0.16
Fever, n (%)	4 (1.6)	0 (0.0)	3 (3.8)	1 (1.2)	0.14
Asthenia, n (%)	133 (53.6)	37 (43.0)	35 (44.9)	61 (72.6)	0.0001
Weight loss, n (%)	109 (44.0)	34 (39.5)	33 (42.3)	42 (50.0)	0.37
Mobility disorders, n (%)	11 (4.4)	0 (0.0)	3 (3.8)	8 (9.5)	0.01
Paraesthesia, n (%)	37 (15.0)	7 (8.1)	9 (11.5)	21 (25.3)	0.004
Voice alterations, n (%)	15 (6.0)	3 (3.5)	3 (3.8)	9 (10.7)	0.09
Swallowing disorders, n (%)	5 (2.0)	0 (0.0)	0 (0.0)	5 (6.0)	0.007
Exanthema, n (%)	14 (5.6)	2 (2.3)	5 (6.4)	7 (8.3)	0.22
Hair loss, n (%)	78 (31.5)	22 (25.6)	21 (26.9)	35 (41.7)	0.04
Sleep disturbances, n (%)	79 (31.9)	22 (25.6)	21 (26.9)	36 (42.9)	0.03
Deterioration of cognitive abilities, n (%)	41 (16.6)	13 (15.3)	5 (6.4)	23 (27.4)	0.001
Mood disturbance, n (%)	66 (26.6)	17 (19.8)	13 (16.7)	36 (42.9)	0.0001
Number of symptoms, mean±SD	3.5±2.4	2.6±2.1	2.9±1.9	5.1±2.4	0.0001
Arthralgias, n (%)	8 (3.2)	4 (4.7)	0 (0.0)	4 (4.8)	0.15
Headache, n (%)	15 (5.2)	2 (2.3)	4 (5.1)	7 (8.3)	0.21
Physical inactivity, n (%)	188 (75.8)	62 (72.1)	54 (69.2)	72 (85.7)	0.03

Discussion

The median sick leave time due to COVID-19 almost doubled the longest optimal time proposed for any other viral pneumonia, regardless of hospital admission. In fact, the median sick leave for the subgroup of patients not requiring hospitalisation was close to three times that of the OSL time. Additionally, long-COVID symptoms such as dyspnoea, asthenia, chest pain and hair loss were significantly associated with LSL. On the other hand, physical activity was associated with a reduction in LSL.

TABLE 3 Multivariate analysis by binary logistic regression of factors associated with longer sick leave of patients evaluated in a post-COVID-19 consultation

Factor	Univariate analysis (OR)	95% confidence interval	p-value	Multivariate analysis (OR)	95% confidence interval	p-value
Men	0.71	0.42–1.21	0.20	0.56	0.27–1.16	0.12
Age	1.04	1.02–1.07	0.001	1.03	0.99–1.01	0.06
Obesity	1.43	0.84–2.44	0.19	1.08	0.58–2.00	0.81
Asthma	2.18	1.03–4.61	0.04	1.54	0.63–3.75	0.34
Dyspnoea	4.92	2.63–9.20	0.0001	3.26	1.59–6.70	0.001
Asthenia	3.39	1.92–5.99	0.0001	1.98	1.04–3.76	0.04
Chest pain	3.45	1.89–6.29	0.0001	2.01	1.01–3.99	0.04
Hair loss	2.01	1.15–3.50	0.01	2.15	1.02–4.55	0.04
Sleep disturbances	2.11	1.21–3.68	0.008	1.07	0.53–2.15	0.85
Mood disturbance	3.35	1.86–6.02	0.0001	1.47	0.70–3.05	0.31
Daily physical exercise	0.52	0.30–0.89	0.009	0.45	0.20–0.98	0.04
Arterial hypertension	0.81	0.45–1.46	0.48			
Dyslipidaemia	1.07	0.58–1.99	0.82			
Diabetes	1.25	0.54–2.89	0.60			
Obstructive sleep apnoea	1.18	0.42–3.38	0.75			
Hospitalisation	1.18	0.57–2.47	0.66			

Variables included in the multivariate analysis: sex (men), age, obesity, asthma, dyspnoea, asthenia, chest pain, hair loss, sleep disturbances, mood disturbance and daily physical exercise of at least 10 min·day^{-1}.

TABLE 4 Sociodemographic characteristics and medical history of patients seen in a post-COVID-19 consultation who required hospitalisation, according to the duration of their sick leave

Characteristic	Total N=209	First tertile (⩽43 days) n=74	Second tertile (⩾44–82 days) n=63	Third tertile (⩾83 days) n=72	p-value
Age, mean±SD years	52.6±10.2	49.5±11.5	53.3±10.4	55.2±7.7	0.003
Sex, men (%)	121 (57.9)	43 (58.1)	40 (63.5)	38 (31.4)	0.45
Obesity, n (%)	89 (42.6)	29 (39.2)	26 (41.3)	34 (47.2)	0.60
Body mass index, mean±SD kg·m^{-2}	29.4±5.8	28.7±5.9	29.1±5.0	30.4±6.1	0.18
Arterial hypertension, n (%)	63 (30.1)	18 (24.3)	25 (39.7)	20 (27.8)	0.13
Dyslipidaemia, n (%)	49 (23.4)	15 (20.3)	16 (25.4)	18 (25.0)	0.72
Asthma, n (%)	26 (12.4)	10 (13.5)	2 (7.7)	14 (19.4)	0.02
Diabetes, n (%)	23 (11.0)	7 (9.5)	7 (11.1)	9 (12.5)	0.84
Obstructive sleep apnoea, n (%)	14 (6.7)	4 (5.4)	4 (6.3)	6 (8.3)	0.77
Ischaemic heart disease, n (%)	5 (2.4)	3 (4.1)	2 (3.2)	0 (0.0)	0.25
Heart failure, n (%)	2 (1.0)	0 (0.0)	2 (3.2)	0 (0.0)	0.10
COPD, n (%)	5 (2.4)	0 (0.0)	4 (6.3)	1 (1.4)	0.04
Days of hospital admission, median (IQR)	11 (7–17)	8.5 (6.8–11.2)	12 (7.0–16.0)	16.5 (11.0–35.0)	0.0001

IQR: interquartile range.

These findings are in line with other population studies, which determined that the duration of COVID-19 sick leave was longer than other infections plausibly of viral aetiology with flu-like symptoms [18]. For practical purposes, factors associated with LSL could be divided into two groups, namely sociodemographic factors (age and sex) and medical history (asthma, obesity), and a second group of long-COVID symptoms.

Older age has been described as a factor associated with LSL due to COVID-19 [19, 20]. In our series, older age was associated with longer sick leaves in the univariate analysis, but not in the multivariate one by a very narrow margin. This might be due to the fact that a good proportion of the patients in our study were from the first and second waves of COVID-19 and presented homogeneous data about their age, with a mean±SD age of 52±10 years and a difference of only 4 years between the 60th and 100th percentiles. This age is considerably lower than in another series from the city of Madrid, where the mean age was nearly 65 years [21]. This suggests an underrepresentation of older working-age individuals, who might have skewed the association measure more strongly towards the logical side: the older the patient, the greater the impact of the disease and, consequently, longer sick leave durations. The fact that age appeared as a protective factor in the Bayesian analysis is notable, but it should be noted that the confidence interval is very close to 1 and, in any case, the Bayesian analysis was not the primary analysis of the study but rather an exploratory one.

Regarding sex, discordant results are also found. Some studies have associated being a woman with LSL [18, 20, 22], while other authors do not find such an association [23], as in our sample. Regarding medical history, the pre-existence of lung diseases was significantly associated with LSL [19, 24]. In our series, the

TABLE 5 Parametric Bayesian proportional hazards analysis of factors associated with longer sick leave of patients evaluated in a post-COVID-19 consultation

Factor	Hazard ratio	95% credibility interval
Men	0.90	0.70–1.14
Age	0.97	0.96–0.99
Obesity	1.28	1.05–1.57
Asthma	1.48	1.06–1.95
Dyspnoea	1.82	1.50–2.20
Asthenia	1.26	1.01–1.57
Chest pain	1.19	0.87–1.60
Hair loss	1.12	0.83–1.49
Sleep disturbances	1.12	0.88–1.34
Mood disturbance	1.25	0.92–1.60
Daily physical exercise	0.91	0.70–1.16

asthmatic population, almost 13% of the patients studied, a percentage representative of the global prevalence [25], seemed to be at greater risk of LSL in the Bayesian analysis. It is possible that the overlap of post-COVID respiratory symptoms and asthma has played a role in prolonging this condition. Finally, obesity, a factor associated with poor clinical outcomes such as an increase in mortality [26] or the probability of hospital admission because it is a more severe clinical condition compared to patients with normal weight [27], was also associated with LSL in the Bayesian analysis. A similar result was found in a study carried out in Sweden on healthcare personnel in nursing homes not requiring hospitalisation [28].

One of the most important findings of our study was that the sick leave observed was longer than that documented in population-based studies from other countries, such as Sweden (35 days) [25, 29], the Netherlands (10 days) [18] and Germany (only 6% of patients with sick leaves longer than 4 weeks) [22]. The fact that more than 80% of our population was hospitalised could explain this difference, but economic and cultural factors may have also played a decisive role. In Spain, the Social Security Service classified COVID-19 as an occupational accident starting on 10 March 2020, meaning that coverage began on day 0 of the infection, along with recognition of up to 75% of the worker's taxable salary. For healthcare professionals, it was recognised as an occupational disease in February 2021, which not only included the same characteristics of day 0 of the infection and 75% of the salary, but also allowed for retrospective claims if the illness was sufficiently well documented, along with other benefits such as a change in workplace or job duties due to disability caused by COVID-19 or its sequelae [30]. In Sweden, the first 2 weeks of sick leave was paid by the employer, after which 60% of the salary was covered by the Swedish social insurance agency. Furthermore, it has been reported that guidelines for COVID-19 were vague due to a lack of knowledge of the prognosis of the disease [29, 31]. All these factors could explain why Swedish workers returned to work sooner than the Spanish ones. The fact that there are significant differences compared to other populations whose social security systems were already generous before the pandemic could be explained by cultural differences. For example, the sick leave for COVID-19 in the Dutch population was 10 days, although it is possible that many patients from the first wave are not sufficiently represented in this study [18]. In the Netherlands, employers must pay benefits to workers on sick leave for a period of 2 years at a statutory rate of 70% of the salary, with a maximum of 70% of the daily wage. In many collective labour agreements, this percentage is topped up to 90 or 100% of the salary or maximum daily wage during the first year of sick leave [32].

It is well known that population-based studies can present significant limitations. Selection bias, poor control of potential confounding variables and a lack of standardisation in error measurement are perhaps the most important ones [33–35]. Although our study focuses on a specific moment during the pandemic and is not large enough to be extrapolated to the general population, it included all patients who attended the outpatient clinic and met the inclusion criteria, including microbiological documentation of COVID-19. Population studies acknowledge the limitation of potentially including patients without confirmation of COVID-19 infection or direct comparators, such as influenza, as these studies often relied on clinical symptoms reported by patients due to the shortage of tests at the beginning of the pandemic [24, 29]. It is also important to note that most of the patients in our study were hospitalised and we have detailed information about their clinical, analytical and radiological evolution, a variable not deeply studied in population-based studies and a major limitation recognised by others [22, 24, 31]. Our study collected information obtained from a strict follow-up protocol and, while only the symptoms reported in the first consultation are presented, a follow-up was conducted to determine the duration and severity of these symptoms. Finally, since we had no more information than what was collected during the consultation, we decided to present not only the raw data on sick leave due to COVID-19 and its possible associated factors but also to consider the worst-case scenario of any other viral pneumonia recognised by the social security system. We compared this with COVID-19 to demonstrate the pandemic's significance and impact on the economically active population. To our knowledge, no other study has addressed this issue from this perspective, as others have compared COVID-19 sick leave with actual influenza sick leave or flu-like symptoms.

While it was no surprise that sicker patients who were hospitalised had LSL, we believe that one of the most interesting findings of our study was that sick leave from less severe patients, those who were not hospitalised, was not statistically different from admitted patients, despite this sick leave being calculated since hospital admission or discharge. Furthermore, hospitalisation was not associated with LSL in the univariate analysis and no significant differences were found in the number of symptoms reported by the two groups at their first visit to the outpatient clinic (supplementary table 4). This addresses the fact that long-COVID symptoms are present not only in patients experiencing the most severe cases in need of hospital treatment, but also in those patients who were less sick during the active infection. In addition, we have demonstrated that these symptoms have a negative impact in their journey back to work. We can only speculate about this result, but we believe that the mandatory lockdown imposed by authorities during most of 2020 and a large part of 2021, which hindered a more favourable physical and mental recovery of nonhospitalised patients, as well as the respiratory and motor rehabilitation programmes that could have better prepared hospitalised patients, may have contributed to this finding. Regarding residual symptoms, there is little literature that associates them with LSL. More than 90% of the patients could fit the definition of long COVID and only a third of them were off sick for more than 12 weeks. This could indicate that a significant percentage of patients returned to work despite continuing to have symptoms. Among these symptoms, the impact of dyspnoea as a relevant disabling factor is predominant, as with other chronic respiratory diseases such as COPD or interstitial diseases. Dyspnoea has also been described in other studies as a symptom associated with LSL [18, 28], but others in our series, such as asthenia, chest pain and hair loss, have not been documented in other similar studies.

The role of vaccination in the pandemic is worth mentioning. There are studies associating the first two doses of vaccines with the probability of sick leave due to symptoms such as fever, asthenia or pain at the puncture site [36]. Comparing the 1 or 2 days of these sick leaves to the median of almost 42 days in our sample, we take a stance in favour of vaccination as beneficial to society, not just from a health status point of view. Along these lines, the socioeconomic impact is notable not only for the direct and indirect costs that the pandemic entailed in terms of prevention and treatment of the disease, but also in the late return to work. Several articles refer to this long-COVID syndrome scenario and the impact it has had on the workplace. For example, in a longitudinal study of patients with long-COVID criteria, the percentage of people who were still on sick leave after a year of follow-up was practically unchanged, with 20.4% at the beginning of the study and 20.6% at the end of the year. In this study, of the sample analysed, about 27% were fired, had resigned or retired early due to long COVID. As a conclusion to these figures, they estimate that 47% of the sample presented income losses due to this cause [37]. Somewhat lower are the figures obtained in a Swedish sample where the percentage of sick leave due to long COVID was 13.3% [31]. The percentage of withdrawals recorded in a German study was much lower, with 5.8% of the entire sample [22], more in line with that obtained in another Swedish study with 5.7% of withdrawals [20].

The benefit of physical activity has been described in various scenarios of respiratory pathology, such as its association with the reduction of mortality due to pneumonia in middle-aged and elderly patients [38], which could fit with the profile included in the study. In our series, it was determined that those patients who performed at least 10 $min \cdot day^{-1}$ of physical activity had a 55% lower probability of having LSL. Evidence of the positive effect of physiotherapy on dyspnoea in patients with long-COVID syndrome has already been described [39, 40]. The promotion of healthy habits, including physical activity, is more than justified, but it is worth mentioning that one of the great difficulties of this type of intervention is maintaining the adherence of the potential beneficiary over time.

The study has several limitations. Its observational nature and a sample size of only 248 patients might have led it to selection bias and loss of data that could overstate its conclusions. To counteract these limitations, the longest OSL time was considered for analysis and multivariate analyses were developed, including one with a Bayesian approach, but attention to all possible confounders is practically impossible. Another limitation is the possible collinearity between some of the variables analysed, especially between symptoms. In this sense, it is important to know that long COVID is a complex and dynamic scenario in which the pathophysiology of the symptoms that simulate respiratory involvement in patients with normal lung function or without manifest parenchymal alterations is still unknown. Regarding physical activity, we acknowledge that asking patients how many minutes per day they exercised was not the best way to address this issue. Some patients show a maladaptive response to exercise, whereas others might have presented reverse causality since those who fully recovered with shorter sick leaves could exercise more, rather than exercise reducing their sick leave duration. Most patients were included during the first waves of the pandemic, when the entire healthcare system collapsed, and we wanted to keep things simple. Nevertheless, we believe that promoting the message that healthy habits, such as daily physical activity, are beneficial for respiratory patients is well-intentioned, despite the potential for maladaptive responses in some individuals, which should be assessed by health professionals. Finally, detailed analysis was not carried out regarding the waves of the pandemic or vaccination status. During the collection and follow-up years, it could be inferred that patients from the first five waves were included, but less than 20% of the patients studied were infected in 2021, the year in which mass vaccination of the population began. Therefore, it is not considered that this would have significantly modified the results.

The paper also has strengths. It is one of the few studies that has analysed in more detail the presence of symptoms possibly framed in long COVID and analytical alterations with LSL, unlike other more population-based works. In this regard, respiratory symptoms were prevalent and rather debilitating to both admitted and nonadmitted patients, which highlights the socioeconomic impact of returning to work for every person affected by COVID-19 and not only to the most severe cases. We also want to point out that our study is specific to a post-COVID outpatient consultation in one of the hospitals most affected in the world by the pandemic during the first wave [41] and this represents the best of our efforts to accompany our patients throughout their recovery.

Conclusions

Sick leave due to COVID-19 was considerably longer than that stipulated for non-SARS-CoV-2 viral pneumonia. To the direct impact of the health cost and the economic disaster caused by the need for isolation, the impact on the working life of the infected economically active population should also be added. A series of factors, such as age and obesity, seems to be associated with LSL, while physical activity is presented as a protective factor. Finally, long-COVID syndrome, with its constellation of symptoms, seems to be a very present factor in the inability of these patients to work.

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