Received: 20 October 2020 | Accepted: 27 April 2021

DOI: 10.1111/ijcp.14301

SYSTEMATIC REVIEW

Respiratory Medicine

THE INTERNATIONAL JOURNAL OF CLINICAL PRACTICE WILEY

Changes in the respiratory function of COVID-19 survivors during follow-up: A novel respiratory disorder on the rise?

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Abstract

Background: The Human Coronavirus Disease 2019 (COVID-19) is a highly contagious respiratory disorder that may result in acute respiratory distress syndrome. The aim of this review was to investigate the incidence and type of respiratory function abnormalities during the follow-up of patients who recovered from COVID-19.

Methods: A systematic search of MEDLINE was conducted, utilising various term combinations. Studies that assessed any respiratory function parameter during the re-evaluation of patients who recovered from COVID-19 and were published as full-text articles in English are included in this review.

Results: Amongst 183 articles initially retrieved, 8 fulfilled the criteria and were included in this review; they involved a total of 341 adult patients. Four were retrospective studies, one was a prospective cohort study, one was a randomised control trial and two were case reports/case series. The follow-up time ranged from 1 month since symptom onset to 3 months after discharge. The most frequent abnormality was reduced lung diffusion for carbon monoxide (DLCO), followed by a restrictive pattern. Other findings are the lack of resting hypoxemia, the reduced respiratory muscle strength and the decreased exercise capacity, although relative data are extremely limited.

Conclusion: Patients who recovered from COVID-19 present with abnormal respiratory function at short-term follow-up, mainly with reduced lung diffusion and a restrictive pattern. However, results are currently very limited in order safe conclusions to be made, regarding the exact incidence of these abnormalities and whether they may be temporary or permanent.

1 | INTRODUCTION

On 12 March 2020, the human coronavirus disease 2019 (COVID-19) outbreak was declared as a pandemic by the World Health Organization. COVID-19 is a highly contagious respiratory disorder that is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel virus that is easily transmitted between humans.[1,2] As of 9 October 2020, there were 36 754 395 confirmed COVID-19 cases including 1 064 838 deaths globally, with numbers continuously rising.[3] A growing body of literature is providing information regarding the epidemiology, pathophysiology and clinical manifestations of the disease, which can vary widely from asymptotic cases to the rapid development of acute respiratory distress syndrome.[4]

Along with the number of casualties that are constantly growing, there is also a considerable proportion of patients that have been discharged from hospital and recovered from the disease, worldwide. Previous studies amongst patients who recovered from other severe respiratory infections, such as Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS)[5,6] or

H_1N_1 influenza[7] indicated that respiratory function abnormalities and exercise capacity impairment may persist for long during follow-up. However, studies that have compared SARS-CoV-2 to influenza infection concluded that COVID-19, besides similarities, has also several distinct features from influenza; these differences refer to underlying pathophysiologic processes (endothelialitis, interferon-γ mediation of host-immune response and lymphopenia[8]), patient characteristics (COVID-19 patients are older but probably with less comorbidities and lower prevalence of respiratory disorders, compared to the ones with influenza[9,10]), clinical course (the fraction of severe and critical infection and the risk ratio for most respiratory and non-respiratory complications amongst patients with COVID-19 is significantly higher, compared to what is observed for influenza infection[9,10]), imaging presentation (ground-glass opacities are probably more often amongst COVID-19 compared to influenza patients[11]) and prognosis. Since influenza infection cannot serve as an accurate model for COVID-19,[8] one can hypothesise that the short and long-term respiratory function abnormalities of COVID-19 patients cannot be predicted by published data on other severe respiratory infections. To the authors' knowledge, no other study has yet reviewed published literature regarding the potential functional abnormalities during short-term follow-up of patients who recovered from COVID-19 disorder. However, such an approach could provide valuable information regarding disease outcomes and prognosis and offer further data towards the optimisation of follow-up.

Based on the aforementioned, the aim of this review is to summarise the available published data regarding the potential changes in: (a) respiratory function parameters, that is spirometric variables, lung volumes, lung diffusion for carbon monoxide and respiratory muscle strength, (b) arterial blood gases and (c) exercise capacity, during the follow-up re-evaluation of patients who were hospitalised and discharged because of COVID-19 disease.

Review criteria

- This review was conducted using MEDLINE database, aiming to evaluate any respiratory function parameter recorded during follow-up of patients who recovered from COVID-19.
- The article screening and data extraction referred to full-text manuscripts published in english between December 2019 and August 2020 and was conducted by two independent reviewers.

Message for the clinic

- Patients that recovered from COVID-19 present with abnormal respiratory function at short term follow-up, mainly a restrictive pattern and impaired diffusion.
- Data is scarce regarding whether these abnormalities may be permanent or temporary and for how long they may insist, thus longitudinal follow-up studies are needed to draw safe conclusions.

2 | MATERIALS AND METHODS

A search of MEDLINE (December 2019–August 2020) was conducted. We used the terms "covid 19," "SARS-CoV-2," "respiratory function," "pulmonary function," "spirometry," "diffusion," "exercise capacity," "6-minute walking test," "functional capacity," "functional assessment," "follow-up," and "longitudinal" in various combinations. The reference list of all relative articles was also reviewed by the authors, in order for further studies to be identified. Studies that assessed any respiratory function parameter during follow-up re-evaluation amongst discharged COVID-19 patients and were published as full-text articles in English are included in this review.

3 | RESULTS

Amongst the 183 studies initially identified, 8 fulfilled the criteria and are reported in this review (Table 1). These studies were all conducted in adults and they included a total of 341 patients (55.7% males; age range: 19-79 years). Four were retrospective studies, one was a prospective cohort study, one was a randomised control trial and two were cases series/case reports. The follow-up time ranged from 1 month since symptom onset to 3 months after discharge. Six studies were conducted in China, one in France and one in Italy.

3.1 | Spirometric parameters and lung volumes

The majority of patients had normal spirometry at follow-up; however, when pulmonary function was abnormal, the restrictive pattern was more frequent than the obstructive one, amongst COVID-19 survivors. In the study of Huag et al,[1] 57 patients with no history of respiratory disease who underwent rehabilitation were retrospectively evaluated a month after hospital discharge. The patient group means of forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), Tiffeneau index (FEV_1/FVC) and total lung capacity (TLC) were normal. However, impairments in FEV_1, FVC and TLC were present amongst 8.8%, 10.5% and 12.5% of patients, respectively, while a low Tiffeneau index compatible with obstructive disorder (<70) was present in one patient with smoking history. Interestingly, TLC was the only lung volume measurement that differed between patients who recovered from mild or severe (as defined by the presence of respiratory failure or shock or need for ICU monitor and treatment) disease.[1] TLC also correlated with the total severity score in the worst chest CT, but not in the follow-up CT.

Fumagalli et al studied 13 COVID-19 survivors who were admitted to ICU because of bilateral pneumonia. At the time of clinical recovery (ie, just before discharge), FEV_1 and FVC were lower than lower limits of normal (LLN) and FEV_1/FVC was higher than upper limits of normal (ULN), indicating a restrictive pattern. At 6 weeks of

TABLE 1 Follow-up studies that were included in this review

First Author	Follow-up timepoints	Study design	Number of patients	Respiratory parameters measured
Fumagalli A[12]	At time of clinical recovery and 6 wk later	Case series	13 adults	FEV_1 (LLN), FVC (LLN), FEV_1/FVC (ULN) Only at clinical recovery: 2-min walking test, nocturnal SpO_2, ABGs
Huang Y[1]	30 d after discharge	Retrospective study	57 adults	FVC, FEV_1, TLC, RV, DLCO, Raw, R_5, R_{20}, PImax, PEmax, 6MWD
Liu K[18]	At baseline and after 6 wk	Randomised control study	36 adult controls (another 36 underwent PR)	FEV_1, FVC, FEV_1/FVC, TLCO, 6MWD
Frija-Masson J[13]	1 mo after infection	Retrospective study	50 adults	FEV_1, FVC, FEV_1/FVC, DLCO, KCO, TLC
Mo X[15]	1 mo after symptom onset	Retrospective cohort study	110 adults	FEV_1, FVC, FEV_1/FVC, MMEF, FEF_{50}, FEF_{75}, DLCO, DLCO/V_A, TLC, RV, RV/TLC, SpO_2
You J[16]	Between 5 and 6 wk after discharge	Prospective cohort study	18 adults	FEV_1, FVC, FEV_1/FVC, MVV, VC, TV, ERV, IRV, IC, MMEF, FEF50, FEF75, SpO_2
Zha L[17]	1st patient: 1 mo after discharge 2nd patient: 2 mo after disease onset and 3 mo after disease onset	Case reports	2 patients	FEV_1, FVC, FEV_1/FVC, DLCO, PaO_2, 6MWD
Zhao Y-M[14]	3 mo after discharge	Retrospective multi-centre cohort study	55 adults	FEV_1, FVC, TLC, DLCO, small airway function (no further data)

Abbreviations: 6MWD, 6-minute walking distance; ABGs, arterial blood gases; DLCO, diffusing capacity for carbon monoxide; FEF, forced expiratory flow; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; KCO, transfer coefficient for carbon monoxide; LLN, low limits of normal; MMEF, maximum mid-expiratory flow; PaO_2, arterial oxygen partial pressure; PEmax, maximum static expiratory pressure; PImax, maximum static inspiratory pressure; R20, central airway resistance at an oscillation frequency of 20 Hz; R5, airway viscosity resistance at an oscillation frequency of 5 Hz; Raw, airway resistance; RV, residual volume; SpO_2, arterial oxygen saturation; TLC, total lung capacity; TLCO, diffusing capacity for carbon monoxide; ULN, upper limits of normal l.

follow-up FEV_1 and FEV_1/FVC were not different than LLN and ULN correspondingly, but FVC remained reduced, indicating a partially persistent pattern of respiratory restriction.[12]

Similarly, in an evaluation of 50 discharged non-critical patients 1 month after symptom onset, the majority of patients had mild impairments of pulmonary function and mean group FEV_1%, FVC%, FEV_1/FVC and TLC% predicted values were normal.[13] Nevertheless, when the patterns of pulmonary function were evaluated, 28% of patients presented with a restrictive pattern (with or without diffusion abnormalities). This percentage increased up to 51% amongst patients who had presented with severe pneumonia, involving >50% of parenchyma extent; the clinical severity of the disease course, though, was not associated with differences in pulmonary function variables.[13]

The longest follow-up evaluation was conducted in the study of Zhao et al, which included 55 eligible patients with non-critical COVID-19 disease who had been discharged from the hospital.[14] In this study, almost one out of four patients still presented with a pulmonary function abnormality during the 3-month follow-up; a restrictive pattern was present amongst 10.9%, an obstructive pattern amongst 9.1% a mixed pattern in 5.5% of individuals, while small airway dysfunction was present in almost 13% of participants, although authors do not report the exact variables that were chosen to indicate airway dysfunction. No correlation was found, though, between FEV_1%, FVC%, TLC% predicted values and the extent of chest X-ray findings.[14]

In the larger study in the field, Mo et al evaluated 110 discharged patients within a month after symptom onset; approximately 9% had reduced FVC, 13.6% reduced FEV_1, while in 5% of patients FEV_1/FVC was <70.[15] The most frequent lung volume abnormality was reduced TLC; it was present amongst 25% of the total patient group, while almost half of these cases were found amongst those who had recovered from severe disease. In this study, clinical severe cases presented with significantly lower TLC% predicted, suggesting a greater impairment of respiratory function amongst those patients. However, Mo et al did not report the extent of parenchyma involvement according to thorax computed tomography (CT) findings and its potential association to spirometric variables, while the spirometric evaluation was conducted quite early in the course of the disease that is 1 month after symptom onset.

In another small study, You et al confirmed that the majority of patients who recovered from COVID-19 presented with normal pulmonary function approximately 5-6 weeks after discharge. Amongst the 18 patients evaluated though, the most common spirometric abnormality was small airway dysfunction which was present in one-third of the participants, while 16.7% presented either an obstructive or a restrictive pattern.[16] Zha et al published the follow-up course of two COVID-19 who recovered, which was significantly different; the first one presented with completely normal lung function approximately 1 month after discharge, while the second one with a restrictive lung function defect (FVC = 62.3% and FEV_1/FVC = 80.1%) at 2-month follow-up after disease onset, which further worsens at 3-month follow-up.[17] In contrast to all other studies, one of the Liu et al indicated that the patients' group mean FEV_1/FVC ratio was lower than 70 at discharge, indicating the presence of obstruction, which persisted at 6 weeks of follow-up. However, this was an open randomised control study to evaluate the effects of respiratory pulmonary rehabilitation (PR) on respiratory function amongst patients without prior obstructive lung disease who recovered from COVID-19, that is a clinical trial in a selective patient group >65 years old, so results can be less easily generalised.[18]

3.2 | Diffusion abnormalities

The most common pulmonary function abnormality encountered during patient follow-up is the impairment of diffusion capacity for carbon monoxide (DLCO), which can be either isolated or in combination with a restrictive pattern. Huang et al[1] reported that at 1-month follow-up after hospital discharge, the majority (52.6%) of 57 participants presented with abnormal DLCO (<80% of predicted); of these patients approximately 13% had moderate DLCO impairment (40%–60% predicted), while in the rest the impairment was mild (>60% predicted). Interestingly, there was a significant difference in impaired diffusing capacity between the two groups, which accounted for 42.5% in non-severe cases and 75.6% in severe cases, respectively. Nevertheless, DLCO %predicted values did not correlate with TTS on worst chest CT during follow-up.[1]

In the study of Frija-Masson, where 50 discharged patients were evaluated 1 month after symptom onset, the mean DLCO %predicted was within normal values. However, 26% of patients had isolated low DLCO, while another 16% presented with abnormal DLCO combined with a restrictive spirometric pattern[13] and the proportion of abnormal values was significantly different between groups according to the CT extent of pneumonia (from none/mild to severe). Similar to the rest of pulmonary function parameters, this study established no difference of DLCO between the stages of clinical severity.

In the larger study of Mo et al, the mean DLCO %predicted value was slightly reduced (78.2 ± 14.3), while low DLCO values (<80% predicted) were noted amongst 47.2% of individuals 1 month after symptom onset.[15] Mean DLCO %predicted values significantly decreased and the proportion of abnormal DLCO significantly increased with varying degrees of disease severity (from mild to severe). Interestingly, for almost one out of two patients with impaired DLCO, the transfer coefficient (DLCO/VA) remained normal.

3.3 | Changes in respiratory muscle function

Currently, the only available data on respiratory muscle function during follow-up of COVID-19 patients come from the study of Huang et al[1]; according to this, more than half of patients presented with impaired respiratory muscle strength. Approximately 30 days after hospital discharge, maximum static inspiratory pressure (Pimax) was below normal expected values in 49% of patients, while another 23% presented with abnormal maximum static expiratory pressure (Pemax). Authors report that no significant difference in respiratory muscle strength was noted between severe clinical cases that were treated with glycocorticosteroids and non-severe ones; however, group comparisons of mean Pimax values yielded a level of significance of 0.059 and no sample size calculation was conducted, so the lack of group difference might be questionable.

3.4 | Arterial blood gases

Data regarding arterial blood gases during patients' follow-up after COVID-19 recovery are scarce. Mo et al reported that mean oxygen arterial saturation (SpO_2%) was normal and over 98% amongst 110 patients who were studied 1 month after symptom onset.[15] In the smaller study of You et al,[16] no patients out of the 18 that were assessed approximately 1 month after hospital discharge presented with resting hypoxemia, as mean SpO_2 was 95% and no difference was noted between patients with severe and non-severe disease. Zha et al reported that in a case of a patient who developed respiratory restriction at 3-month follow-up, arterial oxygen partial pressure was low and just above 60 mmHg.[17] In another small study, 50% of discharge-ready patients with COVID-19 and normal resting oxygen saturation presented with SpO_2 <90% during exercise and, thus, terminated 6MWT early[19]; nevertheless, this assessment was conducted not during follow-up, but just before hospital discharge, so longitudinal studies are needed to identify whether these patients establish exercise-induced desaturation.

3.5 | Exercise endurance and functional capacity

There are extremely limited data regarding the exercise capacity of COVID-19 patients after recovery. In the study of Huang et al, the mean 6-minute walking distance (6MWD) at 1 month of follow-up was approximately 562 m; however, patients with severe disease

were presented with significantly shorter 6MWD than the non-severe ones (517.43 ± 44.55 m vs 573.52 ± 38.38 m; $P = .012$).[1] When the % predicted values were evaluated, the severe cases reached only 88.4% of predicted values, which is significantly lower than the non-severe cases, indicating a significant decrease in short-term exercise capacity amongst them.

Exercise capacity was even worse in the study of Liu et al,[18] where an intervention group (that received respiratory PR after hospital discharge) was compared to a control group (that did not receive respiratory PR); in both groups mean 6MWD very low at baseline (162.7 ± 72.0 vs 155.7 ± 82.1, correspondingly) and it remained invariable in the control group at 6 weeks of follow-up (157.2 ± 71.7). Although the latter study was conducted in elderly individuals with one or more comorbidities, it indicates that exercise capacity can markedly reduce amongst COVID-19 survivors and this reduction may insist for a long.

4 | DISCUSSION

In this review, we summarised the existing literature regarding follow-up lung function abnormalities amongst patients who were discharged after recovering from SARS-CoV-2 infection; the most remarkable finding is that existing data are scarce, as they come from small studies which were conducted during very short-term follow-up. Amongst the abnormalities noted, reduced DLCO was the most frequently encountered, followed by a restrictive pattern, as they may be evident in almost half of patients during follow-up. Other interesting findings are the lack of resting hypoxemia, the reduced respiratory muscle strength and the decreased exercise capacity, although relative data are extremely limited.

Diffusion capacity abnormalities are a common complication amongst patients that survived severe respiratory infections. In a previous meta-analysis, the survivors of SARS and MERS were presented with reduced DLCO that persisted in some cases up to 12 months after recovery[5]; this is consistent with relevant CT findings which have reported that pulmonary fibrosis amongst survivors of SARS can persist for up to 7 years.[20] The CT abnormalities recorded during the follow-up of patients with COVID-19 are similar; You et al reported that after approximately 40 days from discharge, 61.1% of patients presented with ground-glass opacities and pulmonary fibrosis.[16] In a larger study, Huang et al reported that at 30 days of follow-up approximately, 54% of patients had residual abnormalities in thorax CT and this percentage increased up to 94.1% amongst those who had recovered from severe COVID-19 disease.[1] Most of the residual imaging abnormalities were patchy ground-glass opacities with periphery distribution, but pulmonary fibrosis could also be noted amongst severe cases.[1] According to pathological case series, the major pulmonary finding amongst patients who survived or died from COVID-19 was diffuse alveolar damage (DAD) in the acute or organising phases[21,22] with more intense than usual perivascular inflammation/endotheliitis,[22] while focal pulmonary microthrombi could also be present.[21] These imaging and pathologic abnormalities are consistent and may explain the presence of low DLCO amongst surviving COVID-19 patients; however, to what extent and for how long these abnormalities may persist should be further studied.

Respiratory restriction is far more common than obstructive abnormalities amongst these patients. The main respiratory function parameter that was found to be reduced was TLC, which was the only lung volume parameter associated with the severity of disease[15,16] and with the extent of imaging abnormalities.[13] Since peripheral ground-glass opacities with or without pulmonary fibrosis are the main residual abnormality amongst these patients,[1,16] a restrictive respiratory function is compatible with these findings. A previous publication suggested that alveolar volume (VA) might be more compromised than DLCO during follow-up[23]; this hypothesis was based on the fact that amongst COVID-19 patients ready for discharge, DLCO/VA was found near normal, while DLCO abnormal,[15] indicating that complete acini with alveoli and blood vessels surrounding them are affected,[23,24] while in the remaining functionally available alveolar volume, the actual carbon monoxide uptake is possibly near normal. The pathogenetic mechanism that was proposed was that although initial COVID-19 abnormalities might be similar to that of SARS consisting of microvascular injury with some interstitial thickening,[23] it is followed by the development of alveolar abnormalities with gradual loss of the alveolar spaces[24,25] and filling of the alveoli with exudate at a later stage, resulting in decreased lung volume and reduced pulmonary compliance.[23,26] Moreover, decreased alveolar volume in discharged patients may be explained by transient changes in the mechanical properties of the chest wall and respiratory muscles after critical illness [23] ; this hypothesis agrees with the scarce data on reduced respiratory muscle strength which persists at follow-up.[1] Although obstructive pattern with FEV_1/FVC <70 seems to be highly unusual amongst non-COPD patients, small airway dysfunction is a common abnormality, but of low severity. This finding may also be explained by small airway congestion,[15] but this is a hypothesis that needs to be further tested.

Do patients who survived COVID-19 face the risk of a chronic respiratory disorder? Current data seem not yet sufficient to support or reject this notion, as the number of follow-up studies is very limited, the number of patients included small and the follow-up duration short. In the follow-up studies amongst patients who recovered from SARS improvement of pulmonary function abnormalities were noted in several, but not all patients. In the study of Ng et al,[27] lung function abnormalities were present amongst 75.4% survivors of SARS, at 6-month follow-up, while in the study of Ong et al, pulmonary function abnormalities were still present in one-third of the 94 SARS survivors at 1-year follow-up.[6] In a meta-analysis, Ahmed et al[5] indicated that, although lung function significantly improved over time, the reduction in DLCO was still present in 11%-45% of SARS survivors at 12 months, while 6MWD slowly increased after 1 year. Although functional long-term follow-up studies are scarce, Wu et al reported that imaging abnormalities may persist after 7 years amongst SARS survivors, with findings compatible with pulmonary fibrosis, which is a predominance of intralobular and interlobular septal thickening.[20]

Whether this may also be the progress of COVID-19 survivors, remains to be studied.

5 | CONCLUSION

Patients who recovered from COVID-19 present with pulmonary function abnormalities, decreased muscle strength and reduced exercise capacity at short-term follow-up. However, because of the paucity of current data, longitudinal studies, with systematic follow-up assessment of pulmonary function, exercise capacity, respiratory muscles strength and exercise-induced hypoxemia are urgently needed. Such studies would determine whether COVID-19 survivors develop persistent functional impairments, when these impairments become permanent and whether there are any risk factors that may predict this unfavourable clinical outcome. And to go one step further, these studies may facilitate the designing of individualised pulmonary rehabilitation programmes amongst COVID-19 survivors during both the post-acute and the long-term recovery phase, aiming to optimise their long-term outcomes.

DISCLOSURE

The authors declared no conflict of interest.

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REFERENCES

1. Huang Y, Tan C, Wu J, et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. *Respir Res*. 2020;21:163.
2. Boutou AK, Pitsiou G, Kontakiotis T, Kioumis I. Nicotine treatment and smoking cessation in the era of COVID-19 pandemic: an interesting alliance. *ERJ Open Res*. 2020;6:0306-2020
3. WHO Coronavirus Disease (COVID-19) Dashboard [Internet]. https://covid19.who.int. Accessed September 17, 2020.
4. Gavriatopoulou M, Korompoki E, Fotiou D, et al. Organ-specific manifestations of COVID-19 infection. *Clin Exp Med*. 2020;20:493-506.
5. Ahmed H, Patel K, Greenwood DC, et al. Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: a systematic review and meta-analysis. *J Rehabil Med*. 2020;52:jrm00063.
6. Ong K-C, Ng AW-K, Lee LS-U, et al. 1-year pulmonary function and health status in survivors of severe acute respiratory syndrome. *Chest*. 2005;128:1393-1400.
7. Hsieh M-J, Lee W-C, Cho H-Y, et al. Recovery of pulmonary functions, exercise capacity, and quality of life after pulmonary rehabilitation in survivors of ARDS due to severe influenza A (H1N1) pneumonitis. *Influenza Other Respir Viruses*. 2018;12:643-648.
8. Torres Acosta MA, Singer BD. Pathogenesis of COVID-19-induced ARDS: implications for an ageing population. *Eur Respir J*. 2020;56:2002049.
9. Cates J, Lucero-Obusan C, Dahl RM, et al. Risk for in-hospital complications associated with COVID-19 and influenza - Veterans Health Administration, United States, October 1, 2018-May 31, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69:1528-1534.
10. [No authors listed]. WHO: Coronavirus disease (COVID-19): Similarities and differences with influenza. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/q-a-similarities-and-differences-covid-19-and-influenza? Accessed November 18, 2020.
11. Tang X, Du R-H, Wang R, et al. Comparison of hospitalized patients with ARDS caused by COVID-19 and H1N1. *Chest*. 2020;158:195-205.
12. Fumagalli A, Misuraca C, Bianchi A, et al. Pulmonary function in patients surviving to COVID-19 pneumonia. *Infection*. 2021;49:153-157.
13. Frija-Masson J, Debray M-P, Gilbert M, et al. Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post-infection. *Eur Respir J*. 2020;56:2001754.
14. Zhao Y-M, Shang Y-M, Song W-B, et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine*. 2020;25:100463.
15. Mo X, Jian W, Su Z, et al. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J*. 2020;55:2001217.
16. You J, Zhang L, Ni-Jia-Ti M-Y-L, et al. Anormal pulmonary function and residual CT abnormalities in rehabilitating COVID-19 patients after discharge. *J Infect*. 2020;81:e150-e152.
17. Zha L, Shen Y, Pan L, et al. Follow-up study on pulmonary function and radiological changes in critically ill patients with COVID-19. *J Infect*. 2020;82:159-198.
18. Liu K, Zhang W, Yang Y, Zhang J, Li Y, Chen Y. Respiratory rehabilitation in elderly patients with COVID-19: a randomized controlled study. *Complement Ther Clin Pract*. 2020;39:101166.
19. Fuglebjerg NJU, Jensen TO, Hoyer N, Ryrsø CK, Lindegaard B, Harboe ZB. Silent hypoxia in patients with SARS CoV-2 infection before hospital discharge. *Int J Infect Dis*. 2020;99:100-101.
20. Wu X, Dong D, Ma D. Thin-section computed tomography manifestations during convalescence and long-term follow-up of patients with severe acute respiratory syndrome (SARS). *Med Sci Monit*. 2016;22:2793-2799.
21. Bradley BT, Maioli H, Johnston R, et al. Histopathology and ultrastructural findings of fatal COVID-19 infections in Washington State: a case series. *Lancet*. 2020;396:320-332.
22. Konopka KE, Nguyen T, Jentzen JM, et al. Diffuse alveolar damage (DAD) from coronavirus disease 2019 infection is morphologically indistinguishable from other causes of DAD. *Histopathology*. 2020;77:570-578.
23. Nusair S. Abnormal carbon monoxide diffusion capacity in COVID-19 patients at time of hospital discharge. *Eur Respir J*. 2020;56:2001832.
24. Hughes JMB, Pride NB. Examination of the carbon monoxide diffusing capacity (DL(CO)) in relation to its KCO and VA components. *Am J Respir Crit Care Med*. 2012;186:132-139.
25. Ayers LN, Ginsberg ML, Fein J, Wasserman K. Diffusing capacity, specific diffusing capacity and interpretation of diffusion defects. *West J Emerg Med*. 1975;123:255-264.
26. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054-1062.
27. Ng CK, Chan JWM, Kwan TL, et al. Six month radiological and physiological outcomes in severe acute respiratory syndrome (SARS) survivors. *Thorax*. 2004;59:889-891.

How to cite this article: Boutou AK, Georgopoulou A, Pitsiou G, Stanopoulos I, Kontakiotis T, Kioumis I. Changes in the respiratory function of COVID-19 survivors during follow-up: A novel respiratory disorder on the rise?. *Int J Clin Pract*. 2021;75:e14301. https://doi.org/10.1111/ijcp.14301