Impaired pulmonary function, muscle strength and quality of life in critically ill COVID-19 survivors

Flikweert, A. W.; Rettig, T. C.D.; Kant, K. M.; de Backer, I. C.F.; van der Sar-Van der Brugge, S.; van der Meer, N. J.M.; van der Voort, P. H.J.; Grootenboers, M. J.J.H.

Published in:
Netherlands Journal of Critical Care

Publication date:
2022

Submitted February 2021; Accepted May 2021

LETTER TO THE EDITOR

Impaired pulmonary function, muscle strength and quality of life in critically ill COVID-19 survivors

A.W. Flikweert[1], T.C.D. Rettig[2], K.M. Kant[1,2], I.C.F. de Backer[1], S. van der Sar-van der Brugge[1], N.J.M. van der Meer[3], P.H.J. van der Voort[4], M.J.J.H. Grootenboers[1]

[1]Department of Pulmonology and, [2]Department of Intensive Care, Anaesthesiology and Pain Medicine, Amphia Hospital, Breda, the Netherlands

[3]Catharina Hospital, Eindhoven, the Netherlands

[4]Department of Intensive Care, University Medical Centre, Groningen University, Groningen, the Netherlands

Correspondence

A.W. Flikweert - aflikweert@amphia.nl

Keywords - **COVID-19, post-ICU, pulmonary function tests, health-related quality of life**

Dear editor,

The immediate damaging impact of the new coronavirus disease 2019 (COVID-19) on the respiratory system is substantial; furthermore the long-term consequences remain unclear. Limited studies describe the functional outcome of critically ill COVID-19 patients with acute respiratory distress syndrome (ARDS) admitted to the intensive care unit (ICU),[1-3] as most studies have focused on the pulmonary function and quality of life of COVID-19 patients treated outside the ICU. A recent study showed that one year after ICU admission, around 60% of the medical ICU survivors were suffering from new physical, mental and/or cognitive health problems that were impacting on their quality of life.[4] These persistent functional disabilities are largely a result of muscle weakness and wasting and, to a lesser extent, intrinsic pulmonary morbidity.[5] We aimed to determine the impact of COVID-19 induced ARDS on pulmonary function, muscle strength and health-related quality of life of previously critically ill patients two months after hospital discharge.

Methods

We performed a prospective cohort study with an observational design on COVID-19 patients who were admitted to the ICU from 9 March to 9 April 2020 and suffered from ARDS. Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection was confirmed via real-time reverse transcription polymerase chain reaction on sputum or oropharyngeal swab. All patients were admitted to the ICU because of ARDS, defined according to the Berlin definition of ARDS.

Surviving patients received an invitation to visit the pulmonary medicine outpatient clinic two months after hospital discharge. During this visit, we collected pulmonary function variables, hand muscle strength measurements and performed a chest radiograph. Pulmonary function tests included spirometry, total body plethysmography and diffusing capacity for carbon monoxide (DLCO). The degree of severity in DLCO was interpreted according to the European Respiratory Society/ American Thoracic Society recommendation for interpretation of pulmonary function tests.[6]

Health-related quality of life was measured with the Hospital Anxiety and Depression Scale (HADS), and the 36-item Short-Form Survey (SF-36), which assesses both physical and mental health. The maximum HADS score is 21 for either anxiety or depression; a score above 8 indicates an anxiety disorder or depression. The SF-36 items are scored from 0 to 100, higher scores indicating better quality of life and level of functioning. Hand muscle strength was measured on the dominant hand using a JAMAR handheld dynamometer and was compared with the normative value for the Dutch population.[7] Muscle strength was reduced when the value was below the fifth percentile, adjusted for age and gender.

The study was approved by the institutional ethics committee (N2020-0354). Descriptive statistics were used to describe our findings, using SPSS statistics version 26.0 (IBM). Continuous variables were compared between groups with the t-test, categorical variables were compared with the chi-squared test.

Results

At our ICU, 51 patients survived critical COVID-19 between 9 March and 9 April 2020. Of them 16 were lost to follow-up, mostly because of transfer to other hospitals, leaving 35 patients for inclusion. The median age was 60 years (IQR 54-69) and

Table 1. Patient characteristics (n=35)

Age - years	60 (56-69)
Female	9 (25.7)
BMI, kg/m^2	27 (25-31)
Smoker	
Active	0 (0)
Former	20 (57.1)
Comorbidities	
Pre-existing pulmonary disease	
COPD	0 (0)
Asthma	4 (11.4)
OSAS	5 (14.3)
Pre-existing cardiac disease	6 (17.1)
Hypertension	10 (28.6)
Diabetes mellitus	6 (17.1)
History of malignancy	5 (14.3)
Immune compromised	3 (8.6)
ICU characteristics	
APACHE II score	14 (11-18)
Berlin classification of ARDS	
Mild	5 (14.3)
Moderate	25 (71.4)
Severe	5 (14.3)
Treatment	
Corticosteroids	4 (11.4)
Chloroquine	28 (80)
Lopinavir/ritonavir	13 (37.1)
Renal replacement therapy	6 (17.1)
Pulmonary embolism	5 (14.3)
ICU and hospital outcomes	
Total ventilated days	12 (8-22)
Length of ICU stay – days	14 (8-27)
Length of hospitalisation – days	21 (16-39)
Discharge destination	
Home	24 (68.6)
Rehabilitation clinic	11 (31.4)

Data are presented as no. (%) or the median (interquartile range).
APACHE = Acute Physiology And Chronic Health Evaluation; ARDS = acute respiratory distress syndrome; BMI = body mass index; COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; OSAS = obstructive sleep apnoea syndrome

9 patients (25.7%) were female (*table 1*). None of the patients were current smokers and 20 patients (57.1%) were former smokers. A history of asthma was present in 4 patients (11.3%). Patients reported no limitations in activities of daily living before admission to the ICU.

At admission to the ICU, 30 patients (85.7%) were diagnosed with moderate to severe ARDS. The median number of ventilator days was 12 (IQR 8-22). Median length of ICU and hospital stay were 14 days (IQR 8-27) and 21 days (IQR 16-39), respectively. Most patients were discharged home, but 11 patients (31.4%) were discharged to a rehabilitation facility. Patients discharged to a rehabilitation facility required more days on mechanical ventilation (18.4 vs 9.8 days, p=0.01) and ICU-acquired weakness was reported more often (9 patients (81.8%) vs 6 patients (25%), p=0.002). The mean age in the rehabilitation group was higher, 66.6 years vs 58.8 years in the patients discharged to home (p=0.0496).

Pulmonary function tests were completed in 34 patients, except for one failed DLCO test (*table 2*). One patient was unable to perform pulmonary function tests due to a tracheostomy. In 23 patients (65.7%) a reduced DLCO was observed. In patients discharged to a rehabilitation clinic, diffusion capacity was significantly lower (54.3% of predicted vs 72.7%, p=0.016).

Forced vital capacity was reduced in 13 patients (37.1%) Forced expiratory volume in 1 second was reduced in 8 patients (20%), one of whom had a history of asthma. A mild, moderate and severe decrease in diffusion were observed in 8 (22.9%), 13 (37.5%) and 2 (5.7%) patients, respectively.

Chest radiographs revealed persistent abnormalities in 18 patients (54.1%), the dominant feature being a fine reticular interstitial pattern.

The median hand muscle strength was 27.5 kg (IQR 18.7-43.8) and was reduced in 13 patients (37.1%).[7] The median HADS scores for anxiety and depression were 3 (IOR 2-5.5) and 2 (IQR 1-5), respectively. A HADS score ≥8 was found for anxiety in 3 patients (8.6%) and for depression in 6 patients (17.1%). We also observed poor median scores in the SF-36 domains of physical functioning and health change. In 26 patients (74.3%) there was a substantially reduced SF-36 score in one or more domains.

Discussion

In our study, we observed that 66% of the patients surviving COVID-19 related ARDS had a mild to moderate reduction in DLCO two months after hospital discharge. This is in line with previous studies evaluating pulmonary function outcome of other coronavirus pneumonia outbreaks (Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS)) which showed that impaired DLCO was the most common abnormality in survivors.[8] In non-critically ill COVID-19 patients the incidence of impaired pulmonary diffusing capacity varied from 16 to 47%.[1,2] We observed a higher incidence of impaired DLCO, this is most likely explained

Table 2. Results of pulmonary function tests, muscle strength and quality of life at 2-month follow-up visit

Pulmonary function tests	
FVC % of predicted	88.5 (70-93.50)
FVC <80% of predicted	13 (37.1)
FEV1 % of predicted	89 (79.5-102.3)
FEV1 <80% of predicted	8 (22.9)
FEV1/FVC%	84.3 (77-87)
FEV1/FVC < 70%	4 (11.4)
TLC % of predicted	87 (74-97)
TLC <80% of predicted	10 (28.6)
FRC % of predicted	85 (76-99)
FRC <80% of predicted	9 (25.7)
DLCO % of predicted	63 (50.5-79.5)
Severity of decrease in DLCO	
Mild 61-75% of predicted	8 (22.9)
Moderate 40-60% of predicted	13 (37.5)
Severe <40% of predicted	2 (5.7)
KCO % of predicted	91 (69.5-94.5)
KCO <80% of predicted	10 (28.6)
Hand muscle strength, kg	26.6 (18.6-43.6)
Reduced muscle strength*	13 (37.1)
HADS	
Anxiety	3 (2-5)
Depression	2 (1-5.5)
SF-36	
Physical role limitations	25 (0-50)
Emotional role limitations	100 (33.3-100)
Physical functioning	55 (40-85)
Social functioning	62.5 (53.1-96.9)
Mental health	80 (74–92)
Vitality	60 (45-70)
Pain	67.4 (44.9–96)
General health perception	60 (45–75)
Health change	25 (0–25)

Data are presented as median (interquartile range) or number (%). DLCO = diffusing capacity for carbon monoxide; FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity; FRC = functional residual capacity; HADS = Hospital Anxiety and Depression Scale; KCO = carbon monoxide transfer coefficient; SF-36 = 36-item Short Form Health survey; TLC = total lung capacity

* Reduced when the value was below the fifth percentile, adjusted for age and gender

by the severity of the disease, i.e. the presence and severity of ARDS results in more pulmonary, parenchymal damage.

The observed impaired diffusing capacity may be explained by pulmonary and vascular damage due to COVID-19. Pathological data in patients with COVID-19 pneumonia show diffuse alveolar damage with progression to fibrosis and severe endothelial injury with widespread thrombotic microangiopathy in the pulmonary vasculature, both contributing to diffusion impairment.[9,10] This pulmonary damage can be visualised by radiological imaging. In the majority of our patients chest radiography showed interstitial abnormalities. Two previous studies reported abnormal chest CT findings in 54% and 71% of the patients at 30 days and 3 months after hospital discharge, respectively.[2,3]

Many patients reported reduced quality of life with limitations in their daily activities. This may be the result of impaired pulmonary and muscle function. Impaired physical function is also seen in survivors of ARDS that is not COVID-19 related.[11] Moreover, muscle weakness post-ARDS is associated with worse survival.[12] These findings emphasise the importance of rehabilitation programs. As observed in elderly non-critically ill patients with COVID-19, rehabilitation improved respiratory function, quality of life and anxiety.[13]

The main limitation of our study is the small sample size. In addition, baseline pulmonary function tests were not available. Since smoking might decrease DLCO, it is notable that 57% of the patients were former smokers. Many other factors that were not measured in this study could also have had an influence on the outcomes (e.g. Barthel index and psychological function before admission).

In conclusion, functional outcome of survivors of critical COVID-19 with ARDS two months after hospital discharge is characterised by a reduced DLCO, reduced hand muscle strength and physical functioning. To determine the long-term impact of critical COVID-19, future research is required to investigate whether patients develop pulmonary fibrosis. Because muscle weakness is an important factor in delayed recovery, the clinician should focus more on prevention of wasting and remaining muscle strength. As more than 30% of the patients needed clinical rehabilitation, we recommend to involve the rehabilitation physician early in the recovery process, resulting in an individually tailored rehabilitation plan.

Disclosures

All authors declare no conflict of interest. No funding or financial support was received.

References

1. 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: doi:10.1183/13993003.01217-2020.
2. Y-M Zhao, Y-M Shang, W-B Song, et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. EClinicalMedicine. 2020;25: doi:10.1016/j.eclinm.2020.100463.
3. 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: doi:10.1186/s12931-020-01429-6.
4. Geense WW, Zegers M, Peters MAA, et al. New Physical, Mental, and Cognitive Problems 1-year Post-ICU: A Prospective Multicenter Study. Am J Respir Crit Care Med. 2021. doi:10.1164/rccm.202009-3381OC. Online ahead of print.
5. Eden A. One-Year Outcomes in Survivors of the Acute Respiratory Distress Syndrome. Survey Anesthesiol. 2004;44: doi:10.1097/01.sa.0000108427.01685.9a.
6. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26:948-68.
7. Peters MJH, Van Nes SI, Vanhoutte EK, et al. Revised normative values for grip strength with the Jamar dynamometer. Peripher Nerv Syst. 2011;16:47-50.
8. Ahmed H, Patel K, Greenwood DC, et al. Long-term clinical outcomes in survivors of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis. J Rehabil Med. 2020;52: doi:10.2340/16501977-2694
9. Li Y, Wu J, Wang S, et al. Progression to Fibrosing Diffuse Alveolar Damage in a Series of 30 Minimally Invasive Autopsies with COVID-19 Pneumonia in Wuhan, China. Histopathology. 2020. First published: 14 September 2020. doi:10.1111/his.14249.
10. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med. 2020;383:120-8.
11. Bienvenu OJ, Colantuoni E, Mendez-Tellez PA, et al. Depressive symptoms and impaired physical function after acute lung injury: A 2-year longitudinal study. Am J Respir Crit Care Med. 2012;185:517-24.
12. DInglas VD, Aronson Friedman L, Colantuoni E, et al. Muscle Weakness and 5-Year Survival in Acute Respiratory Distress Syndrome Survivors. Crit Care Med. 2017;45:446-53.
13. 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: doi:10.1016/j.ctcp.2020.101166