

¹Programa de Pós-graduação em

²Departamento de Fisioterapia,

Uberaba, MG, Brasil

Not applicable.

Brasil

Fisioterapia, Universidade Federal do

Universidade Federal de Minas Gerais

Federal do Triângulo Mineiro (UFTM),

Presentation of data at an event:

How to cite: Paranhos DB. Annoni R.

Fernandes LFRM. Low mobility in the first 24 hours of admission correlates with worse

clinical outcomes in COVID-19 patients in the

ICU: a cross-sectional study. Brazilian lournal

Study carried out at: Universidade Federal

do Triângulo Mineiro, Uberaba, MG, Brazil.

35820720.0.0000.5145 from the University

*Corresponding author: Darlisson Bueno Paranhos. E-mail: darlisson-2b@hotmail.com

of Respiratory, Cardiovascular and Critical Care Physiotherapy. 2024;15:e00092025.

https://doi.org/10.47066/2966-

Submitted on: January 15, 2025

Accepted on: March 13, 2025

Ethical approval: CAAE:

of Uberaba. nº 4.240.354.

4837.2024.0010en

Instituto de Ciências da Saúde. Universidade

(UFMG), Belo Horizonte, MG, Brasil ³Departamento de Fisioterapia Aplicada,

Triângulo Mineiro (UFTM), Uberaba, MG,

Low mobility in the first 24 hours of admission correlates with worse clinical outcomes in COVID-19 patients in the ICU: a cross-sectional study

Baixa mobilidade nas primeiras 24 horas de admissão correlaciona-se a piores desfechos clínicos em pacientes com COVID-19 na UTI: um estudo transversal

Darlisson Bueno Paranhos¹* (0); Raquel Annoni² (0); Luciane Fernanda Rodrigues Martinho Fernandes³ (0)

Abstract

Background: COVID-19 patients admitted to intensive care units (ICUs) exhibit reduced mobility levels at the time of admission. However, the correlation between the highest mobility level within the first 24 hours of ICU admission and clinical outcomes in the ICU remains uncertain. Aim: To investigate the correlation between the level of mobility within the first 24 hours of ICU admission, APACHE II score, mechanical ventilation (MV) duration, ICU length of stay, post-ICU hospitalization time, and total hospital stay in COVID-19 patients admitted to the ICU. Methods: A cross-sectional study was conducted in an ICU for adult COVID-19 patients. Sociodemographic and clinical data were collected from medical records. The level of mobility during the first 24 hours of ICU admission was assessed using the ICU Mobility Scale (IMS). The correlation between the level mobility within the first 24 hours of ICU admission and clinical outcomes was tested using Spearman's test. Results: A total of 192 patients were included. Within the first 24 hours of ICU admission, 53.1% of patients exhibited no or minimal activity, while only 3.6% achieved high-intensity mobility. The highest level of mobility was significantly correlated with APACHE II (r= -0.369; p< 0.001) and post-ICU hospitalization time (r = -0.361; p= 0.004). **Conclusion:** Patients with low mobility levels within the first 24 hours in the ICU are associated with greater severity and longer post-ICU hospitalization times.

Keywords: COVID-19; Intensive Care Unit; Mobility Limitation; Critical Care.

Resumo

Introdução: Pacientes com COVID-19 internados em unidades de terapia intensiva (UTI) apresentam níveis reduzidos de mobilidade no momento da admissão. Contudo, a correlação entre o maior nível de mobilidade nas primeiras 24 horas de admissão com desfechos clínicos na UTI ainda é incerto. Objetivo: Investigar a correlação entre o nível de mobilidade nas primeiras 24 horas de admissão na UTI, escore APACHE II, tempo de VM, período de internação na UTI, tempo de internação pós-UTI e a duração total da hospitalização em pacientes com COVID-19 internados em UTI. Métodos: Estudo transversal realizado em uma UTI destinada a pacientes adultos com COVID-19. Foram coletados dos prontuários dados sociodemográficos e clínicos. O nível e mobilidade nas primeiras 24 horas de internação na UTI foi avaliado pelo ICU Mobility Scale (IMS). A correlação entre o nível de mobilidade nas primeiras 24 horas de admissão na UTI e desfechos clínicos foi testada através do teste de Spearman. Resultados: Foram incluídos 192 pacientes. Nas primeiras 24 horas de admissão na UTI, 53,1% dos pacientes apresentaram nenhuma ou mínima atividade, enquanto apenas 3,6% atingiram alta intensidade de mobilidade. O maior nível de mobilidade se correlacionou significativamente com APACHE II (r = -0,369; p < 0,001) e tempo de internação após a alta da UTI (r = -0,361; p = 0,004). Conclusão: Pacientes que apresentam baixo nível de mobilidade nas primeiras 24 horas na UTI estão relacionados a maior gravidade e maior tempo de permanência após UTI.

Palavras-chave: COVID-19; Unidade de Terapia Intensiva; Limitação de Mobilidade; Cuidados Críticos.

This article is published in Open Access and distributed under the Creative Commons Attribution NonCommercial ShareAlike License, which allows unrestricted use, distribution, and reproduction in any medium, provided that it is non-commercial and that the original work is correctly cited and does not indicate endorsement of the work done. In addition, any subsequent work must be published under the same license.



INTRODUCTION

Since COVID-19 was officially declared a pandemic by the World Health Organization (WHO) in 2020¹, a growing number of studies have sought to pinpoint the sociodemographic and clinical factors that influence the severity of the disease and its outcomes²⁻⁶. Approximately 20% of patients diagnosed with COVID-19 may require hospitalization, and around 5% of these require intensive care unit (ICU) support, mainly due to respiratory failure⁷. Therefore, understanding these factors is key to outlining the profile most vulnerable to infection, contributing to implementing effective strategies for the prevention, diagnosis, and clinical management of COVID-19⁸.

In addition to sociodemographic and clinical factors, variables concerning functionality have been investigated to assess whether alterations at any functional level may have an impact on the recovery of COVID-19 patients. Specifically in this patient profile, in addition to the typical conditions of ICU patients, such as prolonged immobility, medications, and the use of medical devices, the virus that causes COVID-19, SARS-CoV-2, triggers a systemic inflammatory response, which contributes to the loss of muscle mass, thus causing functional impairment⁹. Evidence suggests that patients with COVID-19 who are considered frail or functionally dependent at the time of admission to the ICU have a significant association with unfavorable clinical outcomes, such as greater need for mechanical ventilation, prolonged periods of invasive mechanical ventilation, longer ICU and hospital stays, and higher mortality rates¹⁰⁻¹³.

Among the variables associated with functionality, the level of mobility stands out as a relevant assessment parameter, as it reflects the interaction of multiple physiological factors, including the integrity of skeletal muscles and cardiorespiratory functional reserve¹⁴. To date, the available data shows that patients admitted to the ICU with or without COVID-19 tend to have a low level of mobility on admission, but with a tendency to improve on discharge^{13,15}. In non-COVID-19 patients, a higher level of mobility on discharge from the ICU correlates with survival of up to 90 days¹⁶. However, in COVID-19 patients, the correlation between the level of mobility in the first 24 hours of admission and clinical outcomes in the ICU remains uncertain.

Therefore, this study aimed to assess the correlation between the level of mobility in the first 24 hours of ICU admission and relevant clinical variables, such as MV time, ICU length of stay, post-ICU length of stay, and total length of hospitalization in COVID-19 patients admitted to the ICU.

METHODS

Study design and population

This is a cross-sectional study carried out from March to August 2021 in an ICU that cares for individuals with COVID-19, located in a university hospital in the city of Uberaba, state of Minas Gerais, Brazil. The research project was approved by the Research Ethics Committee of the University of Uberaba (CAAE: 35820720.0.0000.5145) and by the Teaching, Research, and Extension Center of the hospital where the study was carried out. All the patients included in the study, or their legal guardians, when necessary, signed an Informed Consent Form (ICF). This study followed the standards established by Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)¹⁷.

This study was conducted using a convenience sample, without prior sample calculation, aiming to include as many patients as possible during the data collection period. Adults (age ≥18 years), both sexes, with a clinical diagnosis of COVID-19 and confirmed using a reverse transcription polymerase chain reaction (RT-PCR) laboratory test or serological tests for IgA, IgM, and/or IgG anti-SARS-CoV-2 antibodies were included. Patients transferred to other hospitals before discharge or who died in the ICU and those with an incomplete assessment on admission were excluded.

Sample characterization

For sample characterization, sociodemographic data {sex, age, and comorbidities} and clinical data {Acute Physiology and Chronic Health Evaluation Classification System II (APACHE-II) in the first 24 hours of ICU admission, use of oxygen therapy, respiratory support (non-invasive MV or invasive MV) duration of MV, length of ICU and hospital stay, and hospital outcome (discharge or death)} were collected from medical records.

Mobility level

The level of mobility in the first 24 hours of admission to the ICU was measured by a trained physiotherapist and ICU specialist using the Intensive Care Unit Mobility Scale (IMS). The IMS is an instrument translated and validated into Brazilian Portuguese¹⁸, consisting of an assessment of 11 levels of mobility that increase in complexity, allowing for an evaluation of the level of assistance required for the individual to carry out the proposed activity. Patients were divided into four groups according to their level of mobility in the first 24 hours of ICU stay: no or minimal activity (IMS \leq 2); low intensity (IMS=3); moderate intensity (IMS between 4 and 7); and high intensity (IMS \geq 8)¹⁹.

Statistical analysis

Continuous data are given as mean and standard deviation or median and interquartile range (IQR), then compared between groups according to mobility level via the Kruskal Wallis test. Categorical data are shown as absolute and relative frequencies and compared between groups by the Chi-square test. The correlation between the level of mobility in the first 24 hours of ICU



admission, APACHE II score, MV time, ICU length of stay, post-ICU length of stay, and total length of hospital stay was tested using the Spearman correlation coefficient. Normality was assessed using the Kolmogorov-Smirnov test. The data were analyzed by the Statistical Package for the Social Sciences, version 22 for Windows (SPSS 22), with p <0.05 taken as a significant difference.

RESULTS

Over the study period, 201 patients were admitted to the ICU. Of these, nine were excluded: two due to lack of diagnostic confirmation and seven due to transfer to other health services. Thus, the final sample consisted of 192 patients (Figure 1).

The average age of the patients included in the study was 58 ± 14.8 years, most of them men (64.1%) and predominantly between 25 and 59 years old (53.6%). Comorbidities were present in 64.6% of the cases, the most frequent being Systemic Arterial Hypertension (41.2%) and Diabetes Mellitus (21.9%). The use of MV was observed in 83.8% of the sample. The median length of stay in the ICU was 9 days (IQR: 5-17). The overall mortality rate was 66.7% (Table 1).

In the first 24 hours of admission to the ICU, the patient's level of mobility was distributed as follows: no or minimal activity in 53.1%, low intensity in 38.5%, moderate intensity in 4.7%, and high intensity in 3.6%. The comparative analysis of mobility levels showed that patients with lower mobility (IMS= 0-2) scored significantly

higher on the APACHE II (p<0.001), more frequently used mechanical ventilation (p<0.001), and spent longer in the ICU (median 9 days; IQR: 5-17; p=0.028). In addition, there was a higher proportion of deaths among patients with lower levels of mobility (p<0.001) (Table 1).

The correlation analysis showed that patients with greater clinical severity, as assessed by the APACHE II score on admission, had significantly lower levels of mobility, as measured by the IMS (r = -0.369; p< 0.001). In addition, individuals with worse levels of mobility on admission showed a significant association with a longer length of stay after discharge from the ICU (r = -0.361; p = 0.004) (Figure 2).

DISCUSSION

Our study investigated the correlation between the highest level of mobility in the first 24 hours of ICU admission and relevant clinical variables in COVID-19 patients admitted to the ICU. Our main findings comprised: (I) during the first 24 hours of ICU stay, most patients showed non-existent or minimal levels of physical activity; (II) a negative correlation emerged between severity, as measured by the APACHE II score, and the level of mobility recorded on admission; (III) the level of mobility on admission also showed a negative correlation with the total length of stay after ICU discharge.

Patients who had minimal or no activity levels in the first 24 hours of admission to the ICU showed increased clinical severity, as assessed by the APACHE II score, a

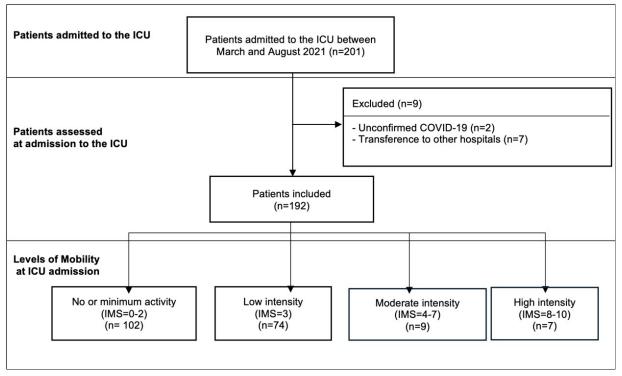


Figure 1. Patient selection flowchart.

Abbreviations: IMS: ICU Mobility Scale; ICU: Intensive Care Unit.

Table	1. Sample	characterization	according to	the mobilit	y level.
-------	-----------	------------------	--------------	-------------	----------

Variables	Total	No or minimal activity (IMS=0-2)	Low intensity	Moderate intensity	High intensity	p-value
	(n=192)	(n=102)	(IMS=3)	(IMS=4-7)	(IMS=8-10)	·
			(n=74)	(n=9)	(n=7)	
Age, years, mean±SD	58.05±14,8	59.21±16.6	57.39±12.59	53.67±8.46	54±4.55	0.408
Age group, n (%)						0,099
18-24 years	1 (0.5)	0 (0)	1 (1.35)	0 (0)	0 (0)	
25-59 years	103 (53.6)	50 (49.02)	39 (52.7)	7 (77.78)	7 (100)	
>60 years	88 (45.8)	52 (50.98)	34 (45.95)	2 (22.22)	0 (0)	
Sex, n (%)						0.825
Male	123 (64.1)	64 (62.74)	50 (67.56)	5 (55.5)	4 (57.14)	
Female	69 (35.9)	38 (37.26)	24 (32.44)	4 (44.5)	3 (42.86)	
Comorbidities, n (%)	124 (64.6)	69 (67.64)	48 (64.86)	3 (33.33)	4 (57.14)	0.218
Comorbidities, n (%)						
SAH, n (%)	83 (41.2)	41 (21.4)	38 (19.8)	1 (0.5)	3 (1.6)	0.104
DM, n (%)	42 (21.9)	25 (13.0)	14 (7.3)	2 (1.0)	1 (0.5)	0.794
Hypothyroidism	20 (10.4)	13 (6.8)	7 (3.6)	0 (0)	0 (0)	0.471
Dyslipidemia	8 (4.2)	4 (2.1)	4 (2.1)	0 (0)	0 (0)	0.802
APACHE II, mean±SD	15.07±9.45	18.2±10.3	12±7.22	8.22±3.87	10.4±5.83	<0.001
Use of oxygen, n (%)	186 (96.9)	99 (97.05)	72 (97.29)	9 (100)	6 (85.71)	0.358
Use of NIV, n (%)	175 (91.1)	91 (89.21)	70 (94.59)	8 (88.8)	6 (85.71)	0.599
Use of MV, n (%)	161 (83.85)	95 (93.13)	65 (87.83)	1 (11.11)	0 (0)	<0.001
MV>48h, n (%)	131 (85.71)	79 (77.45)	58 (78.37)	1 (11.11)	0 (0)	
MV time,	8 (4-17)	7 (3-14.5)	9 (5-20)	20 (20-20)	N/A	0.305
days						
ICU time, days, median (IQR)	9 (5-18.7)	8 (4-16.8)	12 (7-20)	5 (4-8)	9 (7-13)	0.028
Length of hospital stay, days (IQR)	11 (6-20)	9 (4-20.8)	12 (7-20.8)	8 (5-13)	13 (10.5-16.5)	0.293
Outcome, n (%)						<0,001
ICU discharge	64 (33.3)	31 (30.40)	17 (22.98)	9 (100)	7 (100)	
Death	128 (66.7)	71 (69.60)	57 (77.02)	0 (0)	0 (0)	

Abbreviations: APACHE II: Acute Physiology and Chronic Health Evaluation Classification System II; ICU: Intensive Care Unit; MV: Mechanical ventilation; NIV: Non-invasive mechanical ventilation; IQR: interquartile range; n: number of patients; %: Percentage; SD: Standard Deviation; IMS: Intensive Care Unit Mobility Scale; DM: Diabetes mellitus; SAH: Systemic Arterial Hypertension; N/A: not applicable.

higher proportion of MV use, and higher mortality. This result matches that reported in a study investigating the level of mobility of patients affected by COVID-19 in the ICU, in which the lowest levels of mobility were seen in patients undergoing MV and with more severe disease²⁰. These findings can be attributed to the greater severity and clinical instability of these individuals, who often require intensive support and adjuvant therapies. This pattern is reported in the literature and points out that the severity of the disease and hemodynamic instability are among the main factors harming the level of mobility in ICU patients²¹. A study examining functional outcomes in critically ill patients with COVID-19 who required MV found that the median time to first mobilization sitting at the bedside was 7 (4-11) days²². However, it is worth mentioning that, even in non-COVID-19 patients, those who are more severely ill and using MV, a small percentage of patients show higher levels of mobility, such as walking and standing^{23,24}.



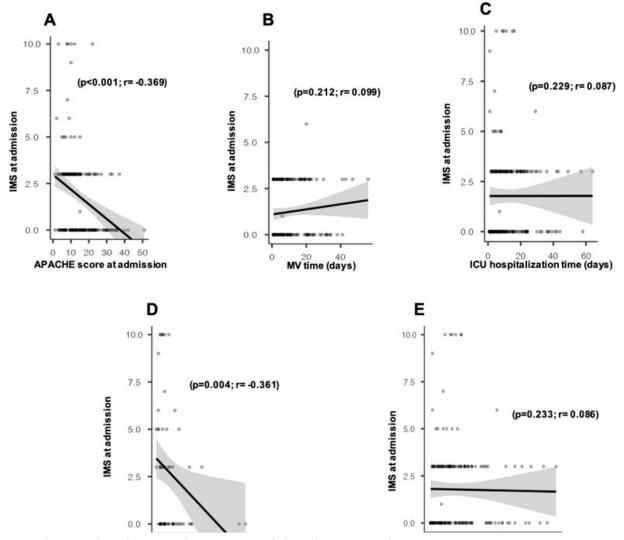


Figure 2. Correlation analyses between admission IMS and clinical outcomes in the ICU. Abbreviations: APACHE II: Acute Physiology and Chronic Health Evaluation Classification System II; IMS: ICU Mobility Scale; ICU: Intensive Care Unit; MV: mechanical ventilation.

The mortality of hospitalized COVID-19 patients varies considerably between studies, especially in cases requiring the use of MV^{2,5,25,26}. The high mortality rates in hospitalized COVID-19 patients, shown in previous studies and corroborated by this study, could be caused by the unfamiliarity of the disease itself, the scarcity of therapeutic options, the severity of the disease in the critical stage, and the negative impact resulting from the high professional demand, which overloads health services and the availability of ICU beds and professionals. It is also worth noting that the patients included in this study often had comorbidities, mainly diabetes and systemic arterial hypertension (SAH), chronic diseases that increase the risk of developing worse clinical and functional outcomes²⁷.

According to this study, the greater the clinical severity of the patient, as assessed by APACHE II, the lower the level of mobility in the first 24 hours of admission. This relationship could mean that patients with greater clinical severity often suffer from hemodynamic instability, respiratory failure, or multiple organ failure, conditions that limit their ability to perform physical activities, even at minimal levels. In a study that investigated the factors associated with improved mobility on discharge from the ICU of patients undergoing MV, greater severity of illness and organ dysfunction measured by the Simplified Acute Physiology Score (SAPS III) and Sequential Organ Failure Assessment (SOFA) was associated with a lower chance of recovery²⁰. In addition, these patients tend to require intensive support, such as mechanical ventilation, sedation, and other invasive procedures, which harm their mobility. This pattern reflects the functional impairment resulting from the severity of the disease and the critical condition.

Patients with lower mobility on admission tend to remain hospitalized for longer after discharge from the ICU. Moreover, patients with a lower level of mobility usually suffer from more severe conditions or greater functional impairment, such as muscle weakness acquired in the ICU and reduced overall functional capacity, which are often associated with post-intensive care syndrome



(PICS)^{28,29}. In a retrospective cohort, most non-mechanically ventilated COVID-19 patients were released from bed on the first day of ICU admission, while ventilated patients were only released on the third day²⁰. These factors hinder recovery and prolong the need for hospital care after discharge from the ICU. In addition, limitations in initial mobility may indicate a functional deficit before the disease. These findings reinforce the importance of early interventions aimed at mobility and functional rehabilitation during the ICU stay, seeking not only to improve immediate outcomes but also to reduce the total length of hospital stay, as well as facilitate the patient's recovery in the post-ICU environment^{30,31}.

The negative clinical outcomes found here could be attributed largely to the pathophysiological characteristics of COVID-19 that distinguish it from other clinical conditions. By using the angiotensin-converting enzyme 2 (ACE2) as a cellular gateway, the SARS-CoV-2 virus triggers changes in the renin-angiotensin-aldosterone system (RAAS), promoting a robust systemic inflammatory response^{32,33}. Current data suggest that this entire inflammatory chain is associated with functional impairment³⁴. Post-COVID-19 patients report functional impairment in many aspects of life, such as compromised daily activities, selfcare, and mobility^{35,36}, interruption or difficulty in returning to work, and once they return, they are unable to revert to their pre-COVID-19 level³⁷⁻³⁹. Furthermore, even six months after discharge from the ICU, patients hospitalized due to COVID-19 have reduced functional capacity compared to the general population, showing persistent impacts of severe infection on physical performance⁴⁰.

LIMITATIONS

This study has some limitations that should be considered when interpreting the results. Firstly, this is a single-center study of specific regional characteristics, which may restrict the scope for generalizing the findings to other populations and contexts. Secondly, the data collection period coincided with the peak of the second local outbreak of the COVID-19 pandemic. This time was marked by a high demand for ICU beds, not only in the city of Uberaba but also in neighboring municipalities and states. Therefore, many patients admitted to the ICU were already in advanced and more severe stages of the disease, which may have influenced the outcomes analyzed. Further multicenter studies carried out during different periods of the pandemic could contribute to validating and expanding our findings.

CONCLUSION

This study showed that in the first 24 hours of ICU admission, most patients showed non-existent or minimal levels of physical activity. Moreover, a negative correlation was found between clinical severity, as measured by the

APACHE II score, and the level of mobility recorded on admission, indicating that as severity increases, mobility tends to decrease. Similarly, mobility on admission showed a negative correlation with the total length of stay after discharge from the ICU, suggesting that patients with lower mobility may remain in the hospital for longer periods.

FUNDING

Nothing to declare.

CONFLICT OF INTEREST

Nothing to declare.

ACKNOWLEDGEMENTS

Nothing to declare.

REFERENCES

- Lauxmann MA, Santucci NE, Autrán-Gómez AM. The SARS-CoV-2 coronavirus and the COVID-19 outbreak. Int Braz J Urol. 2020;46(Suppl 1):6-18. http://doi.org/10.1590/s1677-5538.ibju.2020.s101. PMid:32549071.
- Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, et al. Risk factors associated with mortality among patients with COVID-19 in Intensive Care Units in Lombardy, Italy. JAMA Intern Med. 2020;180(10):1345-55. http://doi. org/10.1001/jamainternmed.2020.3539. PMid:32667669.
- 3. 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(1):163. http://doi. org/10.1186/s12931-020-01429-6. PMid:32600344.
- Zou X, Li S, Fang M, Hu M, Bian Y, Ling J, et al. Acute physiology and chronic health evaluation II score as a predictor of hospital mortality in patients of coronavirus disease 2019. Crit Care Med. 2020;48(8):e657-65. http://doi.org/10.1097/ CCM.000000000004411. PMid:32697506.
- Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York city area. JAMA. 2020;323(20):2052-9. http://doi.org/10.1001/ jama.2020.6775. PMid:32320003.
- Kim L, Garg S, O'Halloran A, Whitaker M, Pham H, Anderson EJ, et al. Risk factors for Intensive Care Unit Admission and in-hospital mortality among hospitalized adults identified through the US coronavirus disease 2019 (COVID-19)associated hospitalization surveillance network (COVID-NET). Clin Infect Dis. 2021;72(9):e206-14. http://doi. org/10.1093/cid/ciaa1012. PMid:32674114.
- Berlin DA, Gulick RM, Martinez FJ. Severe covid-19. N Engl J Med. 2020;383(25):2451. http://doi.org/10.1056/ NEJMcp2009575. PMid:32412710.
- Gomes GGC, Bisco NCB, Paulo MF, Fabrin SCV, Fioco EM, Verri ED, et al. Perfil epidemiológico da Nova Doença Infecciosa do Coronavírus - COVID-19 (Sars-Cov-2) no mundo: estudo descritivo, janeiro-junho de 2020. Braz J Health Rev. 2020;3(4):7993-8007. http://doi.org/10.34119/ bjhrv3n4-064.



- Lin D, Liu L, Zhang M, Hu Y, Yang Q, Guo J, et al. Co-infections of SARS-CoV-2 with multiple common respiratory pathogens in infected patients. Sci China Life Sci. 2020;63(4):606-9. http://doi.org/10.1007/s11427-020-1668-5. PMid:32170625.
- Andrés-Esteban EM, Quintana-Diaz M, Ramírez-Cervantes KL, Benayas-Peña I, Silva-Obregón A, Magallón-Botaya R, et al. Outcomes of hospitalized patients with COVID-19 according to level of frailty. PeerJ. 2021;9:e11260. http://doi. org/10.7717/peerj.11260. PMid:33954054.
- Jung C, Flaatten H, Fjølner J, Bruno RR, Wernly B, Artigas A, et al. The impact of frailty on survival in elderly intensive care patients with COVID-19: the COVIP study. Crit Care. 2021;25(1):149. http://doi.org/10.1186/s13054-021-03551-3. PMid:33874987.
- Yang Y, Luo K, Jiang Y, Yu Q, Huang X, Wang J, et al. The impact of frailty on COVID-19 outcomes: a systematic review and meta-analysis of 16 cohort studies. J Nutr Health Aging. 2021;25(5):702-9. http://doi.org/10.1007/s12603-021-1611-9. PMid:33949641.
- 13. Paranhos DB, Annoni R, Schujmann DS, Fernandes LFRM. Functional dependence prior to ICU admission is associated with worse clinical and functional outcomes in individuals with COVID-19: a prospective observational study. J Intensive Care Med. 2024;39(5):439-46. PMid:37915228.
- McGregor RA, Cameron-Smith D, Poppitt SD. It is not just muscle mass: a review of muscle quality, composition and metabolism during ageing as determinants of muscle function and mobility in later life. Longev Healthspan. 2014;3(1):9. http://doi.org/10.1186/2046-2395-3-9. PMid:25520782.
- Timenetsky KT, Serpa A No, Lazarin AC, Pardini A, Moreira CRS, Corrêa TD, et al. The Perme Mobility Index: A new concept to assess mobility level in patients with coronavirus (COVID-19) infection. PLoS One. 2021;16(4):e0250180. http:// doi.org/10.1371/journal.pone.0250180. PMid:33882081.
- Tipping CJ, Bailey MJ, Bellomo R, Berney S, Buhr H, Denehy L, et al. The ICU mobility scale has construct and predictive validity and is responsive. A multicenter observational study. Ann Am Thorac Soc. 2016;13(6):887-93. http://doi. org/10.1513/AnnalsATS.201510-717OC. PMid:27015233.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453-7. http://doi.org/10.1016/S0140-6736(07)61602-X. PMid:18064739.
- Kawaguchi YMF, Nawa RK, Figueiredo TB, Martins L, Pires-Neto RC. Perme intensive care unit mobility score and ICU mobility scale: translation into Portuguese and cross-cultural adaptation for use in Brazil. J Bras Pneumol. 2016;42(6):429-34. http://doi.org/10.1590/s1806-37562015000000301. PMid:28117473.
- Berney SC, Rose JW, Bernhardt J, Denehy L. Prospective observation of physical activity in critically ill patients who were intubated for more than 48 hours. J Crit Care. 2015;30(4):658-63. http://doi.org/10.1016/j.jcrc.2015.03.006. PMid:25813549.
- Nawa RK, Serpa A No, Lazarin AC, da Silva AK, Nascimento C, Midega TD, et al. Analysis of mobility level of COVID-19 patients undergoing mechanical ventilation support: a single center, retrospective cohort study. PLoS One. 2022;17(8):e0272373. http://doi.org/10.1371/journal. pone.0272373. PMid:35913973.
- 21. Anekwe DE, Koo KKY, de Marchie M, Goldberg P, Jayaraman D, Spahija J. Interprofessional survey of perceived barriers

and facilitators to early mobilization of critically III patients in Montreal, Canada. J Intensive Care Med. 2019;34(3):218-26. http://doi.org/10.1177/0885066617696846. PMid:28355933.

- 22. Yamada K, Kitai T, Iwata K, Nishihara H, Ito T, Yokoyama R, et al. Predictive factors and clinical impact of ICU-acquired weakness on functional disability in mechanically ventilated patients with COVID-19. Heart Lung. 2023;60:139-45. http://doi.org/10.1016/j.hrtlng.2023.03.008. PMid:37018902.
- 23. Nydahl P, Ruhl AP, Bartoszek G, Dubb R, Filipovic S, Flohr HJ, et al. Early mobilization of mechanically ventilated patients: a 1-day point-prevalence study in Germany. Crit Care Med. 2014;42(5):1178-86. http://doi.org/10.1097/ CCM.00000000000149. PMid:24351373.
- 24. Sibilla A, Nydahl P, Greco N, Mungo G, Ott N, Unger I, et al. Mobilization of mechanically ventilated patients in Switzerland. J Intensive Care Med. 2020;35(1):55-62. http://doi.org/10.1177/0885066617728486. PMid:28847238.
- 25. 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. http://doi.org/10.1016/S0140-6736(20)30183-5. PMid:31986264.
- Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and Outcomes of 21 Critically III Patients With COVID-19 in Washington State. JAMA. 2020;323(16):1612-4. http://doi.org/10.1001/ jama.2020.4326. PMid:32191259.
- 27. Vanhorebeek I, Latronico N, Van den Berghe G. ICU-acquired weakness. Intensive Care Med. 2020;46(4):637-53. http://doi. org/10.1007/s00134-020-05944-4. PMid:32076765.
- Sheehy LM. Considerations for postacute rehabilitation for survivors of COVID-19. JMIR Public Health Surveill. 2020;6(2):e19462. http://doi.org/10.2196/19462. PMid:32369030.
- 29. Biehl M, Sese D. Post-intensive care syndrome and COVID-19: implications post pandemic. Cleve Clin J Med. 2020:1-3. http://doi.org/10.3949/ccjm.87a.ccc055.
- 30. Gosselink R, Bott J, Johnson M, Dean E, Nava S, Norrenberg M, et al. Physiotherapy for adult patients with critical illness: recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically III patients. Intensive Care Med. 2008;34(7):1188-99. http://doi.org/10.1007/s00134-008-1026-7. PMid:18283429.
- 31. Wang YT, Lang JK, Haines KJ, Skinner EH, Haines TP. Physical rehabilitation in the ICU: a systematic review and metaanalysis. Crit Care Med. 2022;50(3):375-88. http://doi. org/10.1097/CCM.00000000005285. PMid:34406169.
- McElvaney OJ, McEvoy NL, McElvaney OF, Carroll TP, Murphy MP, Dunlea DM, et al. Characterization of the inflammatory response to severe COVID-19 illness. Am J Respir Crit Care Med. 2020;202(6):812-21. http://doi.org/10.1164/ rccm.202005-1583OC. PMid:32584597.
- Sungnak W, Huang N, Bécavin C, Berg M, Queen R, Litvinukova M, et al. SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. Nat Med. 2020;26(5):681-7. http://doi. org/10.1038/s41591-020-0868-6. PMid:32327758.
- 34. Ceban F, Ling S, Lui LMW, Lee Y, Gill H, Teopiz KM, et al. Fatigue and cognitive impairment in Post-COVID-19 Syndrome: a systematic review and meta-analysis. Brain Behav Immun. 2022;101:93-135. PMid:34973396.
- 35. Frontera JA, Yang D, Lewis A, Patel P, Medicherla C, Arena V, et al. A prospective study of long-term outcomes among hospitalized COVID-19 patients with and without



neurological complications. J Neurol Sci. 2021;426:117486. http://doi.org/10.1016/j.jns.2021.117486. PMid:34000678.

- Johnsen S, Sattler SM, Miskowiak KW, Kunalan K, Victor A, Pedersen L, et al. Descriptive analysis of long COVID sequelae identified in a multidisciplinary clinic serving hospitalised and non-hospitalised patients. ERJ Open Res. 2021;7(3):00205-02021. http://doi.org/10.1183/23120541.00205-2021. PMid:34345629.
- Evans RA, McAuley H, Harrison EM, Shikotra A, Singapuri A, Sereno M, et al. Physical, cognitive and mental health impacts of COVID-19 following hospitalisation: a multicentre prospective cohort study. Lancet Respir Med. 2021;9(11):1275-87.
- Ghosn J, Piroth L, Epaulard O, Le Turnier P, Mentré F, Bachelet D, et al. Persistent COVID-19 symptoms

are highly prevalent 6 months after hospitalization: results from a large prospective cohort. Clin Microbiol Infect. 2021;27(7):1041.e1-4. http://doi.org/10.1016/j. cmi.2021.03.012. PMid:34125067.

- Miskowiak K, Johnsen S, Sattler S, Nielsen S, Kunalan K, Rungby J, et al. Cognitive impairments four months after COVID-19 hospital discharge: Pattern, severity and association with illness variables. Eur Neuropsychopharmacol. 2021;46:39-48. http://doi.org/10.1016/j.euroneuro.2021.03.019. PMid:33823427.
- 40. Neville TH, Hays RD, Tseng CH, Gonzalez CA, Chen L, Hong A, et al. Survival after severe COVID-19: long-term outcomes of patients admitted to an Intensive Care Unit. J Intensive Care Med. 2022;37(8):1019-28. http://doi. org/10.1177/08850666221092687. PMid:35382627.