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Pulmonary function and respiratory muscle strength at hospital discharge in COVID-19 patients after Intensive Care Unit admission

Função pulmonar e força muscular respiratória na alta hospitalar em pacientes com COVID-19 pós internação em Unidade de Terapia Intensiva

Función pulmonar y fuerza muscular respiratoria al alta hospitalaria en pacientes con Covid-19 posingreso en la Unidad de Cuidados Intensivos

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ABSTRACT | This study describes the pulmonary function and respiratory muscle strength (RMS) at hospital discharge of severe COVID-19 patients, correlating them with peripheral muscle strength, duration of mechanical ventilation (MV), length of hospital stay, and use of medication. A cross-sectional study was conducted with COVID-19 patients admitted to the Intensive Care Unit. Assessment at hospital discharge included the following variables: RMS, pulmonary function, and peripheral muscle strength (Medical Research Council score [MRC] and handgrip dynamometry). A total of 25 patients with mean age of 48.7±12.3 years were assessed. Out of these, 72% presented restrictive ventilatory disorder, in addition to reduced RMS (maximum inspiratory pressure [MIP] of 74% and maximum expiratory pressure [MEP] of 78% of the predicted value). RMS (MIP and MEP, respectively) correlated negatively with duration of MV (r=−0.599, p=0.002; r=−0.523, p=0.007) and length of hospital stay (r=−0.542, p=0.005; r=−0.502, p=0.01); and positively with FVC (r=0.825, p=0.000; r=0.778, p=0.000), FEV1 (r=0.821, p=0.000; r=0.801, p=0.000), PEF (r=0.775, p=0.000; r=0.775, p=0.000), and handgrip strength (r=0.656, p=0.000; r=0.589, p=0.002). At hospital discharge, severe COVID-19 patients presented: reduced RMS; changes in lung function; negative correlation between RMS and duration of invasive mechanical ventilation (IMV), and length of hospital stay; and a positive correlation with lung function and hand grip strength.

Keywords | COVID-19; Respiratory Function Tests; Respiratory muscles; Critical Care.

RESUMO | Este estudo teve como objetivo descrever a função pulmonar e a força muscular respiratória (FMR) na alta hospitalar de pacientes com quadros críticos da COVID-19 e correlacioná-las com a força muscular periférica, tempo de ventilação mecânica (VM) e de internação hospitalar e uso de medicações. Trata-se de um estudo transversal, incluindo pacientes que estiveram internados na UTI devido à COVID-19. A avaliação, na alta hospitalar, incluiu as seguintes variáveis: FMR, função pulmonar e força muscular periférica (escore *Medical Research Council* (MRC) e dinamometria de preensão palmar). Foram incluídos 25 pacientes, com idade média de 48,7±12,3 anos. Observou-se que 72% dos pacientes apresentaram distúrbio ventilatório restritivo, além de redução da FMR (pressão inspiratória máxima (PImáx) de 74% e pressão expiratória máxima (PEmáx) de 78% do predito). A FMR (PImáx e PEmáx, respectivamente) apresentou correlação negativa com o tempo de VM (r=−0,599, p=0,002; r=−0,523, p=0,007) e de internação hospitalar (r=−0,542, p=0,005; r=−0,502, p=0,01) e correlação positiva com a capacidade vital forçada (CVF) (r=0,825, p=0,000; r=0,778, p=0,000), o volume expiratório forçado no primeiro segundo

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(VEF1) (r=0,821, p=0,000; r=0,801, p=0,000), o pico de fluxo expiratório (PFE) (r=0,775, p=0,000; r=0,775, p=0,000) e a força de preensão palmar (r=0,656, p=0,000; r=0,589, p=0,002). Concluímos que pacientes com quadros críticos da COVID-19 apresentaram, na alta hospitalar: redução da FMR; alterações da função pulmonar; correlação negativa entre a FMR e o tempo de ventilação mecânica invasiva (VMI) e de internação hospitalar; e correlação positiva com a função pulmonar e a força de preensão palmar.
Descritores | COVID-19; Testes de Função Respiratória; Músculos Respiratórios; Cuidados Críticos.

RESUMEN | Este estudio tuvo como objetivo describir la función pulmonar y la fuerza muscular respiratoria (FMR) al alta hospitalaria de pacientes con condiciones críticas del Covid-19 y correlacionarlas con la fuerza muscular periférica, el tiempo de ventilación mecánica (VM) y de hospitalización y uso de medicamentos. Se trata de un estudio transversal con pacientes que ingresaron en Unidades de Cuidados Intensivos por Covid-19. La evaluación en el alta hospitalaria incluyó las siguientes variables: FMR, función pulmonar y fuerza muscular periférica (puntuación Medical Research Council –MRC– y dinamometría manual). Participaron 25 pacientes, con una edad media de 48,7±12,3 años. Se observó que el 72% de los pacientes presentó trastorno ventilatorio restrictivo, además de una reducción de la FMR (presión inspiratoria máxima –PImáx– del 74% y presión espiratoria máxima –PEmáx– del 78% del valor predicho). La FMR (PImáx y PEmáx, respectivamente) mostró una correlación negativa con la duración de la VM (r=−0,599, p=0,002; r=−0,523, p=0,007) y la hospitalización (r=−0,542, p=0,005; r=−0,502, p=0,01), pero una correlación positiva con la capacidad vital forzada (CVF) (r=0,825, p=0,000; r=0,778, p=0,000), el volumen espiratorio forzado en el primer segundo (VEF1) (r=0,821 , p=0,000; r=0,801, p=0,000), el flujo espiratorio máximo (FEM) (r=0,775, p=0,000; r=0,775, p=0,000) y la fuerza de agarre (r=0,656, p=0,000; r =0,589, p=0,002). Se concluye que los pacientes en condiciones críticas del Covid-19 presentaron al alta hospitalaria: reducción de FMR; cambios en la función pulmonar; correlación negativa entre la FMR y de tiempo de ventilación mecánica invasiva (VMI) y de hospitalización; y correlación positiva con la función pulmonar y la fuerza de agarre.
Palabras clave | COVID-19; Pruebas de Función Respiratoria; Músculos Respiratorios; Cuidados Críticos.

INTRODUCTION

The COVID-19 pandemic has been the cause of a significant number of hospitalizations worldwide[1]. Recent studies highlight the significant impairment of the lung, with pathological changes including diffuse destruction of the alveolar epithelium; capillary damage; hyaline membrane formation; alveolar septal fibrous proliferation; and pulmonary consolidation[2,3]. At hospital discharge, patients with COVID-19 pneumonia still had abnormalities on chest tomography, mainly ground glass opacity[2].

The first studies of pulmonary function in post-COVID-19 patients suggested impaired pulmonary function. A recent systematic review and meta-analysis revealed that about 40% of patients presented diffusion capacity , followed by restrictive disorders in 15%[2,4].

Considering the importance of better understanding the effect of COVID-19 on the pulmonary function of patients with critical conditions, this study aims to evaluate the pulmonary function and respiratory muscle strength (RMS) in the hospital discharge of patients who required Intensive Care Unit (ICU) care for COVID-19, and associate pulmonary function, RMS, peripheral muscle strength, duration of mechanical ventilation (MV), length of hospital stay, and use of medications.

METHODOLOGY

This is an observational, cross-sectional study with patients admitted to the ICU of the Hospital de Clínicas de Porto Alegre due to COVID-19 from June to August 2020. Participants agreed to participate and signed an informed consent form.

The study included patients older than 18 years who required ICU admission for COVID-19 for at least 72 hours and who used invasive mechanical ventilation (IMV), non-invasive mechanical ventilation (NIV), or high-flow nasal cannula (HFNC) to treat acute respiratory failure (ARF). Patients with previous functional impairment; use of tracheostomy; incapable of communicating and understanding commands; and who were unable to perform the proposed evaluations were excluded.

At hospital discharge or within 24 hours prior to discharge, patients were evaluated for:

- Respiratory muscle strength (RMS): to evaluate maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), a digital manovacuometer—model MVD300, brand Globalmed—was used. Technical procedures and the criteria of acceptability and reproducibility were based on the American Thoracic Society/European Respiratory Society[5]. The values obtained were compared with the values predicted by the equation proposed by Neder et al.[6] for Brazilian adults.
- Pulmonary function: to evaluate pulmonary function by spirometry, a portable spirometer—Sibelmed brand, Datospir Micro C model—was used, which provided the following data: forced vital capacity (FVC); forced expiratory volume in the first second (FEV1); FEV1/FVC ratio; peak expiratory flow (PEF); forced expiratory flow 50% (FEF50%); and intermediate forced expiratory flow (FEF25-75). The evaluation followed the recommendations of the American Thoracic Society[7]. The values obtained were compared with the reference values for the population[8].
- Peripheral muscle strength: measured by the Medical Research Council (MRC) score and handgrip strength. The MRC score was obtained by evaluating 12 muscle groups in the upper and lower limbs, and for each muscle group, a score from 0 (complete paralysis) to 5 (normal strength) was assigned. The maximum score was 60 points[9]. The hand grip strength of the dominant hand was evaluated with the elbow positioned at 90°, using a hydraulic hand dynamometer (Saehan brand). Three evaluations were carried out; the highest result was considered for analysis.

Based on the review of the patient's electronic medical record, demographic and anthropometric data and information on pre-existing comorbidities, treatments, and complications during hospitalization were collected. Also, data on length of hospital and ICU stay; need for ventilatory support and time of use; medications; and ICU readmission rate were also collected.

Statistical analysis

The sample size was calculated to test whether the Spearman correlation coefficient between FVC and FMR was greater than zero using the PSS Health tool, online version[10]. Considering a 5% significance level, 80% power, and an expected correlation of 0.5, the total sample size of 23 subjects was reached. Adding 5% for possible losses and refusals, the sample size should be 25.

Data normality was assessed using the Shapiro–Wilk normality test. Data were expressed as mean±standard deviation or median (interquartile range) for continuous variables and number (%) for categorical variables. The MIP and MEP values and lung function obtained were compared with the predicted values using the t-test for paired samples for parametric data and the Wilcoxon test for non-parametric data. The correlations were evaluated by Spearman's test and a very strong correlation coefficient was considered for values from 0.9 to 1; strong, from 0.7 to 0.89; and moderate, from 0.5 to 0.69[11]. The Statistical Package for Social Science, version 17.0, was used for data analysis and $p<0.05$ was considered significant.

RESULTS

During the study period, 66 patients who were hospitalized in the ICU for more than 72 hours were discharged and, of these, 25 were included in the study (Figure 1). Most patients were male (68%), with a mean age of 48.7±12.3 years, and had more than two preexisting comorbidities; systemic arterial hypertension and obesity been the most prevalent (Table 1). The median length of ICU stay and hospital stay was 15 (8–29) and 21(12–33) days, respectively, and most patients (80%) required IMV (Table 2).

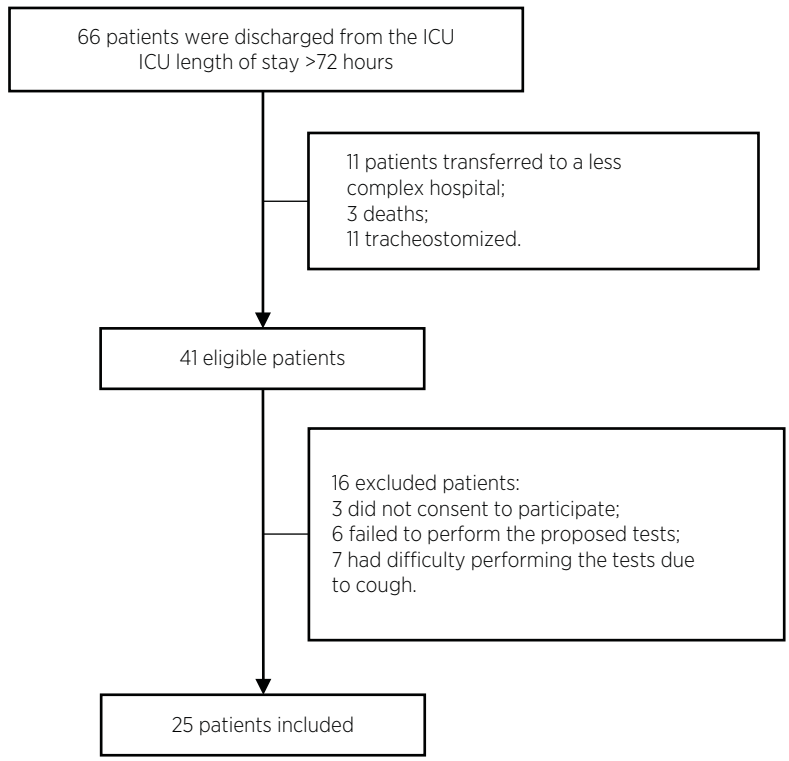

Figure 1. Flowchart of inclusion of patients in the study

ICU: Intensive Care Unit.

Table 1. Sample characteristics

Characteristic	(n=25)
Age (years)	48.7±12.3
Male	17 (68)
White	21 (84)
Body Mass Index (kg/m²)	30.2±6.4
Preexisting comorbidities	
Arterial hypertension	11 (44)
Obesity	10 (40)
Diabetes mellitus	7 (25)
Asthma	6 (24)
Chronic kidney disease	2 (8)
Chronic obstructive pulmonary disease	1 (4)
Cardiac disease	1 (4)
Number of comorbidities	
0	3 (12)
1	6 (24)
2-3	11 (44)
>3	5 (20)
Smoker	2 (8)
Alcohol consumption	2 (8)

Values expressed as mean±standard deviation or n (%).

Table 2. Hospitalization characteristics

Characteristic	n=25
Length of hospital stay (days)	21 (12–33)
Length of ICU hospitalization (days)	15 (8–29)
ICU readmission	1 (4)
Ventilatory support	
IMV	20 (80)
Post-extubation NIV	10 (50)
HFNC only	2 (8)
HFNC+NIV	2 (8)
NIV only	1 (4)
Time of IMV	11 (3-20)
Medication	
Antibiotics	25 (100)
Steroids	22 (88)
Sedation	20 (80)
Neuromuscular blocker	18 (72)
Vasopressors	17 (68)
Other treatment	
Prone position	9 (36)
Hemodialysis	6 (24)
Nitric oxide	2 (8)
Extracorporeal membrane oxygenation	1 (4)

ICU: Intensive Care Unit; HFNC: High Flow Nasal Cannula; NIV: non-invasive mechanical ventilation; IMV: invasive mechanical ventilation.

Values expressed as median (Q1–Q3) or n (%).

Maximum respiratory pressure values were significantly lower when compared to predicted values (obtained MIP and MEP: 74% and 78% in relation to predicted values; p<0.001). Regarding pulmonary function, patients had lower values of FVC, FEV1, and PEF when compared to the reference values (p≤0.01). Moreover, 72% of the patients had FVC<80% of predicted, indicating the presence of restrictive ventilatory disorder (Table 3).

The median MRC score at hospital discharge was 60 (58–60) points. Only three patients (12%) scored <48 points, characterizing the persistence of muscle weakness acquired in the ICU at hospital discharge. Median handgrip strength was 24 (22–32)Kgf.

MIP and MEP were positively correlated with FVC, PEF, FEV1, and handgrip strength, and negatively correlated with duration of MV and length of hospital stay, but did not correlate with MRC score at hospital discharge. The FVC also had a positive correlation with PEF, FEV1, and handgrip strength (Table 4). MIP, MEP, and FVC did not correlate with time on sedatives, neuromuscular blockers, and steroids.

Table 3. Characterization of pulmonary function and respiratory muscle strength at hospital discharge

Characteristic	n=25
Pulmonary Function	
FVC	3.67±1.16
FVC%pred	73.77±14.22
<80% pred	18 (72)
FEV1	3.20±1.01
FEV1%pred	81.28±14.79
<80% pred	13(52)
FEV1/FVC	87.54±9.55
FEV1/FVC%pred	113.97±12.76
PEF	6.67±2.07
FEF%pred	71.98±11.35
FEF50	4.16±1.21
FEF50%pred	88.59±18.29
FEF25–75	3.52±0.98
FEF25–75%pred	98.63±21.96
Maximum respiratory pressures	
MIP	79.16±19.39
<80%pred	17 (68)
MEP	87.48±20.51
<80%pred	15(60)

FVC: forced vital capacity; FEV1: forced expiratory volume in the first second; PEF: peak expiratory flow; FEF50: forced expiratory flow 50%; FEF25–75: intermediate forced expiratory flow; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure.
Values expressed as mean±standard deviation or n(%).

Table 4. Correlation between variables

	MIP	MEP	FVC	PEF	FEV1	MV (days)	Hospitalization (days)	MRC
MEP	0.948*	1						
FVC	0.869*	0.855*	1					
PEF	0.775*	0.753*	0.819*	1				
FEV1	0.821*	0.801*	0.857*	0.894*	1			
MV (days)	−0.599*	−0.523*	−0.422	−0.246	−0.188	1		
Hospitalization (days)	−0.542*	−0.502*	−0.323	−0.190	−0.158	0.820*	1	
MRC Score	0.355	0.373	0.327	0.209	0.190	−0.608*	−0.482*	1
Dynamometry	0.656*	0.589*	0.573*	0.669*	0.543*	−0.691*	−0.392	0.612*

MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; FVC: forced vital capacity; PEF: peak expiratory flow; FEV1: forced expiratory volume in one second; MV: mechanical ventilation; MRC: Medical Research Council score.

DISCUSSION

At hospital discharge, COVID-19 patients admitted to the ICU showed a reduction in RMS and changes in lung function characterized by a reduction in FVC, FEV1, and PEF when compared to the reference values.

In our study, patients showed a decrease in RMS. The reduction in MRF had already been reported in a study conducted by Huang et al.[12], in which approximately 30% of the patients were considered severe or critical, and more than half had a decrease in MRF. In this study, 49% and 23% of the patients, respectively, had MIP and MEP values lower than 80% of the predicted value; and 13 patients had moderate MRF impairment, 11 of which had mild COVID-19 conditions[12]. The authors stress the role of hypoxemia, which can lead to long in-bed periods, resulting in muscle disorders and respiratory muscle weakness. Furthermore, the systemic use of steroids may cause myopathy; however, we did not observe statistical significance in the MRF when analyzing the patients grouped by steroid administration. This result indicates that steroids were not the main cause of respiratory muscle weakness in the study by Huang et al.[12], which also found no difference in the decline in MRF between the severe and mild groups.

Prolonged MV increases the risk of diaphragmatic dysfunction[13]. The literature suggest that diaphragm weakness occurs primarily as a consequence of

ventilator-induced diaphragm inactivity, progressing as duration of mechanical ventilation increases[14,15]. This hypothesis is in line with our outcomes, which revealed a negative correlation of RMS with the duration of IMV and length of hospitalization.

Studies on pulmonary function in post-COVID-19 patients report impairment of diffusion capacity[2,12,16], airway dysfunction[4] and restrictive ventilatory changes[2,4,12,16-18]. The evaluation of pulmonary function by spirometry, performed in our study, revealed that patients with COVID-19 admitted to the ICU had, at hospital discharge, a reduction in FVC, FEV1, and PEF, compared to our predictions. This impairment of pulmonary function can be explained by the changes observed in autopsies of patients who died due to COVID-19, who presented different degrees of destruction in the alveolar structure and interstitial pulmonary fibrosis[19,20]. Computed tomography analysis of patients admitted to the ICU for acute respiratory distress syndrome (ARDS) showed that 70.2% of patients had abnormalities, 49.1% of which were reticular lesions and 21.1% of which were fibrotic, even three months after the acute event[21]. In addition to lung injury, respiratory muscle weakness, observed in the patients included in our study, can also lead to decreased lung function[12], reinforcing the correlation found between MIP and MEP values with FVC, FEV1, and PEF.

RMS and lung function (FVC, FEV1, and PEF) showed no correlation with the MRC score; however, there was a positive correlation with handgrip strength. This result may have suffered interference due to the fact that most evaluated patients had an MRC score close to or equal to 60 points (maximum score). Handgrip strength values varied even among patients who presented maximum MRC score (22–51Kgf). Both MRC and dynamometry are reliable methods for diagnosing ICU-acquired muscle weakness[22,23]. In our study, individuals with maximum MRC score, the handgrip dynamometry seemed to offer a more accurate assessment of strength. This fact can be explained by a potential ceiling effect that has already been previously suggested as a limitation of the MRC score[24].

This study has some limitations. This is a cross-sectional study, with a small sample size, exclusively investigating pulmonary function and RMS at hospital discharge. We did not follow-up the patients after discharge and, therefore, we cannot say whether the alterations found persisted or if they were related to the acute infection. The age range of the evaluated patients in our study is lower than the mean age of other studies involving critically ill patients. Moreover, many patients with long ICU stay were transferred to less complex hospitals for continuity of care, or were excluded due to tracheostomy. These factors may have contributed to a sample with muscle strength close to the maximum score at discharge.

In our study, most patients required IMV (80%) and prolonged hospital stay. These data reinforce the severity of the included patients, differing from other studies that evaluated the pulmonary function of post-COVID-19 patients, in which only patients with mild or moderate cases were included, or even small percentages of severe patients[2,12,16-18]. Finally, we highlight the importance of studies that assess the medium- and long-term effect of COVID-19 on lung function and RMS of patients with severe disease.

CONCLUSION

At hospital discharge, COVID-19 patients admitted to the ICU showed a reduction in RMS and changes in lung function characterized by restrictive ventilatory disorder. The FMR showed a negative correlation with the duration of IMV and length of hospital stay and a positive correlation with pulmonary function and handgrip strength.

REFERENCES

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5.
2. Mo X, Jian W, Su Z, Chen M, Peng H, Peng P, et al. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. Eur Respir J. 2020;55(6):2001217. doi: 10.1183/13993003.01217-2020.
3. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis. 2020;20(4):425-34. doi: 10.1016/S1473-3099(20)30086-4.
4. You J, Zhang L, Ni-jia-Ti M, Zhang J, Hu F, Chen L, et al. Anormal pulmonary function and residual CT abnormalities in rehabilitating COVID-19 patients after discharge. J Infect. 2020;81(2):e150-2. doi: 10.1016/j.jinf.2020.06.003.
5. American Thoracic Society; European Respiratory Society. ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med. 2002;166(4):518-624. doi: 10.1164/rccm.166.4.518.
6. Neder JA, Andreoni S, Lerario MC, Nery LE. Reference values for lung function tests. II. Maximal respiratory pressures and

voluntary ventilation. Braz J Med Biol Res. 1999;32(6):719-27. doi: 10.1590/S0100-879X1999000600007.

7. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, et al. Standardization of spirometry 2019 update. An official american thoracic society and European Respiratory Society technical statement. Am J Respir Crit Care Med. 2019;200(8):e70-88. doi: 10.1164/rccm.201908-1590ST.
8. Pereira CAC, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. J Bras Pneumol. 2007;33(4):397-406. doi: 10.1590/s1806-37132007000400008.
9. De Jonghe B, Sharshar T, Lefaucheur JP, Authier FJ, Durand-Zaleski I, Boussarsar M, et al. Paresis acquired in the Intensive Care Unit: a prospective multicenter study. JAMA. 2002;288(22):2859-67. doi: 10.1001/jama.288.22.2859.
10. Borges RB, Mancuso ACB, Camey SA, Leotti VB, Hirakata VN, Azambuja GS, et al. Power and sample size for health researchers: uma ferramenta para cálculo de tamanho amostral e poder do teste voltado a pesquisadores da área da saúde. Clin Biomed Res. 2020;40(4):247-53. doi: 10.22491/2357-9730.109542.
11. Mukaka MM. Statistics corner: a guide to appropriate use of correlation coefficient in medical research. Malawi Med J. 2012;24(3):69-71.
12. Huang Y, Tan C, Wu J, Chen M, Wang Z, Luo L, 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.
13. Supinski GS, Callahan LA. Diaphragm weakness in mechanically ventilated critically ill patients. Crit Care. 2013;17:R120. doi: 10.1186/cc12792.
14. Petrof BJ, Jaber S, Matecki S. Ventilator-induced diaphragmatic dysfunction. Curr Opin Crit Care. 2010;16(1):19-25. doi: 10.1097/MCC.0b013e328334b166.
15. Jaber S, Jung B, Matecki S, Petrof BJ. Clinical review: ventilator-induced diaphragmatic dysfunction – human studies confirm animal model findings! Crit Care. 2011;15:206. doi: 10.1186/cc10023.
16. Frija-Masson J, Debray MP, Gilbert M, Lescure FX, Travert F, Borie R, et al. Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post-infection. Eur Respir J. 2020;56(2):2001754. doi: 10.1183/13993003.01754-2020.
17. Li X, Wang C, Kou S, Luo P, Zhao M, Yu K. Lung ventilation function characteristics of survivors from severe COVID-19: a prospective study. Crit Care. 2020;24:300. doi: 10.1186/s13054-020-02992-6.
18. Zhao YM, Shang YM, Song WB, Li QQ, Xie H, Xu QF, 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. doi: 10.1016/j.eclinm.2020.100463.
19. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420-2. doi: 10.1016/S2213-2600(20)30076-X.
20. Yao XH, Li TY, He ZC, Ping YF, Liu HW, Yu SC, et al. A pathological report of three COVID-19 cases by minimal invasive autopsies. Chin J Pathol. 2020;49(5):411-7. doi: 10.3760/cma.j.cn112151-20200312-00193.
21. González J, Benítez ID, Carmona P, Santisteve S, Monge A, Moncusí-Moix A, et al. Pulmonary function and radiologic features in survivors of critical COVID-19: a 3-month prospective cohort. Chest. 2021;160(1):187-98. doi: 10.1016/j.chest.2021.02.062.
22. Bragança RD, Ravetti CG, Barreto L, Ataíde TBLS, Carneiro RM, Teixeira AL, et al. Use of handgrip dynamometry for diagnosis and prognosis assessment of intensive care unit acquired weakness: a prospective study. Heart Lung. 2019;48(6):532-7. doi: 10.1016/j.hrtlng.2019.07.001.
23. Ali NA, O'Brien JM Jr, Hoffmann SP, Phillips G, Garland A, Finley JCW, et al. Acquired weakness, handgrip strength, and mortality in critically ill patients. Am J Respir Crit Care Med. 2008;178(3):261-8. doi: 10.1164/rccm.200712-1829OC.
24. Kress JP, Hall JB. ICU-acquired weakness and recovery from critical illness. N Engl J Med. 2014;370(17):1626-35. doi: 10.1056/NEJMra1209390.