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CASE REPORT

Pulmonary function in patients surviving to COVID-19 pneumonia

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Abstract

Purpose The aim of our study was to assess respiratory function at the time of clinical recovery and 6 weeks after discharge in patients surviving to COVID-19 pneumonia.

Methods Our case series consisted of 13 patients with COVID-19 pneumonia.

Results At the time of clinical recovery, FEV1 (2.07 ± 0.72 L) and FVC (2.25 ± 0.86 L) were lower compared to lower limit of normality (LLN) values (2.56 ± 0.53 L, $p = 0.004$, and 3.31 ± 0.65 L, $p < 0.001$, respectively), while FEV1/FVC (0.94 ± 0.07) was higher compared to upper limit of normality (ULN) values (0.89 ± 0.01, $p = 0.029$). After 6 weeks pulmonary function improved but FVC was still lower than ULN (2.87 ± 0.81, $p = 0.014$).

Conclusion These findings suggest that COVID-19 pneumonia may result in clinically relevant alterations in pulmonary function tests, with a mainly restrictive pattern.

Keywords COVID-19 · Pneumonia · Spirometry

Introduction

The spread of COVID-19 has taken on pandemic proportions, affecting more than 6, 5 million people and causing almost 400,000 deaths worldwide [1].

Fever, fatigue, cough and expectoration are the most frequent presenting symptoms, but muscle soreness, anorexia, chest tightness, dyspnea, nausea, vomiting, diarrhea, headache also occurred frequently. The majority of patients developing COVID-19 pneumonia had bilateral lung lesions (75.7%, 95% CI = 65.7–84.5%) and respiratory failure or acute respiratory distress syndrome (ARDS) occurred in 9.5% (95% CI = 5.0%, 40.3%) of patients [2].

As a new infectious disease carrying a high risk of severe course and intensive care unit admission, it is particularly important to explore COVID-19 clinical characteristics, which may help to manage properly its sequelae in the post-acute phase. It is worth noting that evidence about pulmonary function tests among COVID-19 patients is currently limited to a trial showing that 6-week respiratory rehabilitation can improve respiratory function, quality of life and anxiety of older patients [3]. Therefore, we aimed at assessing respiratory function at the time of clinical recovery and 6 weeks after discharge in patients surviving to COVID-19 pneumonia.

Methods

Our study included 13 adult patients with COVID-19 bilateral pneumonia admitted to the respiratory acute care ward at IRCCS INRCA hospital in Merate (Lombardy, Italy), between March 14th and April 14th, 2020. Inclusion criteria were the availability of written informed consent to

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participate in the study and ability to perform pulmonary function tests correctly. The study was approved by the Ethics Committee of the IRCCS INRCA.

COVID-19 bilateral pneumonia was diagnosed by positive polymerase chain reaction (PCR) testing on nasopharyngeal swab and presence of bilateral lung infiltrates on chest X-ray upon admission.

Patient history, body mass index (BMI), smoking habit, signs and symptoms, complete laboratory panel and setting transitions were collected.

Chest high-resolution computed tomography (CT), spirometry, 2-min walking test and arterial blood gas analysis at the time of clinical recovery (i.e. the day before discharge) were included in the study. Clinical recovery was defined by the presence of all of the following: absence of fever for at least 48 h, PaO_2 greater than 60 mmHg on arterial blood gas testing on room air, and negative C-reactive protein (CRP) on two consecutive blood samples performed at least 48 h apart.

2-minute walking test was performed on room air under the supervision of a respiratory therapist in the patients' room. Nocturnal pulse oximetry was also recorded on room air. PalmSAT 2500 pulse oximeters were used for recordings (Nonin, USA).

Arterial blood gases analysis was performed regularly during hospitalization to monitor oxygen requirements by Cobas b 123 (Roche, Switzerland) point-of-care testing system.

Pulmonary function tests were performed using Microlab portable spirometer (Viasys Healthcare, USA). Forced expiratory volume in the first second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio were included in the analysis. For each patient lower limit of normality (LLN) values for FEV_1, FVC, and upper limit of normality (ULN) values fo FEV_1/FVC were also calculated by Global Lung Function 2012 equations [4]. Correct performance of forced expiration was ensured by medical personnel who observed the patients at security distance to minimize the risk of infection due to droplet spreading. Pulmonary function tests were repeated 6 weeks after discharge.

Descriptive data were presented as mean ± SD for continuous variables or number (percentage) for categorical ones. Paired data *t* test was used when appropriate. Statistical analysis was carried out by SPSS V.24 statistical software package (SPSS for Windows V24, SPSS Inc., Chicago, IL, USA).

Results

Overall, patients enrolled in the study were aged 57.8 ± 10.0 years (range 34–73 years) and almost exclusively male (12 patients, 92.3%). Additionally, all patients were no smokers. Fever ($N=13$), dyspnea ($N=11$) and cough ($N=10$) were the most frequently observed symptoms at presentation. Pre-existing comorbidities are reported in Table 1. Patients included in the analysis did not exhibit respiratory comorbidities with the exception of one patient with pre-existing history of asthma. Seven out of 13 patients had BMI > 30 kg/m^2. The average length of hospital stay was 29.5 ± 9.8 days.

CT scan at the time of clinical recovery showed persistent multifocal ground glass opacities in 12 patients, crazy paving in 6 patients, linear opacities in 7 patients and consolidation pattern associated to multifocal ground glass opacities in 5 patients.

Interestingly, walked distance was less than 100 m in only 4 patients, and limited burden of dyspnea and fatigue was observed. Additionally, blood gas analysis showed only mild hypoxemia in 7 patients. Nevertheless, average nocturnal SaO_2 was compatible with clinically relevant night-time hypoxemia in 7 out of 13 patients.

Figure 1 shows pulmonary function variables of patients studied. At the baseline, the average FEV_1/FVC was higher compared to ULN values ($p=0.029$), while FVC ($p<0.001$) and FEV_1 ($p=0.004$) were lower compared to respective LLN values in enrolled patients. After 6 weeks, an overall improvement in pulmonary function was observed (see also supplementary Table 1), but FVC was still lower than LLN.

Discussion

Results of the present case series suggest that COVID-19 pneumonia may result in clinically relevant alterations in pulmonary function tests, with a restrictive pattern in 10 out of 13 patients at the time of hospital discharge. After 6 weeks, pulmonary function improved, but some degree of restrictive alteration still persisted.

Patients surviving to COVID-19 pneumonia may present with a restrictive pulmonary pattern, which is known to be associated with increased risk of life-threatening comorbidities [5, 6]. While the need of further data with DLCO and plethysmography deserves to be recognized, our results suggest that survivors to COVID-19 pneumonia should be carefully screened for pulmonary function and rehabilitation needs at the end of acute phase, and eventually referred to specific care pathways to monitor and manage clinically relevant sequelae during follow-up.

Our data suggest that pulmonary function needs to be carefully investigated in COVID-19 patients, as it was already done for other atypical pneumonia. Indeed, pulmonary function tests were found to improve significantly in the first 3 months but with no further significant improvement from 3 to 6 months after discharge among survivors to severe influenza A (H1N1) pneumonia [7], and other studies

Table 1 Demographic and pulmonary function parameters of COVID-19 patients studied

	All patients ($N=13$)	Pt 1	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7	Pt 8	Pt 9	Pt 10	Pt 11	Pt 12	Pt13
Age	57.8 ± 10.0	64	55	57	68	73	53	46	65	63	57	34	57	59
Sex, M	12 (92.3%)	M	M	M	M	F	M	M	M	M	M	M	M	M
BMI, kg/m^2	30.5 ± 5.6	22.6	26.6	31.5	25.2	28.1	40.6	38.6	31.7	35.3	26.1	24.8	30.7	34.8
Comorbidities														
Hypertension	3 (23.1%)	N	N	N	N	N	N	N	Y	Y	N	N	Y	N
Heart failure	–	N	N	N	N	N	N	N	N	N	N	N	N	N
Coronary artery disease	1 (7.7%)	N	N	N	N	N	N	N	Y	N	N	N	N	N
COPD	–	N	N	N	N	N	N	N	N	N	N	N	N	N
Asthma	1 (7.7%)	N	Y	N	N	N	N	N	N	N	N	N	N	N
Diabetes	1 (7.7%)	N	N	N	N	N	Y	N	N	N	N	N	N	N
Atrial fibrillation	1 (7.7%)	N	N	N	Y	N	N	N	N	N	N	N	N	N
Dementia	1 (7.7%)	N	N	N	Y	N	N	N	N	N	N	N	N	N
Stroke	1 (7.7%)	N	N	N	Y	N	N	N	N	N	N	N	N	N
CKD	–	N	N	N	N	N	N	N	N	N	N	N	N	N
Blood gas analysis														
PaO_2, mmHg	68.8 ± 7.1	67.2	76.8	80.1	67.0	62.8	76.0	66.0	73.0	60.0	68.5	74.1	68.7	57.2
$PaCO_2$, mmHg	35.5 ± 3.6	34.6	39.9	35.3	37.0	35.4	28.0	37.0	31.0	34.6	40.7	39.2	37.0	31.9
SaO_2, %	95.9 ± 1.7	95.0	96.7	97.5	99.0	94.0	98.0	95.0	96.0	93.0	95.6	96.3	95.0	94.2
HCO_3, mmol/l	24.5 ± 1.5	24.3	25.5	22.9	26.1	22.0	24.5	24.7	22.6	26.0	26.9	25.3	24.1	23.8
pH	7.4 ± 0.0	7.46	7.42	7.43	7.46	7.42	7.51	7.44	7.45	7.49	7.43	7.42	7.43	7.46
Functional status														
2-min walked distance, m	134.4±61.6	82	140	140	70	100	133	154	84	168	80	294	168	n.a
Borg scale dyspnea	2.5 ± 1.8	1	3	1	4	2	2	6	4	4	0	0	3	n.a
Borg scale fatigue	1.5 ± 1.7	1	3	0	0	0	2	5	0	3	1	0	3	n.a
Nocturne SaO_2, %	91.2 ± 1.8	92.5	93.5	90.7	91.0	90.8	92.0	87.0	91.3	89.5	90.3	94.1	90.9	91.4

Data are means ± SD or number (percentage)

COPD chronic obstructive pulmonary disease, *CKD* chronic kidney disease, *n.a.* not able to perform

showed a complete normalization of pulmonary function 6 months after H1N1-related ARDS [8]. At variance, about 80% of survivors to ARDS not caused by influenza A H1N1 had reduced diffusing capacity, 20% had airway obstruction, and 20% had restrictive pattern 12 months after recovery [9].

If our data will be confirmed by a more comprehensive diagnostic assessment, it will likely be necessary to rethink the pneumology services with an increase in the availability of respiratory rehabilitation units in the areas most violently affected by the pandemic. The recent demonstration that six-week respiratory rehabilitation can effectively improve respiratory function in older patients with COVID-19 [3] is in keeping with this view.

The small sample size and the simple spirometric approach are main limitations of the present study. Additionally, pulmonary function tests before COVID-19 infection are not available for our patients. Nevertheless, our results may represent an important first step in the knowledge of COVID-19 consequences in terms of pulmonary function.

In conclusion, COVID-19 pneumonia may result in significant alterations in lung function, with a mainly restrictive pattern, partly persisting at 6 weeks after recovery. Further studies are needed to confirm this observation on wider populations and with a more detailed diagnostic work-up. However, given the potential implications of spirometric restrictive patterns in terms of quality of life and independency of patients [10], it will be necessary to prevent the tsunami of post-COVID-19 patients from catching healthcare systems unprepared again after the pandemic.

Availability of data and material

Data are locally available for participating researchers and stored in the data repository of the IRCCS INRCA.

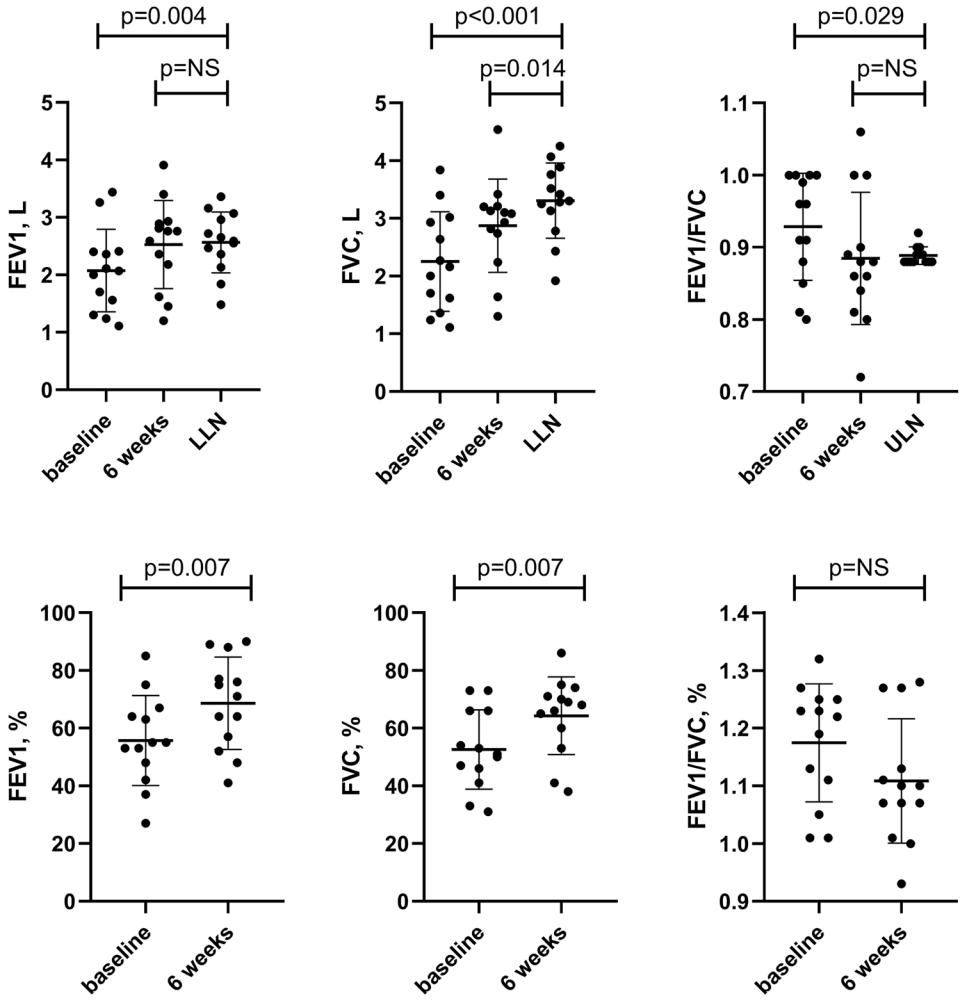

Fig. 1 Pulmonary function tests at the time of clinical recovery (i.e. the day before discharge) and 6 weeks after discharge in the patients studied

Author contributions Study design: AF, CM, DC; Literature Search: AC, MDR, LS; Data Collection: AF, CM AB, NB, SL, SM, DRB, DC; Data Analysis: AC, MDR, LS; Drafting paper: AF, CM, AC, MDR, LS, FL; Manuscript Reviewing-all authors.

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Compliance with ethical standards

Conflict of interest All Authors declare to have no conflict of interest/competing interest to disclose with this manuscript.

Ethics approval The study was approved by the Ethics Committee of the Italian National Research Center on Aging (IRCCS INRCA), study #20008/2020 and deliberation #141/DGEN/2020.

Consent to participate All patients signed a written informed consent to be enrolled in the study.

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