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BRIEF REVIEW

Pulmonary Post-Acute Sequelae of COVID-19

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Abstract

Introduction: Persistent symptoms have been observed in a substantial proportion of survivors of COVID-19 since relatively early in the pandemic. Among these post-acute sequelae of COVID-19 (PASC), respiratory symptoms appear to be the most prevalent.

Methods: We conducted a literature review of peer-reviewed publications in English on the clinical and epidemiological features of respiratory PASC in cohorts of 100 or more patients with a follow-up of four weeks or more after acute infection. Included studies reported the prevalence of persistent respiratory symptoms and/or the results of follow-up pulmonary function tests.

Results: On our review included 14 studies across eight countries with a total of 2,380 patients. Subacute PASC was reported in 876 patients, and chronic PASC in 1,504 patients. The median age ranged from 44 to 67 years. The most common symptoms observed were fatigue (44%), dyspnea (40%), and cough (22%). Lung disease as a comorbidity was found in 13% of patients on average. Predominance of males was seen in all studies of subacute PASC and six out of eight studies of chronic PASC. The rates of comorbidities for subacute *vs.* chronic PASC were: hypertension 32% *vs.* 31%, cardiovascular disease 10% *vs.* 7%, diabetes mellitus 15% *vs.* 12%, kidney disease 7% *vs.* 4%, and lung disease 19% *vs.* 10%.

Conclusion: Respiratory PASC seems to be more predominant as a chronic presentation, more common in male adults, and less common in older persons. Respiratory PASC is most often associated with fatigue, dyspnea, and cough. There was no strong correlation of severity of illness, acute respiratory distress syndrome, or intensive care unit admission with respiratory PASC.

Introduction

The post-acute sequelae of COVID-19 (PASC) is a novel syndrome increasingly reported in the literature.[1] However, the characterization of these sequelae in the literature remains vague and incomplete. Across four systematic reviews of PASC, respiratory sequelae were consistently reported among the most studied [2, 3] and most prevalent.[4, 5] A systematic review and meta-analysis of 43 studies of PASC found that the most commonly reported sequelae longer than 12 weeks after infection were fatigue (48%), sleep disturbance (44%), and dyspnea (39%).[5] A second systematic review and meta-analysis of ten studies reported that the most prevalent respiratory sequelae were fatigue (52%), dyspnea (37%), chest pain (16%), and cough (14%).[6] The authors of both meta-analyses and three systematic reviews highlighted the heterogeneity of study design in the literature, particularly concerning the lack of stratification by severity of illness and the lack of consistency in the timing of follow-up.[3-7]

A systematic review and meta-analysis of seven studies evaluated pulmonary function tests (PFTs) in 380 patients. A prevalence of 39% (95% CI 24–56, $P<0.01$, $I^2=86\%$) was found for altered diffusion capacity of the lungs for carbon monoxide (D_{LCO}), 15% (95% CI 9–22; $P=0.03$, $I^2=59\%$) for restrictive pattern, and 7% (95% CI 4–11; $P=0.31$, $I^2=16\%$) for obstructive pattern.[7]

There is a need to better characterize the incidence, prevalence, and most common symptoms associated with PASC. PASC have been defined as symptoms persisting more than four weeks after the onset of acute COVID-19.[8] Nalbandian *et al.* further defined subacute PASC as the persistence of symptoms and other abnormalities 4–12 weeks after the onset of acute infection and chronic PASC as symptoms and other abnormalities persisting for longer than 12 weeks.[9] A detailed characterization of PASC will guide the optimal

diagnosis and management of patients suffering from this health condition. The objective of the review was to examine peer-reviewed publications to characterize the respiratory sequelae of patients with a prior diagnosis of SARS-CoV2 infection, in particular those with community-acquired pneumonia (CAP).

Methods

Database Search Strategy

We conducted a search of the PubMed database using terms such as "post-acute sequelae of COVID-19", "post-acute COVID-19 syndrome", "post-COVID syndrome", "long COVID", and "COVID-19 sequelae" in combination with "lung", "pulmonary", and "respiratory".

Inclusion Criteria

Peer-reviewed prospective and retrospective studies in English of patients with SARS-CoV-2 infection with follow-up after hospital discharge were included. Prospective studies and studies with a specific focus on the pulmonary sequelae of SARS-CoV-2 CAP were prioritized. Studies were selected if they included more than 100 participants. Following the definitions provided by Nalbandian *et al.* [9], the length of patient follow-up was categorized as follows:

Subacute PASC: symptoms and abnormalities present from 4 to 12 weeks beyond acute COVID-19.

Chronic PASC: symptoms and abnormalities persisting or present beyond 12 weeks of the onset of acute COVID-19.

Day 0 of either symptom onset, hospital admission, or hospital discharge and either the mean or median were used to report length of follow-up in a given study. If multiple day 0s were reported within a single study, symptom onset was preferred in accordance with the definitions provided by Nalbandian *et al.*[9]

Exclusion Criteria

Non-peer-reviewed studies and studies of patients without SARS-CoV-2 infection were excluded. Any studies with fewer than 100 participants or follow-up of less than four weeks post-infection were excluded from this review.

Assessment of Findings

Weighted mean average frequencies of dichotomous variables were calculated from summary statistics reported in the included studies. Due to the variety of summary statistics used to report continuous variables—median *vs.* mean averages, interquartile ranges *vs.* standard deviations, and raw values *vs.* proportions of expected values—accurate statistical comparisons were not possible. All analysis was performed using R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 14 studies fulfilled the inclusion and exclusion criteria.[10-23] The selected studies were either retrospective or case series and comprised four from the United Kingdom (29%), three from Italy (21%), two from Spain (14%), and one each from Belgium, Canada, China, France, and Mexico (7% each). Six studies fulfilled the criteria for subacute PASC, and eight studies fulfilled the criteria for chronic PASC (**Figure 1**). Arnold *et al.* reported follow-up a median 83 days after hospital admission, but 90 days after symptom onset.[11]

The total patient count for all studies was 2,380. Overall, the average (mean or median) age ranged from 44 to 67 years old. Males made up a higher proportion of participants than females in 12 out of 14 studies that reported the sex distribution (**Table 1**). Among the studies that provided the data, the three most common symptoms were fatigue (44%), dyspnea (40%), and cough (22%).

The findings of patients with subacute and chronic PASC are shown in **Tables 2** and **3**, respectively. The total patient counts for subacute and chronic PASC were 876 and 1,504, respectively. The average (mean or median) age in subacute cohorts ranged 47–67 years and 44–63.2 years in chronic cohorts. Males made up a higher proportion of participants than females in all of the subacute PASC studies (**Table 2**) and in six out of eight chronic PASC studies. In all studies of chronic PASC that reported smoking status, nonsmokers formed the majority of participants. The weighted mean percentages of reported comorbidities for subacute *vs.* chronic PASC were as follows: hypertension 32% *vs.* 31%, cardiovascular disease 10% *vs.* 7%, diabetes mellitus 15% *vs.* 12%, kidney disease 7% *vs.* 4%, and lung disease 19 *vs.* 10%. The three most common respiratory symptoms of subacute PASC were fatigue (49%), dyspnea (38%), and chest pain (23%), and of chronic PASC were dyspnea (41%), fatigue (40%), and cough (21%).

Studies that included pulmonary function tests (PFTs), lung computed tomography (CT) scans, and assessments of functional impairment are shown in **Table 4**. In this particular subset of studies, average patient age ranged from 47 to 67 years, with six of seven studies having a predominantly male cohort. The highest frequency of lung disease as a comorbidity was 19%. Overall, the proportion of patients with severe illness

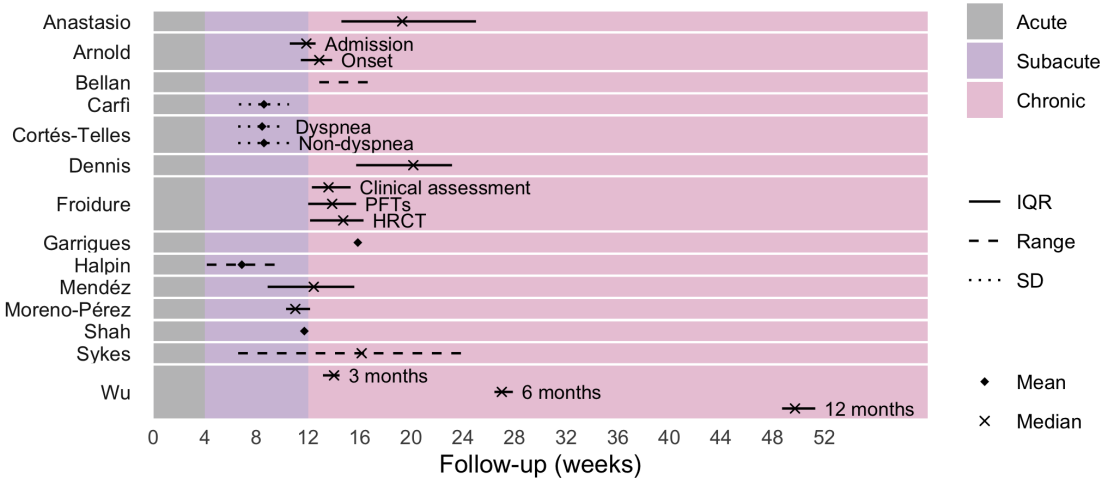

Figure 1. Length of follow-up for all included studies. While several studies reported ranges crossing the 12-week threshold, only one (Arnold *et al.*) reported multiple averages falling on either side of the 12-week threshold. In accordance with the definitions given by Nalbandian *et al.*, the measurement from symptom onset was preferred, and the study was considered chronic. Overall, either time of onset of symptoms, time of hospital admission, or time of hospital discharge was considered as day 0, as reported by different studies.

and/or who were admitted to the ICU was 22% or lower, excluding Wu *et al.*, whose cohort was entirely composed of ICU patients. The most common symptoms reported in these studies were dyspnea (31%), fatigue (30%), chest pain (11%), and cough (11%). The rate of D_{LCO} <80% ranged from 25% to 55%, and only one study reported a marginal airway obstruction (FEV1/FVC 0.789). Abnormal CT of the lungs was reported in 24% to 78% of patients.

Discussion

Our review of respiratory PASC revealed that the majority of participants were male, in accordance with the findings of three systematic reviews that reported total participants by sex.[3, 6, 7] However, a fourth systematic review with a participant total greater than the former three combined was split 40% male and 60% female.[5] Other reviews have found PASC to be more common in females.[24, 25] García-Abellán *et al.* found that female sex was associated with 2.41 times greater odds than male sex of persistent symptoms at six months, although at two months, the association was not statistically significant.[26] It is possible that males are more likely to be enrolled in studies of PASC and less likely to be diagnosed with the condition.

By weighted arithmetic mean, the prevalence of respiratory sequelae at subacute follow-up was: fatigue 49%, dyspnea 38%, and chest pain 23%; at chronic follow-up: dyspnea 41%, fatigue 40%, and cough 21%. Cares-Marambio *et al.* similarly found prevalence of fatigue 52%, dyspnea 37%, chest pain 16%, and cough 14%.[6] Willi *et al.* reported fatigue prevalence ranging 39–73% and dyspnea 39–74%.[27] The persistent dyspnea may reflect chronic lung inflammation and fibrosis resulting in fatigue, similar to advanced interstitial lung fibrosis.

By weighted arithmetic mean, about 13% of patients had a history of lung disease, and 15% were admitted to the ICU. Hypertension, cardiovascular disease, diabetes mellitus, kidney disease, and lung disease were slightly less prevalent among patients with chronic PASC compared to those with subacute PASC. These findings suggest that these comorbidities may not be predictors of chronic PASC. We also found no evidence that the severity of acute disease correlates with the incidence of subacute or chronic sequelae.

We did an analysis of studies that included PFTs, lung CT, and assessment of the functional impairment of patients with PASC. The rate of DLCO <80% ranged from 25% to 55%, and the rate of abnormal CT of the lungs ranged from 24% to 78%. Overall, PASC does not seem to correlate with the severity of acute illness; therefore, factors other than ARDS and cytokine storm may be the cause of the symptoms and laboratory abnormalities.

The pathogenesis of pulmonary PASC is not yet well understood. Proposed mechanisms include diffuse alveolar epithelium destruction formation of hyaline membrane, capillary bleeding, fibrosis of alveolar septum, and proliferation and pulmonary consolidation.[28] There is also a suggested mechanism of extensive injury to alveolar epithelial cells and subsequent remodeling, which causes lung fibrosis or can cause pulmonary hypertension.[29] A prospective observational study reported that serum troponin-I levels dur-

Table 1. Summary averages of dichotomous variables across all included studies.

	All included studies			Subacute PASC			Chronic PASC		
	Studies	Participants	WAM	Studies	Participants	WAM	Studies	Participants	WAM
Baseline characteristics									
Male	14	2,380	55%	6	876	58%	8	1,504	53%
Female	14	2,380	45%	6	876	42%	8	1,504	47%
Smoker	10	1,773	35%	3	389	36%	7	1,384	34%
Non-smoker	10	1,773	65%	3	389	64%	7	1,384	66%
Comorbidities									
Hypertension	14	2,380	31%	6	876	32%	8	1,504	31%
CVD	8	1,443	8%	3	431	10%	5	1,012	7%
Diabetes mellitus	14	2,380	13%	6	876	15%	8	1,504	12%
Kidney disease	9	1,462	4%	4	413	7%	5	1,049	4%
Lung disease	7	1,258	13%	3	447	19%	4	811	10%
Hospitalization features									
Pneumonia	5	1,016	75%	2	420	78%	3	596	74%
Oxygen therapy	9	1,304	64%	4	412	53%	5	892	69%
NIV	7	867	35%	4	412	25%	3	455	44%
Invasive ventilation	8	1,113	8%	3	302	7%	5	811	8%
Persistent respiratory symptom(s) at follow-up									
Dyspnea	16	2,414	40%	6	876	38%	10	1,538	41%
Cough	10	1,839	22%	4	633	22%	6	1,206	21%
Chest pain	9	1,645	21%	3	439	23%	6	1,206	20%
Fatigue	11	2,022	44%	5	816	49%	6	1,206	40%
ICU	9	1,583	15%	3	520	14%	6	1,063	16%

Abbreviations: CVD, cardiovascular disease; ICU, intensive care unit; NIV, non-invasive ventilation; WAM, weighted arithmetic mean.

ing acute illness were significantly associated with the onset of fatigue after discharge at three months' follow-up of 76 patients.[30] Baig *et al.* proposed that persistent oxidative stress and inflammation lead to weak immunological response from the host and therefore incomplete viral eradication.[31] For symptoms such as breathlessness and chest pain, SARS-CoV-2 has been indicated to cause deconditioning, hypovolemia, and immune-mediated autonomic system injury.[32]

Our review is limited due to the data quality of the best publications available. It is unlikely that our results are comprehensive or precisely representative of available evidence regarding pulmonary PASC complications. Heterogeneity in study design precluded precise statistical comparisons between the findings of different studies, even after studies were excluded that did not report the frequency of pulmonary sequelae or follow-up PFT results. The distinction between subacute (4–12 weeks after acute infection) and chronic ($\geq$12 weeks after acute infection) was useful, but it was not always possible to distinguish studies precisely because follow-up was measured from different points (symptom onset, hospital admission, hospital discharge, *etc.*) and reported using different summary statistics (median and interquartile range, mean and standard deviation, etc.) in different studies. Additionally, some studies did not report summary statistics for their entire cohort, providing only subgroup analyses or the results of regression analyses.

In conclusion, respiratory PASC is characterized predominantly by a chronic presentation that is more common in male adults but less common in older persons. Respiratory PASC is most often associated with fatigue, dyspnea, and cough. There was no strong correlation of severity of illness, ARDS, or ICU admission with respiratory PASC.

Table 2. Predictors and outcomes in studies of patients with subacute PASC.

	Halpin (*n*=100)	Carfi (*n*=143)	Cortes-Telles (*n*=186)	Moreno-Pèrez (*n*=277)	Shah (*n*=60)	Arnold (*n*=110)
Follow-up	48 (29–71)[a]	60±13.6	59±13[b] 60±14[e]	77 [72–85]	81.9[c]	83 [74–88][d] 90 [80–97][f]
Baseline characteristics						
Age	70.5 (20–93)[g] 58.5 (34–84)[h]	56.5±14.6	47±13	56.0 [42.0–67.5]	67 [54–74]	60 [46–73]
Male	54 (54)	90 (62.9)	61%	146 (52.7)	41 (68)	68 (62)
Female	46 (46)	53 (37.1)	39%	131 (47.3)	19 (32)	42 (38)
Active smokers		15 (10.5)	20%		23 (38)	
Previous smokers		65 (45.4)				
Non-smokers		63 (44.1)	80%		37 (62)	
Comorbidities						
Hypertension	41 (41)	50 (35.0)	20%	101 (36.5)	21 (35)	27 (25)
Cardiovascular disease				18 (6.9)[i]	6 (10)[j]	20 (18)[k]
Diabetes mellitus	29 (29)	10 (7.0)	16%	32 (11.6)	13 (22)	19 (17)
Kidney disease	15 (15)	2 (2.1)[l]			4 (7)	7 (6)[m]
Lung disease				50 (18.1)	8 (13)	28 (25)
Hospitalization features						
Pneumonia		104 (72.7)		223 (80.5)		
Oxygen therapy	78 (78)	77 (53.8)			46 (78)[n]	18 (16)
NIV	30 (30)	21 (14.7)			34 (58)[n]	16 (15)
Invasive ventilation	1 (1)	7 (4.9)			12 (20)[n]	
ICU	32 (32)	18 (12.6)		24 (8.7)		
Persistent respiratory symptom(s) at follow-up						
Dyspnea	50 (50)	43.4	38%	95 (34.4)	12 (20)	43 (39)
Cough			30%	59 (21.3)	12 (20)	13 (12)
Chest pain		21.7	30%			14 (13)
Fatigue	64 (64)	53.1	67%[o]	96 (34.8)		43 (39)
Pulmonary function tests						
DLCO,%			99±27[p]		77±16[p]	
FVC			83±18[p]		94±16[p]	
FEV1			88±18[p]		93±16[p]	
FEV1/FVC			85±8[p]		90±13[p]	

Abbreviations: D_{LCO}, diffusing capacity of the lungs for carbon monoxide; ECMO, extracorporeal membrane oxygenation; FVC, forced vital capacity; FEV, forced expiratory volume; ICU, intensive care unit; NIV, non-invasive ventilation.
Dichotomous variables are displayed as n (%); continuous variables are displayed as median [interquartile range] or mean±standard deviation, except where otherwise specified. [a] Mean (range); [b] Dyspnea; [c] Mean; [d] Admission; [e] Non-dyspnea; [f] Symptom onset; [g] Ward, median (range); [h] ICU, median (range); [i] Out of 261 patients; [j] Coronary heart disease; [k] Heart disease; [l] Kidney failure; [m] Severe kidney disease; [n] Out of 59 patients; [o] Fatigue on effort; [p] % of predicted.

Table 3. Predictors and outcomes in studies of patients with chronic PASC.[12, 15-17, 19, 22, 23, 33]

First author	Wu (*n*=83)				Dennis	Anastasio	Bellan	Mendez	Sykes	Froidure	Garrigues
	3 months	6 months	9 months	12 months	(*n*=201)	(*n*=379)	(*n*=238)	(*n*=215)	(*n*=134)	(*n*=134)	(*n*=120)
Follow-up	98 [92–101]	189 [185–195]		348 [341–359]	141 [110–162]	135 [102–175]	3–4 months	87 [62–109]	113 (46–167)[a]	95 [86–107][b]	110.9±11.1
Baseline characteristics											
Age, years		60 [52–66]			44 ±11.0	56 [49–63]	61 [50–71]	55 [47–66]	59.6±14.0	60 [53–68]	63.2±15.7
Male		47 (57)			69 (29.4)	174 (45.9)	142 (59.7)	130 (60.5)	88 (65.7)	79 (59)	75 (62.5)
Female		36 (43)			142 (70.6)	205 (54.1)	96 (40.3)	85 (39.5)	46 (34.3)	55 (41)	45 (37.5)
Current smoker		N/A[c]			6 (3.0)	25 (6.6)	25 (10.5)	64 (29.8)	59 (44.0)	30 (22)	
Former smoker		N/A			62 (30.8)	128 (33.8)	74 (31.1)				
Non-smoker		83 (100)			133 (66.2)	226 (59.6)	139 (58.4)	151 (70.2)	75 (56.0)	104 (78)	
Comorbidities											
Hypertension		N/A			13 (6.5)	112 (29.6)	98 (41.2)	67 (31.2)	55 (41.0)	63 (47)	56 (46.7)
Cardiovascular		N/A			9 (4.5)	44 (11.6)		12 (5.6)[d]	6 (4.5)		
Diabetes		N/A			4 (2.0)	24 (6.3)	36 (15.1)	32 (14.9)	31 (23.1)	29 (22)	26 (21.7)
Kidney disease		N/A				13 (3.4)	15 (6.3)	3 (1.4)	6 (4.5)		
Lung disease		N/A				32 (8.4)		27 (12.6)	19 (41.2)[e]	25 (19)	
									11 (8.2)[f]		
									3 (2.2)[g]		
Hospitalization features											
Pneumonia		83 (100)				222 (58.6)			134 (100)		
O_2 therapy		83 (100)				135 (60.8)[h]	172 (72.3)	111 (51.6)	116 (87)		
NIV		46 (55)					49 (20.6)		107 (79.9)		
Inv vent		N/A				34 (9.0)[h]	21 (8.8)		9 (6.7)	15 (11)	
ICU						34 (9.0)[h]	28 (11.8)	40 (18.6)	27 (20)	30 (22)	24 (20)
ECMO									1 (0.7)		
Persistent respiratory symptoms at follow-up											
Dyspnea	67 (81)	25 (30)	10 (12)	4 (5)	176 (88.0)	162 (42.7)	13 (5.5)		80 (59.7)	45/126 (35)	50 (41.7)
Cough					146 (73.0)	23 (6.1)	6 (2.5)		47 (35.1)	14/126 (10)	20 (16.7)
Chest pain					152 (76.0)	45 (11.9)	1 (0.4)		24 (17.9)	6/126 (4)	13 (10.8)
Fatigue					196 (98.0)	113 (29.8)	14 (5.9)		53 (39.6)[i]	32/126 (25)	66 (55.0)
Pulmonary function tests											
D_{LCO}<80%	46 (55)	45 (54)		27 (33)			113/219 (51.6)	53 (24.7)			
D_{LCO}<60%	12 (15)	11 (13)		4 (5)			34/219 (15.5)	13 (6.0)		33 (27)	
D_{LCO},%	77 [67–87]	76 [68–90]		88 [78–101]			79 [69–89]	88 [80–99]		74 [61–89]	
D_{LCO}/VA						101 [89–112]		102 [90–112]			
FVC	92 [81–99][j]	94 [85–104][j]		98 [89-109][j]		106 [95–117]	98.5 [90–109]	106 [96–116]		88 [78–98][j]	
FEV1	90 [76–100][j]	92 [80–101][j]		96 [85–110][j]		107 [96–117]	101 [91.5–112.0]	103 [92–113]		91 [81–102][j]	
FEV1/FVC	81 [77–84][j]	81 [78–84][j]		82 [79–86][j]		82 [80–86]		78.9 [75.3–83.5]		96 [83–106][j]	
Imaging											
Abnormal CT	65 (78)	40 (48)	22 (27)	20 (24%)							

Abbreviations: D_{LCO}, diffusing capacity of the lungs for carbon monoxide; ECMO, extracorporeal membrane oxygenation; FVC, forced vital capacity; FEV, forced expiratory volume; ICU, intensive care unit; Inv vent, invasive ventilation; NIV, non-invasive ventilation. Dichotomous variables are displayed as n (%); continuous variables are displayed as median [interquartile range] or mean±standard deviation, except where otherwise specified. [a] Median (range); [b] Clinical assessment 95 [86–107], pulmonary function tests 97 [84–110] days, high-resolution computed tomography 103 [85–114] days; [c] Wu *et al.* excluded current/former smokers, patients with comorbidities, and patients who required invasive ventilation from their study. [d] Heart disease ; [e] Asthma; [f] Chronic obstructive pulmonary disease; [g] History of venous thromboembolism; [h] Out of 222 pneumonia patients; [i] Extreme fatigue; [j] % of predicted.

Table 4. Predictors and outcomes for studies involving pulmonary function tests.

First author	Wu (*n*=83)			Anastasio	Bellan	Mendez	Froidure	Cortes-Telles	Shah
	3 months	6 months	12 months	(*n*=379)	(*n*=238)	(*n*=215)	(*n*=134)	(*n*=186)	(*n*=60)
Baseline characteristics									
Age		60 [52-66]		56 [49–63]	61 [50–71]	55 [47–66]	60 [53-68]	47±13	67 [54–74]
Male		47 (57)		174 (45.9)	142 (59.7)	130 (60.5)	79 (59)	61%	41 (68)
Female		36 (43)		205 (54.1)	96 (40.3)	85 (39.5)	55 (41)	39%	19 (32)
Active smokers		0		25 (6.6)	25 (10.5)	64 (29.8)	30 (22)	20%	23 (38)
Previous smokers		0		128 (33.8)	74 (31.1)				
Non-smokers		83 (100)		226 (59.6)	139 (58.4)	151 (70.2)	104 (78)	80%	37 (62)
Comorbidities									
Hypertension		0		112 (29.6)	98 (41.2)	67 (31.2)	63 (47)	20%	21 (35)
Cardiovascular disease		0		44 (11.6)		12 (5.6)[a]			6 (10)[b]
Diabetes mellitus		0		24 (6.3)	36 (15.1)	32 (14.9)	29 (22)	16%	13 (22)
Kidney disease		0		13 (3.4)	15 (6.3)	3 (1.4)			4 (7)
Lung disease		0		32 (8.4)		27 (12.6)	25 (19)		8 (13)
Hospitalization features									
Pneumonia		83 (100)		222 (58.6)					
Oxygen therapy		83 (100)		135 (60.8)[c]	172 (72.3)	111 (51.6)			46 (78)[d]
NIV		46 (55)			49 (20.6)				34 (58)[d]
Invasive ventilation		0		34 (9.0)[c]	21 (8.8)		15 (11)		12 (20)[d]
ICU				34 (9.0)[c]	28 (11.8)	40 (18.6)	30 (22)		
Persistent symptom(s) at follow-up									
Dyspnea	67 (81)	25 (30)	4 (5)	162 (42.7)	13 (5.5)		45[e](35)	38%	12[f](20)
Cough				23 (6.1)	6 (2.5)		14[e](10)	30%	12[f](20)
Chest pain				45 (11.9)	1 (0.4)		6[e](4)	30%	
Fatigue				113 (29.8)[g]	14 (5.9)		32[e](25)	67%[h]	
Pulmonary function tests									
DLCO<80%	46 (55)	45 (54)	27 (33)		113 (51.6)[i]	53 (24.7)			
DLCO<60%	12 (15)	11 (13)	4 (5)		34 (15.5)[i]	13 (6.0)	33 (27)		
DLCO,%	77 [67–87]	76 [68–90]	88 [78–101]		79 [69–89]	88 [80–99]	74 [61–89]	99±27%	77±16%
DLCO/VA				101 [89–112]		102 [90–112]		93±16%	
FVC	92 [81–99][j]	94 [85–104][j]	98 [89–109][j]	106 [95–117]	98.5 [90–109]	106 [96–116]	88% [78–98]	83±18%	94±16%
FEV1	90 [76–100][j]	92 [80–101][j]	96 [85–110][j]	107 [96–117]	101 [91.5–112]	103 [92–113]	91% [81–102]	88±18%	93±16%
FEV1/FVC	81 [77–84][j]	81 [78–84][j]	82 [79–86][j]	82 [80–86]		78.9 [75.3–83.5]	96% [83–106]	85±8%	90±13
Imaging									
Abnormal CT	65 (78)	40 (48)	20 (24)						

Abbreviations: CT, computed tomography; D_{LCO}, diffusing capacity of the lungs for carbon monoxide; ECMO, extracorporeal membrane oxygenation; FVC, forced vital capacity; FEV, forced expiratory volume; ICU, intensive care unit; NIV, non-invasive ventilation.

Dichotomous variables are displayed as n (%); continuous variables are displayed as median [interquartile range] or mean±standard deviation, except where otherwise specified.

[a] Heart disease; [b] Coronary heart disease; [c] Out of 222 patients with pneumonia; [d] Out of 59 patients; [e] Out of 126 patients; [f] Out of 60; [g] Extreme fatigue; [h] Fatigue on effort; [i] Out of 219 patients; [j] % of predicted.

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