Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
**Short communication**

**Decreased quality of life and spirometric alterations even after mild-moderate COVID-19**

Alberto Ordinola Navarro, Javier Cervantes-Bojalil, Orestes de Jesús Cobos Quevedo, Andrea Avila Martínez, Carlos Alberto Hernández-Jiménez, Esperanza Pérez Álvarez, Andrea González Gil, Ana Lilia Peralta Amaro, Olga Vera-Lastra, Bruno Ali Lopez Luis.

**ARTICLE INFO**

**Keywords:** COVID-19, Pulmonary Rehabilitation, Post-COVID, Quality of life, Respiratory infection, SARS

**ABSTRACT**

**Background:** The follow-up of recovered COVID-19 patients is still limited. We aimed to evaluate the changes in quality-of-life (QOL) and spirometric alterations in the convalescent phase of 115 patients with at least 30 days post-COVID-19.

**Methods:** We included patients with confirmed COVID-19 infection, available past medical records and at least 30 days after the onset of symptoms. All patients were asked to rate their general health condition before and after COVID-19 using the EQ-5D-5L standardized questionnaire and perform a spirometry at evaluation.

**Results:** In this study, that included 70% (81/115) of patients with mild or moderate COVID-19; there was a severe decrease in QOL up to 56% (64/115). Alterations in usual activities and anxiety/depression were present in 59% of patients with a severe decrease in QOL. The persistence of symptoms was present in 63% (72/115). Restrictive lung impairment was the most common spirometric alteration in 17% (20/115), of whom 65% (13/20) had mild COVID-19.

**Conclusions:** Spirometric alterations are presented even in mild COVID-19, and more remarkably, there is a high rate of alterations in quality of life after the recovery of this disease.

**1. Introduction**

The world has been affected by the biggest pandemic in recent years, coronavirus disease 2019 (COVID-19), of which we are learning through extensive research during the last months. The follow-up of post-COVID-19 patients is still limited, but the persistence of symptoms early after the disease has already been described [1]. Moreover, coronavirus infections have been reported as a cause of altered lung function, mostly related to the disease severity [2]. This study aimed to evaluate the changes in quality-of-life (QOL) and spirometric changes in the early convalescent phase of a group of recovered COVID-19 patients.

**2. Methods**

This follow-up study included patients evaluated for COVID-19 in The Hospital de Especialidades “Dr. Antonio Fraga Mouret,” Centro Médico Nacional La Raza, M´exico, between Apr 01 to Jul 30, 2020. The local ethics committee approved this study (registration number, R-2020-3501-158). Informed consent was obtained from all participants. The inclusion criteria were as follows: (1) Confirmed COVID-19 infection by SARS-CoV-2 real-time qPCR using nasopharyngeal swaps. (2) Available past medical records and the radiological evaluation with chest computed tomography scan (CT). (3) Patients with at least 30 days after the onset of symptoms until the time of the spirometric evaluation. Patients with baseline lung disease were excluded from the study.

Spirometry was done using a portable spirometer (MIR Spirolab®). The performance and acceptability criteria were based on ATS-ERS guidelines [3]. Normal spirometric was defined as no airflow obstruction, FEV1/FVC ≥ 0.7 with FVC > 80% of the predicted values, according to NHANES III. Restrictive pattern was diagnosed as an FVC < 80% of the predicted values.
predicted value and an FEV1/FVC ratio >70%.

All patients were asked to rate their general health condition before and after COVID-19 disease as well as symptoms persistence at the time of the evaluation using a standardized questionary. In order to evaluate QOL, the EQ-5D-5L instrument was used [4]. It consists of a visual analogue scale from 0 (worst health) to 100 (best health) and five items: mobility, usual activities, self-care, pain/discomfort and anxiety/depression. We defined a severe decline in QOL as a decrease ≥10 points in the EQ-5D-5L visual analogue scale.

Qualitative variables were presented as proportions and quantitative variables as mean (standard deviation) or medians (interquartile range) when appropriate. Statistical comparisons were performed between
patients who had a severe decline in the EQ-5D-5L scale and who did not after COVID-19. Categorical variables were compared using the Chi-square test or Fisher’s exact test, and for continuous variables, the Student t-test, Wilcoxon rank-sum test and signed-rank test were used. Comparisons in perceived alterations pre and post COVID-19 were performed using the MacNemar test for paired data. Statistical significance was considered with a \( P < 0.05 \). All analyses were done using R Software version 3.6.3 (R-Foundation).

3. Results

Overall, 140 patients met the inclusion criteria, of whom 16 refused to participate, and 9 were excluded because of unacceptable spirometry. In the final analysis, 115 patients were evaluated, their median age was 40 years, and 57% were women (65/115). The median body mass index (27.76 kg/m²) was in the range of overweight, and 27% (31/115) required hospitalization with a median length of hospital stay of 10 days (IQR, 6–12). The mean time since onset of symptoms until the evaluation was 58 ± 18 days. The persistence of symptoms was present in 63% (72/115), of whom 19% (14/72) had at least two symptoms. The median score of the EQ-5D-5L visual analogue scale pre-COVID-19 was 95 (IQR; 90–100), and after was 85 (IQR; 75–90), \( P < 0.001 \). There were no significant differences in the patients’ baseline characteristics with a severe decline in QOL compared to those who did not have such decline, as shown in Table 1. Moreover, the frequency of spirometric alterations and persistence of symptoms did not significantly differ between both groups. However, in the severe decline group, the percentage of patients with altered items of health status such as usual activities and anxiety/depression were significantly higher (Table 1). All the health state parameters evaluated had a significantly higher proportion of abnormalities post-COVID-19 than pre-COVID-19, as shown in Fig. 1.

Spirometric alterations were present in 17% (20/115) of patients. All

---

**Fig. 1.** Graphics showing EQ-5D-5L health state evaluation before and after COVID-19. *Statistical comparison was performed using the MacNemar test for paired data between no problems versus all alterations levels.*
of them had a restrictive impairment. The patients with spirometric alterations were significantly older (median of age, 48 vs. 39 years, \( P = 0.003 \)), the presence of comorbidities such as type 2 diabetes (4/20), hypertension (3/20), smoking (4/20), overweight (10/20), and obesity (6/20) were similar in patients with and without spirometric alterations. Up to 65% (13/20) of patients with spirometric alterations had the antecedent of a mild COVID-19 disease, which was significantly higher than in the patients without spirometric alterations (32% [30/95]), \( P = 0.01 \). However, the former patients had a higher proportion of bilateral consolidations in the chest CT (25% [5/20]) vs. 3% [3/95], \( P = 0.02 \), which was performed early from symptom onset (median 4 days; IQR, 1–7). The mean of FEV1% (79.2 ± 8), PEF% (91 ± 17), FEF 25–75% (98 ± 21) and FVC% (73 ± 7) was lower than the patients with no spirometric alterations (99 ± 10, 106 ± 19, 109 ± 26 and 97 ± 11, respectively). An FEF 25–75% < 65% was present in 2/115 patients, one with a restrictive pattern. PEF<80% was present in 12/115 patients, of whom five had a restrictive pattern. The median score of the QOL visual analo- 
eg scale was lower in the post-COVID-19 period than in the pre-
COVID-19 period in both groups with (median 80 vs. 95, \( P < 0.001 \)) and without (median 85 vs. 95, \( P < 0.001 \)) alterations in the spirometry. However, the median score in the post-COVID-19 period was significantly lower in patients with spirometric alterations than without these (median 80 vs. 85, \( P = 0.02 \)).

4. Discussion

In this follow-up study of recovered COVID-19 patients, we found a high proportion of patients with a decrease in QOL, and this finding seemed not to have a relation with the disease severity and the persistence of symptoms. Moreover, alteration in health parameters such as usual activities and anxiety/depression were present. Restrictive impairment was the most common spirometric alteration even after mild COVID-19, and these patients had a higher decrease in QOL.

An Italian study of patients recovered from COVID-19, which included 72% of patients with pneumonia with only 20% requiring mechanical ventilation, reported a worsened QOL in 44% of patients and persistent symptoms in 87% [1]. In addition, neurocognitive sequelae have recently been reported in case series of patients from Virginian, USA, who required intensive care attention [5]. Of note, 73% of our study group were outpatients, and there was a significant worsening in all the parameters of QOL and a high proportion of persistent symptoms even in mild or moderate disease.

Spirometric alterations as sequelae of the Middle East respiratory syndrome have previously been related to the disease severity [2]. We found a high proportion of restrictive impairment and only a minority with small-airway dysfunction. Moreover, there was no relationship between lung function test and the severity of illness, although the antecedent of bilateral consolidations on CT was predominant in patients with spirometric alterations. Mo et al. [6], evaluated the spirometric patterns of post-COVID-19 patients, finding 9% of them with restrictive impairment associated with the disease severity. A recent Chinese study [7] found in cases of prior severe COVID-19 up to 33% of a restrictive pattern and in 16% small airway dysfunction; however, in that study, there were no significant differences in comparison with prior mild disease. These findings suggest that the severity of disease or CT alterations are not the only factor associated with impairment of respiratory function [8].

This study’s limitations include the absence of pre-COVID-19 spirometry, the inclusion of patients with obesity and diabetes that might already have restrictive lung impairment and a decreased QOL. However, these comorbidities were present in the same proportions in the group with and without spirometric alterations and with and without severe decrease in QOL. The incomplete respiratory tests, the patient’s heterogeneity, the retrospective evaluation of the medical records and the lack of adjustment by multiple confounders avoided obtaining definitive conclusions.

In conclusion, post-COVID-19 alterations comprised a decrease in QOL, persistent symptoms and lung function impairment. All the latter are in concordance with the called “long-haulers” [9], or “post-
COVID-19 syndrome” [10] who are beginning to be recognized. We hope this study provides insights into this new disease and promotes intervention trials such as early respiratory rehabilitation and psycho-

Conflict of interest disclosures

None reported.

Additional information

The study was approved by the local Review Board (number, R-2020-3501-158).

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Specific author contributions

Drs. Ordinola and Lopez Luis had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization and Methodology: Ordinola, Cervantes, Cobos, Ávila, Hernández, Peralta Lopez Luis. Acquisition, analysis, or interpretation of data: Ordinola, Cervantes, Cobos, Ávila, Hernández, Pérez, González, Lopez Luis. Writing - Original Draft: Ordinola, Cervantes, Cobos, Hernández, Lopez Luis. Writing - Review & Editing: Cobos, Ávila, Perez, González, Vera. Formal analysis: Ordinola, Lopez Luis. Supervision and visualization: Per-

References

[1] A. Carfì, R. Bernabei, F. Landi, For the gemelli against COVID-19 post-acute care study group. Persistent symptoms in patients after acute COVID-19, J. Am. Med. Assoc. 324 (6) (2020) 603–605, https://doi.org/10.1001/jama.2020.12603.
[2] L. Xie, Y. Liu, Y. Xiao, Follow-up study on pulmonary function and lung radiographic changes in rehabilitating severe acute respiratory syndrome patients after discharge, Chest 127 (2005) 2119–2124.
[3] Brian L. Graham, et al., Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement, Am. J. Respir. Crit. Care Med. 200 (8) (2019) e70–e88, https://doi.org/10.1164/ rajc.2019–3501-158.
[4] EuroQol Research Foundation, EQ-5D-5L user guide. https://euroqol.org/publicati 
on/user-guides, 2019.
[5] C. Ramani, E.M. Davis, J.S. Kim, J.J. Provençco, K.B. Enfield, A. Kddl, PostIntensive care unit COVID-19 outcomes—a case series, Chest (2020), https://doi.org/ 10.1016/j.chest.2020.08.2056.
[6] X. Mo, W. Jian, Z. Su, M. Chen, H. Peng, P. Peng, C. Lei, R. Chen, N. Zhong, S. Li, Abnormal pulmonary function in COVID-19 patients at time of hospital discharge, Eur. Respir. J. 55 (6) (2020) 2001217, https://doi.org/10.1183/13993003.01217- 2020. PMCID: PMC2831497; PMCID: PMC7263826.
[7] J. ou, L. Zhang, M.Y. Ni-Jia-Ti, J. Zhang, F. Hu, L. Chen, Y. Dong, K. Yang, B. Zhang, S. Zhang, A normal pulmonary function and residual CT abnormalities in rehabilitating COVID-19 patients after discharge, J. Infect. 81 (2) (2020) e150–e152, https://doi.org/10.1016/j.jinf.2020.06.005. Epub 2020 Jan 05. PMID: 32551202; PMCID: PMC7271314.
[8] Y. Huang, C. Tan, J. Wu, M. Chen, Z. Wang, L. Luo, X. Zhou, X. Liu, X. Huang, S. Yuan, C. Chen, F. Gao, J. Huang, H. Shan, J. Liu, Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase, Respir. Res. 21 (1) (2020) 163, https://doi.org/10.1186/s12931-020-01429-6. PMID: 3260344; PMCID: PMC7323373.
[9] R. Babun, As their numbers grow, COVID-19 ‘long haulers’ stump experts, J. Am. Med. Assoc. (2020), https://doi.org/10.1001/jama.2020.17709 . Epub ahead of print.
[10] Y.M.J. Goertz, M. Van Herck, J.M. Delbressine, A.W. Vaes, R. Meys, V. C. Machado, S. Houben-Wilke, C. Burtin, R. Ponthuma, F.M.E. Fransens, N. van Loon, B. Hajiain, Y. Spies, H. Vlijmbrief, A.J. van ’t Hul, D.J.A. Janssen, M.A. Spruit, Persistent symptoms 30months after a SARS-COV-2 infection: the post-COVID-19 syndrome? ERJ Open Res (2020), 00542-2020. doi: 10.1183/23120541.00542- 2020. PMCID: PMC7491255.