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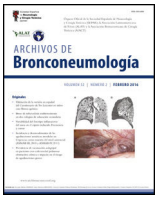

Scientific Letter

Long-term Outcomes in Critical COVID-19 Survivors: A 2-Year Longitudinal Cohort

To the Director,

With the progression of the coronavirus disease 2019 pandemic (COVID-19), evidence has pointed critically ill survivors as one of the populations most at risk of experiencing long-term impairment and persistent COVID-19 symptoms.[1,2] Despite the large number of ICU admissions that COVID-19 has caused and the impact of this on health care systems worldwide,[3] ICU patient cohorts remain underrepresented in studies of COVID-19 survivors.[1] Additionally, studies focusing on post-ICU COVID-19 patients are limited to one-year follow-up periods without exploring all health care outcome domains and their trajectories.[2–4] For these reasons, our objective was to explore 24-month health outcomes in a cohort of patients who required ICU admission to describe the longitudinal progress of (1) pulmonary function tests, (2) radiological abnormalities, (3) symptoms and (3) quality of life, as well as to determine their (4) impact on health care resources consumption during the follow-up. This was a prospective observational study among patients who required ICU admission due to severe COVID-19 between March and December 2020 at the University Hospitals Arnau de Vilanova and Santa Maria of Lleida, Catalonia, Spain. This study was a sub-study of the CIBERESUCICOVID study (ClinicalTrials.gov Identifier: NCT04457505) and details of the protocol and follow-up were previously described.[5–7]

During the study period, a total of 209 critical COVID-19 patients survived, and 180 were eligible to be followed in the post-COVID consultation. Patients were evaluated at 6, 12 and 24 months after hospital discharge. Finally, 109 completed all visits over 24 months after hospital discharge. Five patients died during the follow-up. Baseline characteristics and ICU data are summarized in Table 1A. Over 2 years, patients showed a progressive recovery of lung function and exercise capacity (Fig. 1). However, at 24 months, there were still 45.7% with impairment in lung diffusing capacity (DLCO), and 18.7% of them was moderate to severe (Table 1A). Importantly, patients who required invasive mechanical ventilation (IMV) showed worse DLCO values with an adjusted difference (95% confidence interval (CI)) of −11.03% (−17.03 to −4.93; $p < 0.001$) compared to non-intubated patients. Furthermore, these patients had a higher risk of presenting impairment of other lung function parameters and in the six-minute walking test (6MWT) (Table 1B). Something similar happens regarding radiological abnormalities (Table 1B and Fig. 1). At 2 years, more than half of the patients (53.9%) presented some type of lesion (39.2% reticular lesions and 12.7% fibrotic involvement). Again, pulmonary lesions were more prevalent among intubated patients, with an adjusted odds ratio (OR) (95% CI) of 2.63 (1.10–6.28; p value = 0.0293) for reticular lesions and 4.01 (1.61–9.99; p value = 0.0029) for interlobular septal thickening. The fibrotic pattern was more frequent among intubated patients (20.4% vs. 8.3%), and the mean (SD) total severity score (TSS) was higher (2.23 [2.38] vs. 1.33 [1.92]) (Table 1B).

A global progressive improvement was observed in symptoms, anxiety, depression, quality of life and cognition levels (Fig. 1), with scores and punctuations similar to those of general population (Table 1B). Nevertheless, 35%, 14%, 10.9%, and 7.9% had persistently abnormal scores for fatigue, cognition, anxiety and depression at 2 years, respectively. There were no differences between intubated or non-intubated patients (Table 1B). Additionally, at this time point, patients presented a mean (SD) number of persisting symptoms of 5.87 (4.56), with a total of 54.3% of patients meeting the post-COVID syndrome or long COVID definition.[8] The burden of symptoms and comorbidities was associated with quality of life and with consumption of health resources, but not with lung functional status or radiological abnormalities on the chest CT (data not shown). During the second year, a significant reduction was observed in outpatient clinic visits compared to the previous year (mean difference of −7.21 [5.35–9.06; $p < 0.001$]) and in emergency visits (37.64% at first-year follow-up vs. 21.27% at two-year follow-up; $p < 0.001$). A total of 61 (57.54%) patients attended a pulmonary rehabilitation program during the follow-up and 24.6% had not returned to work two years after hospital discharge.

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Table 1A
Baseline Sociodemographic and Clinical Characteristics (at Hospital and ICU Admission) According to Invasive Mechanical Ventilation Requirement at the 24-Month Follow-up Visit.

	Global (*N* = 109) Median [p25;p75] or *n* (%)	ICU (*N* = 50) Median [p25;p75] or *n* (%)	ICU + IMV (*N* = 59) Median [p25;p75] or *n* (%)	*p* Value	*N*
Sociodemographic data					
Age, years	60.0 [52.0;66.0]	57.5 [49.2;64.0]	62.0 [53.5;67.0]	0.132	109
Sex, women	34 (31.2%)	19 (38.0%)	15 (25.4%)	0.228	109
Smoking history				0.922	107
Nonsmoker	49 (45.8%)	22 (44.0%)	27 (47.4%)		
Current smoker	2 (1.87%)	1 (2.00%)	1 (1.75%)		
Former smoker	56 (52.3%)	27 (54.0%)	29 (50.9%)		
BMI	28.7 [26.2;33.5]	28.3 [26.1;33.7]	29.7 [26.8;33.5]	0.328	109
Comorbidities					
Obesity	43 (39.4%)	16 (32.0%)	27 (45.8%)	0.205	109
Hypertension	50 (45.9%)	21 (42.0%)	29 (49.2%)	0.580	109
Diabetes mellitus (type I/II)	21 (19.3%)	4 (8.00%)	17 (28.8%)	0.012	109
Chronic heart disease	8 (7.34%)	3 (6.00%)	5 (8.47%)	0.724	109
COPD/bronchiectasis	5 (4.59%)	2 (4.00%)	3 (5.08%)	1.000	109
Asthma	7 (6.42%)	3 (6.00%)	4 (6.78%)	1.000	109
Hospital data					
Symptoms to hospital admission, days	7.00 [5.00;8.00]	7.00 [4.00;8.00]	7.00 [5.00;8.00]	0.753	108
Arterial blood gas					
Partial pressure of oxygen (PaO_2)	64.0 [53.5;73.8]	67.0 [55.2;75.2]	61.0 [50.2;72.8]	0.247	100
Partial pressure of carbon dioxide ($PaCO_2$)	34.0 [31.0;38.0]	33.0 [31.0;37.0]	34.0 [31.0;38.8]	0.693	100
PaO_2 to FiO_2 ratio	203 [133;271]	220 [142;295]	189 [128;238]	0.048	100
ICU data					
Symptoms to ICU admission, days	8.00 [7.00;11.0]	9.00 [5.75;12.0]	8.00 [7.00;10.0]	0.312	107
Hospitalization before ICU admission, days	1.00 [0.00;2.00]	1.00 [0.00;3.00]	0.00 [0.00;2.00]	0.128	108
APACHE score	10.0 [8.50;12.5]	9.00 [8.00;11.0]	10.5 [9.00;13.0]	0.170	31
Arterial blood gas					
Respiratory rate, bpm	27.0 [22.0;32.0]	27.0 [23.0;29.5]	26.0 [22.0;32.0]	0.956	105
Partial pressure of oxygen (PaO_2)	69.5 [55.0;92.8]	69.0 [58.5;88.0]	70.5 [52.5;98.8]	1.000	88
Partial pressure of carbon dioxide ($PaCO_2$)	36.0 [32.2;41.0]	36.0 [33.5;39.5]	37.0 [31.5;43.0]	0.517	90
PaO_2 to FiO_2 ratio	134 [95.0;176]	134 [110;150]	133 [86.9;189]	0.701	85

Table 1A (*Continued*)

	Global (*N* = 109) Median [p25;p75] or *n* (%)	ICU (*N* = 50) Median [p25;p75] or *n* (%)	ICU + IMV (*N* = 59) Median [p25;p75] or *n* (%)	*p* Value	*N*
Pharmacological treatment					
Hydroxychloroquine	57 (52.3%)	17 (34.0%)	40 (67.8%)	0.001	109
Corticosteroids	89 (81.7%)	40 (80.0%)	49 (83.1%)	0.872	109
Antibiotics	100 (91.7%)	42 (84.0%)	58 (98.3%)	0.011	109
Remdesivir	21 (19.3%)	16 (32.0%)	5 (8.47%)	0.004	109
Tocilizumab	53 (48.6%)	24 (48.0%)	29 (49.2%)	1.000	109
Procedures					
Ventilatory support					
NIMV	68 (62.4%)	32 (64.0%)	36 (61.0%)	0.903	109
NIMV (days)	1.00 [0.00;3.00]	2.00 [0.00;4.00]	1.00 [0.00;3.00]	0.062	104
IMV	59 (54.1%)	0 (0.00%)	59 (100%)		109
IMV (days)			15.0 [9.00;25.0]		59
Prone positioning	58 (53.7%)	10 (20.4%)	48 (81.4%)	<0.001	108
Prone position duration (h)	4.00 [0.00;38.5]	0.00 [0.00;0.00]	28.0 [11.0;68.0]	<0.001	103
Ventilatory setting and pulmonary mechanics					
FiO_2, %			75.0 [60.0;94.5]		59
PEEP, cmH_2O			14.0 [12.0;15.0]		59
Driving pressure, cmH_2O[a]			12.0 [10.0;14.0]		46
Ventilatory ratio[a]			1.50 [1.30;1.96]		48
Hospital outcomes					
Hospitalization (days)	23.0 [14.0;37.0]	15.0 [11.0;18.8]	34.0 [23.0;44.5]	<0.001	109
ICU stay (days)	12.0 [6.00;22.0]	6.00 [4.00;8.00]	20.0 [14.5;31.0]	<0.001	109
Hospital complications					
Bacterial pneumonia	10 (9.26%)	1 (2.04%)	9 (15.3%)	0.021	108
Pulmonary embolism	2 (1.85%)	1 (2.04%)	1 (1.69%)	1.000	108
Bacteraemia	24 (22.2%)	1 (2.04%)	23 (39.0%)	<0.001	108
Acute renal failure	23 (21.3%)	1 (2.04%)	22 (37.3%)	<0.001	108
Infectious complications	28 (25.9%)	1 (2.04%)	27 (45.8%)	<0.001	108

Abbreviations: COPD, chronic obstructive pulmonary disease; NIMV, noninvasive mechanical ventilation; IMV, invasive mechanical ventilation.

[a] Defined as plateau pressure – PEEP.

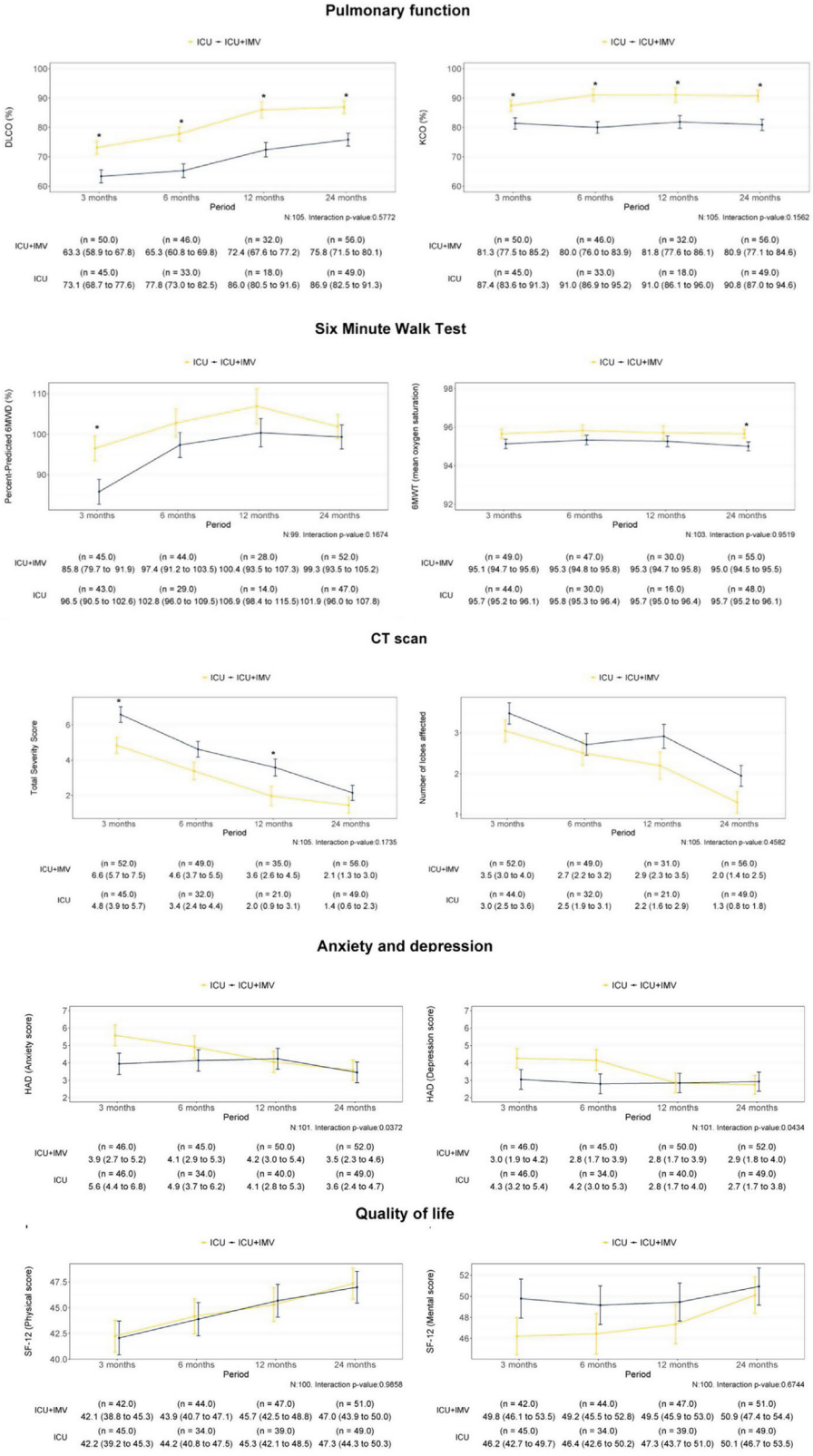

Fig. 1. Longitudinal progression of outcomes according to severity. Outcome evolution was fitted using linear mixed models that were adjusted for confounding factors (age, sex and body mass index). Estimated marginal means (±standard errors) of outcomes over time are described in the figure. Statistically significant differences between groups are indicated with an asterisk. Longitudinal progression of lung function and exercise capacity at follow-up points (3, 6, 12 and 24 months). Note: Lung function and exercise capacity parameters were classified as invasive mechanical ventilation (IMV) required (ICU + IMV) and non-intubated patients (ICU). Longitudinal progression of CT scan findings at follow-up points (3, 6, 12 and 24 months). Note: Total severity score and number of lobes affected were classified as IMV required (ICU + IMV) and non-intubated patients (ICU). *Abbreviations*: D_{LCO}, diffusing capacity for carbon monoxide; IMV, invasive mechanical ventilation; KCO, carbon monoxide transfer coefficient; 6MWT, six-minute walking test; CT, computed tomography. Longitudinal progression of anxiety, depression and quality of life during the follow-up. Outcome evolution was fitted using linear mixed models that were adjusted for confounding factors (age, sex and body mass index). Estimated marginal means (±standard errors) of outcomes over time are described in the figure. Statistically significant differences between groups are indicated with an asterisk. *Abbreviations*: ICU, intensive care unit; IMV, invasive mechanical ventilation; HADS, Hospital Anxiety and Depression Scale.

Table 1B
Pulmonary Function, Exercise Test, CT Findings, Symptoms and Quality of Life, Anxiety, and Depression Questionnaire Results at the 24-Month Follow-up Visit.

	Global (*N* = 109) Median [p25;p75] or *n* (%)	ICU (*N* = 50) Median [p25;p75] or *n* (%)	ICU + IMV (*N* = 59) Median [p25;p75] or *n* (%)	*N*	Adjusted* OR (95% CI) or Mean Difference (95% CI)
Pulmonary function	(*N* = 105)	(*N* = 49)	(*N* = 56)		
DLCO, %	81.1 (16.4)	87.1 (15.7)	75.9 (15.3)	105	−11.03 (−17.13 to −4.93; *p* value = 0.0006)
Abnormal (<0.8)	48 (45.7%)	13 (26.5%)	35 (62.5%)	105	4.25 (1.80 to 10.01; *p* value = 0.0009)
KCO, %	84.8 (14.9)	90.7 (15.3)	79.7 (12.6)	105	−8.91 (−13.97 to −3.86; *p* value = 0.0008)
FEV1, %	94.9 (15.2)	98.5 (13.5)	91.7 (15.9)	105	−7.33 (−12.81 to −1.86; *p* value = 0.0100)
Abnormal (<0.8)	14 (13.6%)	3 (6.25%)	11 (20.0%)	103	3.51 (0.88 to 14.09; *p* value = 0.0764)
FVC, %	90.4 (14.9)	93.1 (13.6)	88.0 (15.6)	105	−5.74 (−11.18 to −0.31; *p* value = 0.0410)
Abnormal (<0.8)	26 (25.2%)	9 (18.8%)	17 (30.9%)	103	2.11 (0.80 to 5.56; *p* value = 0.1306)
FEV1 to FVC ratio	80.5 (6.41)	81.4 (6.29)	79.8 (6.49)	105	−0.94 (−3.37 to 1.48; *p* value = 0.4475)
TLC, %	93.0 (16.0)	93.4 (14.1)	92.7 (17.5)	105	−0.93 (−6.98 to 5.11; *p* value = 0.7629)
Abnormal (<0.8)	20 (19.0%)	8 (16.3%)	12 (21.4%)	105	1.49 (0.53 to 4.18; *p* value = 0.4439)
RV, %	104 (31.6)	103 (30.0)	106 (33.2)	105	3.56 (−8.93 to 16.04; *p* value = 0.5779)
RV/TLC, %	38.3 (7.01)	37.4 (7.32)	39.0 (6.71)	105	2.17 (−0.36 to 4.70; *p* value = 0.0963)
6MWT	(*N* = 103)	(*N* = 48)	(*N* = 55)		
Distance, m	450 (81.8)	460 (66.4)	441 (92.9)	103	−20.06 (−50.12 to 10.01; *p* value = 0.1941)
PP-6MWD (%)	96.1 (22.0)	98.9 (23.2)	93.6 (20.8)	99	−2.52 (−10.11 to 5.08; *p* value = 0.5175)
Oxygen saturation, %					
Initial	96.5 (1.34)	96.8 (0.95)	96.3 (1.57)	103	−0.42 (−0.92 to 0.07; *p* value = 0.0991)
Final	95.2 (2.09)	95.8 (2.03)	94.7 (2.03)	103	−0.93 (−1.73 to −0.14; *p* value = 0.0231)
Minimal	94.3 (2.20)	94.7 (2.12)	94.0 (2.22)	103	−0.67 (−1.52 to 0.18; *p* value = 0.1247)
Average	95.3 (1.61)	95.7 (1.43)	95.0 (1.69)	103	−0.63 (−1.24 to −0.02; *p* value = 0.0469)
Initial RPE	0.39 (1.08)	0.31 (0.88)	0.46 (1.24)	102	0.21 (−0.22 to 0.64; *p* value = 0.3361)
Final RPE	1.52 (2.30)	1.17 (1.71)	1.83 (2.70)	102	0.67 (−0.25 to 1.59; *p* value = 0.1547)
Chest CT scan findings	(*N* = 103)	(*N* = 49)	(*N* = 54)		
Density					
Ground-glass	44 (43.1%)	19 (39.6%)	25 (46.3%)	102	1.24 (0.54 to 2.83; *p* value = 0.6149)
Consolidation	3 (2.94%)	0 (0.00%)	3 (5.56%)	102	n.a.
Internal structures					
Interlobular septal thickening	66 (64.7%)	23 (47.9%)	43 (79.6%)	102	4.01 (1.61 to 9.99; *p* value = 0.0029)
Bronchiectasis	57 (55.9%)	22 (45.8%)	35 (64.8%)	102	1.99 (0.86 to 4.60; *p* value = 0.1095)
Atelectasis	20 (19.6%)	11 (22.9%)	9 (16.7%)	102	0.69 (0.25 to 1.88; *p* value = 0.4636)
Lesions					
Fibrotic	15 (14.7%)	4 (8.33%)	11 (20.4%)	102	2.44 (0.71 to 8.42; *p* value = 0.1583)
Reticular	40 (39.2%)	13 (27.1%)	27 (50.0%)	102	2.63 (1.10 to 6.28; *p* value = 0.0293)
No. of lobes affected by ground-glass or consolidative opacities	1.63 (1.79)	1.22 (1.61)	1.98 (1.88)	105	0.62 (−0.05 to 1.29; *p* value = 0.0710)
TSS	1.81 (2.21)	1.33 (1.92)	2.23 (2.38)	105	0.73 (−0.10 to 1.55; *p* value = 0.0870)
Sequelae symptoms					
Number of symptoms	5.87 (4.56)	5.60 (4.89)	6.12 (4.26)	99	0.90 (−0.88 to 2.68; *p* value = 0.3251)
Smell or taste disorder	28 (28.0%)	13 (26.5%)	15 (29.4%)	100	1.15 (0.46 to 2.83; *p* value = 0.7668)
Headache	20 (20.2%)	10 (20.8%)	10 (19.6%)	99	1.09 (0.39 to 3.04; *p* value = 0.8699)
Reduced fitness	61 (61.0%)	28 (57.1%)	33 (64.7%)	100	1.49 (0.64 to 3.46; *p* value = 0.3592)
Muscle weakness	52 (52.0%)	23 (46.9%)	29 (56.9%)	100	1.54 (0.69 to 3.48; *p* value = 0.2940)
Joint complaints	52 (52.0%)	24 (49.0%)	28 (54.9%)	100	1.40 (0.62 to 3.17; *p* value = 0.4140)
Hair loss	33 (33.0%)	16 (32.7%)	17 (33.3%)	100	1.15 (0.48 to 2.78; *p* value = 0.7528)
Concentration and/or memory problems	46 (46.0%)	24 (49.0%)	22 (43.1%)	100	0.96 (0.42 to 2.24; *p* value = 0.9316)
Sleeping problems	35 (35.0%)	13 (26.5%)	22 (43.1%)	100	2.63 (1.07 to 6.46; *p* value = 0.0343)
Tingling and/or pain in extremities	40 (40.0%)	18 (36.7%)	22 (43.1%)	100	1.42 (0.62 to 3.23; *p* value = 0.4073)
Questionnaires					
BC-CCI, total score	4.05 (4.76)	3.82 (4.69)	4.27 (4.87)	100	0.47 (−1.46 to 2.41; *p* value = 0.6327)
Abnormal (≥5)	35 (35.0%)	16 (32.7%)	19 (37.3%)	100	1.21 (0.52 to 2.80; *p* value = 0.6556)
FACIT, total score	42.6 (10.0)	42.5 (9.68)	42.6 (10.4)	100	0.06 (−4.02 to 4.13; *p* value = 0.9785)
Abnormal (<30)	14 (14.0%)	5 (10.2%)	9 (17.6%)	100	1.81 (0.55 to 5.95; *p* value = 0.3308)
Dyspnoea, score	0.47 (0.68)	0.39 (0.57)	0.53 (0.75)	107	0.14 (−0.13 to 0.40; *p* value = 0.3104)
Abnormal (>0)	39 (36.4%)	17 (34.7%)	22 (37.9%)	107	1.19 (0.53 to 2.68; *p* value = 0.6752)
Quality of life (SF12)					
Physical score	47.7 (9.38)	47.7 (10.0)	47.8 (8.85)	100	−0.14 (−3.94 to 3.66; *p* value = 0.9433)
Mental score	51.0 (9.40)	50.2 (10.6)	51.7 (8.13)	100	1.00 (−2.76 to 4.75; *p* value = 0.6041)
Anxiety score	3.21 (3.53)	3.47 (3.78)	2.96 (3.31)	101	−0.23 (−1.64 to 1.17; *p* value = 0.7465)
Abnormal (≥8)	11 (10.9%)	7 (14.3%)	4 (7.69%)	101	0.63 (0.16 to 2.45; *p* value = 0.5050)
Depression score	2.68 (3.38)	2.65 (3.07)	2.71 (3.68)	101	−0.02 (−1.38 to 1.35; *p* value = 0.9806)

Table 1B (*Continued*)

	Global (*N* = 109) Median [p25;p75] or *n* (%)	ICU (*N* = 50) Median [p25;p75] or *n* (%)	ICU + IMV (*N* = 59) Median [p25;p75] or *n* (%)	*N*	Adjusted* OR (95% CI) or Mean Difference (95% CI)
Abnormal (≥8)	8 (7.92%)	4 (8.16%)	4 (7.69%)	101	0.81 (0.19 to 3.51; *p* value = 0.7798)
No return to work[a]	15 (24.6%)	7 (22.6%)	8 (26.7%)	61	1.61 (0.46 to 5.67; *p* value = 0.4614)

Abbreviations: ICU, intensive care unit; IMV, invasive mechanical ventilation; D_{LCO}, diffusing capacity for carbon monoxide; KCO, carbon monoxide transfer coefficient; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; TLC, total lung capacity; RV, residual volume; 6MWT, six-minute walking test; PP-6MWT, percentile predicted six-minute walking test; RPE, rate of perceived exertion scale; CT, computed tomography; TSS, total severity score; BC-CCI, British Columbia Cognitive Complaints Inventory; FACIT, Functional Assessment of Chronic Illness Therapy; SF-12, 12-Item Short Form Survey.

[a] Patients with previous job.

* adjusted for confounding factors (age and sex)

In addition to COVID-19[1] and SARS,[9] long-term studies of patients who survive to an acute respiratory distress syndrome (ARDS) have yielded similar results. One of the largest and most important studies,[10] which followed 64 patients with ARDS for 5 years, curiously found worse functional results than ours at 24 months, with mean DLCO values of 78% (IQR: 63–89) and a percentile predicted six-minute walking distance (PP-6MWD) of 68%. The study also demonstrated an alteration in quality of life, and the proportion of patients who returned to work was lower (65%). Persistent symptoms were also present, and the number of comorbidities was also related to high health care consumption during follow-up. Additionally, mechanical ventilation[11,12] and its adjunctive therapies (neuromuscular blockade, sedation, prone positioning, recruitment manoeuvres, etc.),[13] as well as its classic complications (ventilator-induced pneumonia, sepsis, multiorgan failure, etc.),[14] increase patients' susceptibility to long-term sequelae.[15] Thus, severe lung injury implies important long-term multidimensional sequelae that go beyond respiratory involvement. Research priorities must include a deep understanding of severe lung injury consequences to develop more effective follow-up involving rehabilitation programs for long-term outcomes after critical illness.

Regarding symptoms and post-COVID syndrome our results are in line with others.[1] Curiously, despite the high number of symptoms and cases of long COVID, most survivors returned to work, as previously described in COVID-19 and SARS.[16] Due to the heterogeneity of follow-up and the definition of long COVID in the studies, comparing symptoms, mental disorders, quality of life and the proportion of patients with post-COVID syndrome is methodologically challenging. Additionally, most symptoms are unspecific, and quality of life and mental disorders are influenced by multiple factors, such as isolation, loss of loved ones, financial crises, and baseline comorbidities.[17] In general, patients progress and tend to return to normal daily life[1]; however, as our results suggest, symptom burden is related to health care consumption. For this reason, it is urgent to advance the knowledge of the pathogenesis of long COVID to apply effective interventions and improve the follow-up of survivors.

Our study has some limitations. First, this was a small observational study from a single city conducted during the early stages of the pandemic, which may reduce the generalizability of the findings and might not directly extend to the long-term consequences of patients infected with later SARS-CoV-2 variants. However, patients were well characterized, and the data were thoroughly revised and validated, in contrast to registry-based studies. The loss to follow-up implied that patients who did not participate had fewer symptoms, which might result in an overestimated prevalence of long COVID symptoms. However, great effort was made to avoid loss to follow-up, and our proportion was lower than that in other studies. Finally, there was no information on pulmonary function test, symptoms or quality of life prior to infection.

In conclusion, critical COVID-19 survivors showed longitudinal improvements in respiratory symptoms and quality of life, and most of them returned to work within 2 years. However, there was still a high proportion of patients with functional and radiological abnormalities, especially intubated patients. A high burden of symptoms and post-COVID syndrome were present in the long term, affecting quality of life and implying high health care consumption. These results highlight the urgent need to explore in depth the pathogenesis not only of long COVID but also of the sequelae of severe lung injury.

Ethical Approval

The study was approved by the Medical Ethics Committee (CEIC/2273) and complies with the tenets of the Declaration of Helsinki. Informed consent was acquired from all patients in accordance with the ethics approval guidelines for the study.

Authors' Contributions

Ferran Barbé is the guarantor of the paper, taking responsibility for the integrity of the work as a whole, from inception to publication of the article. Jessica González, Maria Zuil, Ivan de Benítez, David de Gonzalo, Jordi de Batlle, Antoni Torres, and Ferran Barbe were responsible for the conception, design, interpretation, and drafting of the manuscript for important intellectual content. Statistical analyses were performed by Ivan de Benítez. Patient recruitment and evaluation were performed by Maria Aguilà, Sally Santisteve, Aida Monge, Natalia Varvara, Anna Montcusí, Faty Seck, Clara Gort-Paniello, Rafaela Vaca, Olga Mínguez, Jesus Caballero and Carmen Barberà.

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Competing Interests

None declared.

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References

1. Huang L, Li X, Gu X, Zhang H, Ren L, Guo L, et al. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study. Lancet Respir Med. 2022;10:863–76.
2. Heesakkers H, van der Hoeven JG, Corsten S, Janssen I, Ewalds E, Simons KS, et al. Clinical outcomes among patients with 1-year survival following intensive care unit treatment for COVID-19. JAMA. 2022;327:559–65.
3. Tan E, Song J, Deane AM, Plummer MP. Global impact of coronavirus disease 2019 infection requiring admission to the ICU: a systematic review and meta-analysis. Chest. 2021;159:524–36.
4. Taniguchi LU, Aliberti MJR, Dias MB, Jacob-Filho W, Avelino-Silva TJ. Twelve months and counting: following clinical outcomes in critical COVID-19 survivors. Ann Am Thorac Soc. 2023;20:289–95, http://dx.doi.org/10.1513/AnnalsATS.202207-630OC.
5. Torres A, Arguimbau M, Bermejo-Martín J, Campo R, Ceccato A, Fernandez-Barat L, et al. CIBERESUCICOVID: a strategic project for a better understanding and clinical management of COVID-19 in critical patients. Arch Bronconeumol. 2021;57:1–2, http://dx.doi.org/10.1016/J.ARBRES.2020.10.021.
6. González J, Zuil M, Benítez ID, de Gonzalo-Calvo D, Aguilar M, Santisteve S, et al. One year overview and follow-up in a post-COVID consultation of critically ill patients. Front Med. 2022;9:897990.
7. González J, Benítez ID, Carmona P, Santisteve S, Monge A, Moncusí-Moix A, et al. Pulmonary function and radiologic features in survivors of critical COVID-19. Chest. 2021;160:187–98, http://dx.doi.org/10.1016/j.chest.2021.02.062.
8. Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis. 2022;22:e102–7.
9. Lam MH-B, Wing Y-K, Yu MW-M, Leung CM, Ma RC, Kong AP, et al. Mental morbidities and chronic fatigue in severe acute respiratory syndrome survivors: long-term follow-up. Arch Intern Med. 2009;169:2142–7.
10. Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N, Cooper A, et al. Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med. 2011;364:1293–304.
11. Belli S, Balbi B, Prince I, Cattaneo D, Masocco F, Zaccaria S, et al. Low physical functioning and impaired performance of activities of daily life in COVID-19 patients who survived hospitalisation. Eur Respir J. 2020;56:2002096.
12. González J, Benítez ID, de Gonzalo-Calvo D, Torres G, de Batlle J, Gómez S, et al. Impact of time to intubation on mortality and pulmonary sequelae in critically ill patients with COVID-19: a prospective cohort study. Crit Care. 2022;26:18.
13. González J, Benítez ID, Motos A, Torres A, Barbé F. Driving pressure and adjunctive therapies in pulmonary sequelae of covid-19 patients under invasive ventilation. Intensive Care Med. 2023;49:244–7, http://dx.doi.org/10.1007/s00134-022-06951-3.
14. Martin-Loeches I, Motos A, Menéndez R, Gabarrús A, González J, Fernández-Barat L, et al. ICU-acquired pneumonia is associated with poor health post-COVID-19 syndrome. J Clin Med. 2021;11:224.
15. González J, de Batlle J, Benítez ID, Torres G, Santisteve S, Targa ADS, et al. Key factors associated with pulmonary sequelae in the follow-up of critically ill COVID-19 patients. Arch Bronconeumol. 2023;59:205–15, http://dx.doi.org/10.1016/j.arbres.2022.12.017.
16. Jacobsen PA, Andersen MP, Gislason G, Phelps M, Butt HJ, Køber L, et al. Return to work after COVID-19 infection – a Danish nationwide registry study. Public Health. 2022;203:116–22.
17. Saunders C, Sperling S, Bendstrup E. A new paradigm is needed to explain long COVID. Lancet Respir Med. 2023;11:e12–3, http://dx.doi.org/10.1016/S2213-2600(22)00501-X.

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