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RESEARCH ARTICLE

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Longer length of stay, days between discharge/first readmission, and pulmonary involvement ≥50% increase prevalence of admissions in ICU in unplanned readmissions after COVID-19 hospitalizations

Sarah G. Peixoto[1] | Jonas M. Wolf[2] | Andressa B. Glaeser[2] | Juçara G. Maccari[3] | Luiz A. Nasi[4]

[1]Internal Medicine, Hospital Moinhos de Vento, Porto Alegre, Rio Grande do Sul, Brazil

[2]Value Management Office, Medical Manager at Hospital Moinhos de Vento, Porto Alegre, Rio Grande do Sul, Brazil

[3]Medical Manager, Hospital Moinhos de Vento, Porto Alegre, Rio Grande do Sul, Brazil

[4]Chief Medical Officer, Hospital Moinhos de Vento, Porto Alegre, Rio Grande do Sul, Brazil

Correspondence

Jonas M. Wolf, Hospital Moinhos de Vento, 333 Tiradentes St, 13 Floor, Porto Alegre – RS, 90560-030, Brazil.
Email: jonas.wolf@hmv.org.br

Abstract

Hospital readmissions due to COVID-19 are one of the main concerns for the health system due to risks to the patient's life and increased use of health resources. Studies focusing on this issue are important to understand the risk factors and create strategies to avoid readmissions. We evaluated the readmission of patients with confirmed COVID-19 in a private hospital in southern Brazil, between March 2020 and 2021. Also, the characteristics and clinical outcomes of patients admitted to the intensive care unit (ICU) and nonadmitted were compared. Poisson regression models with prevalence ratio (PR) with 95% confidence intervals (95% CIs) were applied to confirm the association between variables and ICU admission. Of the 2084 hospitalized patients with COVID-19, 1806 were discharged alive. Among them, 106 were readmitted for unplanned reasons during one year. Early hospital readmission (≤30 days) occurred in 52.8% of the cases. The main reasons were respiratory, gastroenterological, kidney, and cardiac disease. The median age was 73.0 years old and women correspond to 52.8%. The presence of at least one comorbidity was detected in 87.7% of patients. Hypertension, diabetes, cardiac, and lung disease were more frequent. The ICU admitted patients ($n = 43$; 40.5%) mostly had 4–5 comorbidities, pulmonary involvement ≥50%, length of stay (LOS), and days between discharge and first readmission. Longer LOS (PR: 3.46; 95% CI: 1.24–5.67), days between discharge/first readmission (PR: 2.21; 95% CI: 1.15–5.88), and pulmonary involvement (≥50%; PR: 1.59; 95% CI: 1.11–3.54) were independently associated with ICU admission. Longer LOS, longer days between discharge/first readmission, and pulmonary involvement (≥50%) were associated with ICU admission in readmitted patients. Readmissions evaluation is pivotal and may help in ensuring safe care transition and postdischarge follow-up.

KEYWORDS

comorbidities, coronavirus, healthcare system, hospital readmission, oxygen therapy

1 | INTRODUCTION

The first confirmed case of coronavirus disease 2019 (COVID-19) was in China in December 2019. Since then, more than 500 million people have been affected by this virus causing more than 6.2 million deaths.[1] This disease led to a world pandemic problem that has never been seen before. Multiple centers all over the world have been focusing research on understanding more about this virus.[2–5]

Hospital readmissions are directly associated with poor patient outcomes and increased health resource necessity.[4,5] Analyzing this type of data gives more knowledge about the probability of gravity after discharging the patient as well as improving patient care. Hospital readmission is a public health concern due to its costs, negatively affecting the benefits of health services.[4–7]

Readmissions study is key and may help in defining optimal timing for patient discharge and ensuring safe care transition. We aimed to characterize the readmission of patients with confirmed COVID-19, risk factors for intensive care unit (ICU) admission, describing the patient profile and the main reasons to return.

2 | METHODS

2.1 | Data collection

The study was conducted at a single center in southern Brazil from March 2020 to March 2021. We identified COVID-19 hospitalizations and performed a retrospective review of unplanned readmission causes and patient data. We included patients with a positive test for SARS-CoV-2, age ≥ 18 years old and the initial hospitalization was for treatment or management of coronavirus disease. Readmissions for planned reasons (e.g., elective surgeries or chemotherapy) were excluded from the study. Unplanned readmissions were clustered by the primary cause of hospitalization, considering reasons respiratory (if COVID-19, pneumonia, or chronic obstructive pulmonary disease), cardiac (if heart failure, acute myocardial infarction or angina), neurological (if seizure or stroke), renal (if urinary tract infection), psychiatric (if anxiety or depression), gastroenterological (if colitis, gastroenteritis, gastric ulcer, or digestive bleeding), vascular (if thrombosis) or other, in cases of specificity to another medical specialty. The classification was defined and reviewed by leading doctors. Demographic and clinical variables, including age, sex, comorbidities, and laboratory data were extracted from electronic medical records with a standardized data collection form. Laboratory testing was defined as the first test results available, within 24 h of admission. The pulmonary involvement was assessed on a visual scale by two independent chest radiologists trained to interpret COVID-19 patients and classified as typical (ground-glass opacity) or atypical.[8] All participants signed an informed consent form and the study was previously approved by the clinical research ethics committee with protocol number 4.497.118.

2.2 | Statistical analysis

The frequencies of qualitative variables were compared between patients using Pearson's chi-square and/or Fisher's exact tests. Quantitative variables were demonstrated by medians with interquartile ranges (IQRs). To evaluate the normality of the continuous data, the Kolmogorov–Smirnov test with Lilliefors correction was performed. Mann–Whitney test was used to compare quantitative variables. Poisson regression models with covariates were used to assess the possible association between variables with ICU admission. A priori confounders considered in the multivariable analysis were age, sex, length of stay (LOS), days between discharge and first readmission, oxygen therapies methods (oxygen catheter, Hudson mask, noninvasive ventilation, high flow oxygen, and invasive mechanical ventilation), and pulmonary involvement. Prevalence ratio (PR) and 95% confidence intervals (95% CIs) were estimated. SPSS, Version 23.0 for Windows (SPSS Inc.), and R software (R Foundation for Statistical Computing; http://www.R-project.org) were used for data analysis. All estimates were bilateral with a significance level of 5% ($p \leq 0.05$).

3 | RESULTS

A total of 2084 hospitalizations were initially enrolled in the current study. Of the total, 278 died during hospitalization, limiting our sample to 1806 recovered patients. Among patients discharged alive, 149 readmissions were identified, being 135 (7.5%) readmissions for unplanned reasons ($n = 29$, 21,5% demonstrated more than one readmission for COVID-19 reason) and 106 patients were eligible for analysis (Figure 1). Of these patients, 43 (40.5%) were admitted to the ICU.

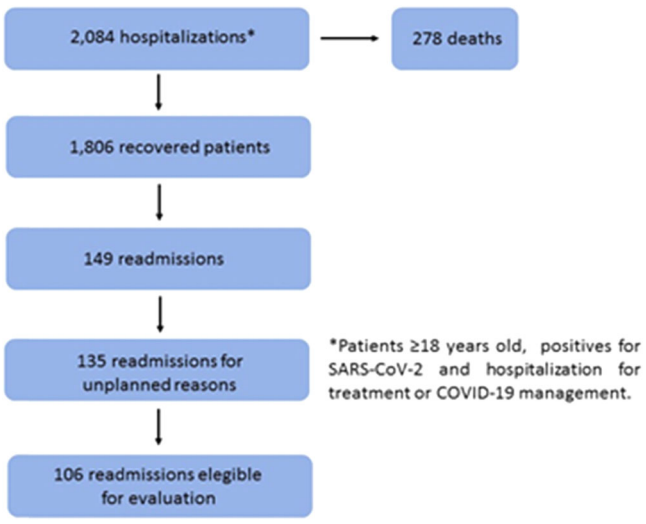

FIGURE 1 Flowchart showing the selection criteria of the patients readmitted by COVID-19.

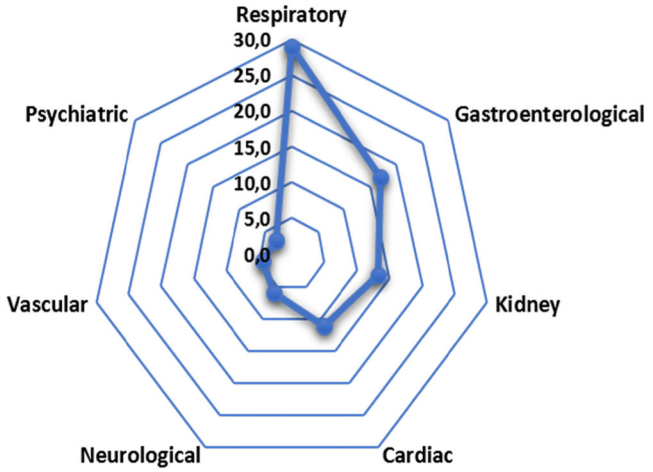

FIGURE 2 Radar chart with percentual of causes of unplanned readmissions of COVID-19 between March 2020 and 2021.

The most common reasons for unplanned readmission were respiratory (28.8%), gastroenterological (18.2%), renal (13.8%), and cardiac problems (11.1%; Figure 2). The median of days between discharge and first readmission was 25.5 (IQR: 9.2–79.7), with 56 (52.8%) patients readmitted between ≤30 days, 30 (28.3%) between 31 and 90 days, and 20 (18.9%) >90 days.

The median age was 73.0 years old (IQR: 58.3–85.5), 56 (52.8%) were women, the body mass index (BMI) was 27.3 (IQR: 24.1–31.4), the LOS was 13.0 (IQR: 7.0–30.0) days, and the time between discharge/first readmission was 25.5 days (IQR: 9.2–79.7). The symptoms more frequently observed were cough in 53.8% of cases ($n = 57$), fever in 44.3% ($n = 47$), dyspnea in 39.6% ($n = 42$), myalgia in 22.6% ($n = 24$), adynamia in 20.8% ($n = 22$), and headache in 17.9% ($n = 19$). The presence of at least one comorbidity was present in 93 patients (87.7%). Hypertension was the chronic medical condition most prevalent, being detected in 59.4% (63), followed by diabetes in 31.1% ($n = 33$), cardiac disease in 28.3% ($n = 30$), and lung disease in 22.6% ($n = 24$). The CT with typical findings was detected in 59.4% of cases ($n = 63$) and 21.5% ($n = 15$) showed pulmonary involvement ≥50%. The clinical characteristics of the index admission are described in Table 1. Additionally, Supporting Information: Table S1 reports the laboratory data of patients evaluated.

The overall hospitalization showed a median of 13.0 days (IQR = 7.0–30.5), 40.6% of patients needed treatment in the ICU and the median LOS was 11.0 days (IQR: 5.8–28.3). During the first hospitalization, 77 (72.6%) of the readmitted patients used oxygen therapy: an oxygen catheter was used in 72 (67.9%), a Hudson mask in 27 (25.5%), noninvasive ventilation in 23 (21.7%), high flow oxygen in 22 (20.8%), and invasive mechanical ventilation in 21 (19.8%). All oxygen therapy methods were statistically more frequent in ICU admitted than not admitted patients. Regarding the clinical outcome of readmissions, 13 (9.6%) resulted in death, being 5 of them due to respiratory causes.

When comparing patients admitted to the ICU with those not admitted to the ICU regarding the presence of comorbidities, it was possible to observe that the ICU patients had 1–2 (58.1%) and 3–5 comorbidities (37.2%). Nevertheless, there was no significant difference between the groups ($p = 0.14$). Comparisons between ICU admitted and not admitted patients are presented in Table 2.

Also, pharmacological treatment and types of comorbidities were compared between ICU admitted and not admitted patients (Supporting Information: Table S2). Treatment with antibiotics (e.g., ceftriaxone and piperacillin/tazobactam), convalescent plasma, vasopressor, and anticoagulant were more frequent in ICU patients (93.0% vs. 74.2%, 32.6% vs. 4.8%, 41.9% vs. 0%, 39.5% vs. 11.3%;

TABLE 1 Characteristics of COVID-19 patients readmitted.

Variables	*n*	%
Sex (*n*= 106)		
Female	56	52.8
Male	50	47.2
Age in years, median (IQR; *n*= 106)	73.0 (58.3–85.5)	
BMI, median (IQR; *n*= 104)	27.3 (24.1–31.4)	
Length of stay, median (IQR; *n*= 106)	13.0 (7.0–30.0)	
Days between discharge/first readmission, median (IQR; *n*= 106)	25.5 (9.2–79.7)	
Symptoms (*n*= 106)		
Cough	57	53.8
Fever	47	44.3
Dyspnea	42	39.6
Myalgia	24	22.6
Adynamia	22	20.8
Headache	19	17.9
Others	42	39.6
Comorbidities (*n*= 106)		
0	13	12.3
1	31	29.2
2	25	23.6
3	25	23.6
4	8	7.5
5	4	3.8
CT classification (*n*= 106)		
SARS-CoV-2 typical	63	59.4
SARS-CoV-2 atypical	38	35.8
Not available	5	4.8
CT graduation (*n*= 70)		
Pulmonary involvement (<50%)	55	78.5
Pulmonary involvement (≥50%)	15	21.5

Abbreviations: BMI, body mass index; CT, computerized Tomography; IQR, interquartile range.

TABLE 2 Characteristics of patients with COVID-19 not admitted to the ICU versus admitted to the ICU.

Variables	Not admitted (n = 63)		Admitted (n = 43)		
	n	%	*n*	%	*m*
Sex (n= 106)					
Female	28	44.5	22	51.2	0.54
Male	35	55.5	21	48.8	
Self-reported skin color (white; n= 102)	58	92.1	40	93.0	0.80
Age in years, median (IQR; n= 106)	74.5 (55.8–87.0)		71.0 (61.0–75.0)		0.82
Length of stay, median (IQR; n= 106)	8.0 (5.0–13.0)		25.0 (15.0–64.0)		**<0.01**
Days between discharge/first readmission, median (IQR; n= 106)	23.0 (7.5–79.0)		31.0 (13.5–79.5)		**<0.01**
Number of comorbidities (n= 106)					
0	11	17.5	2	4.7	0.14
1–2	31	49.2	25	58.1	
3–5	21	33.3	16	37.2	
CT classification (n = 106)					
SARS-CoV-2 typical	37	59.7	26	60.5	0.98
CT graduation (n= 70)					
Pulmonary involvement (≥50%)	3	7.1	12	42.9	**<0.01**
Oxygen therapy (n= 106)					
Oxygen catheter	35	56.5	37	86.0	**<0.01**
Hudson mask	8	12.9	19	44.2	**<0.01**
Noninvasive ventilation	4	6.5	19	44.2	**<0.01**
High-flow nasal oxygen	1	1.6	21	48.8	**<0.01**
Invasive mechanical ventilation	0	0	21	48.8	**<0.01**

Note: Significant p values are highlighted in bold.

Abbreviations: CT, computerized tomography; ICU, intensive care unit; IQR, interquartile range.

$p < 0.01$). Types of comorbidities did not show significant differences between these groups (Supporting Information: Table S2).

Thirteen patients died in this cohort, eight women and five men, with ages between 29 and 92 years old. Five patients were admitted to ICU, three needed invasive ventilation and four noninvasive ventilation. Also, the comorbidities more frequent were cancer (n = 6) and hypertension (n = 5; Supporting Information: Table S3). The LOS varied between 1 and 101 days in readmitted patients. Additionally, the LOS of unplanned readmitted patients was statistically higher than those who were not readmitted, respectively (median: 13.0; IQR: 7.0–30.0 vs. median: 9.0; IQR: 9.0–18.0, $p < 0.01$; Figure 3). Additionally, the LOS was significantly higher in patients with pulmonary involvement ≥50% than those with <50% (median: 18.0; IQR: 10.0–50.0 vs. 10.0; IQR: 5.0–20.0 vs. 18; $p < 0.01$; Figure 4).

In patients admitted to the ICU (n = 43), 34.8% showed thrombosis and 41.9% showed a secondary bacterial infection. In the subgroup of patients >80 years (n = 31), 41.9% were admitted to the ICU, showed a median of LOS of 18.1 (IQR: 14.4–39.8), and days between discharge/first readmission was 15.5 (8.5–48.2), all showed comorbidities and were underwent to oxygen therapy. In this subgroup of patients, 48.4% showed thrombosis, 54.9% showed secondary bacterial infection, and respiratory reason of readmission was predominant (48.4%).

In the multivariable analysis by Poisson regression, the variables independently associated with ICU admission were: longer LOS (PR: 3.46; 95% CI: 1.24–5.67; $p < 0.01$), longer days between discharge/first readmission (PR: 2.21; 95% CI: 1.15–5.88; $p < 0.01$), and pulmonary involvement ≥50% (PR: 1.59; 95% CI:1.11–3.54; $p < 0.01$; Table 3).

4 | DISCUSSION

In the present study, approximately 8.0% of patients were readmitted, this frequency is similar to a study that evaluated 126 137 patients from March to July 2020 in the United States (9.0%).[3] Respiratory, gastroenterological, renal, and cardiac diseases were clinical medical conditions more prevalent. This epidemiological pattern was similar to data reported from China,[9] Italy,[2] Netherlands,[10], and the United States.[3,5,6] COVID-19 symptoms such as

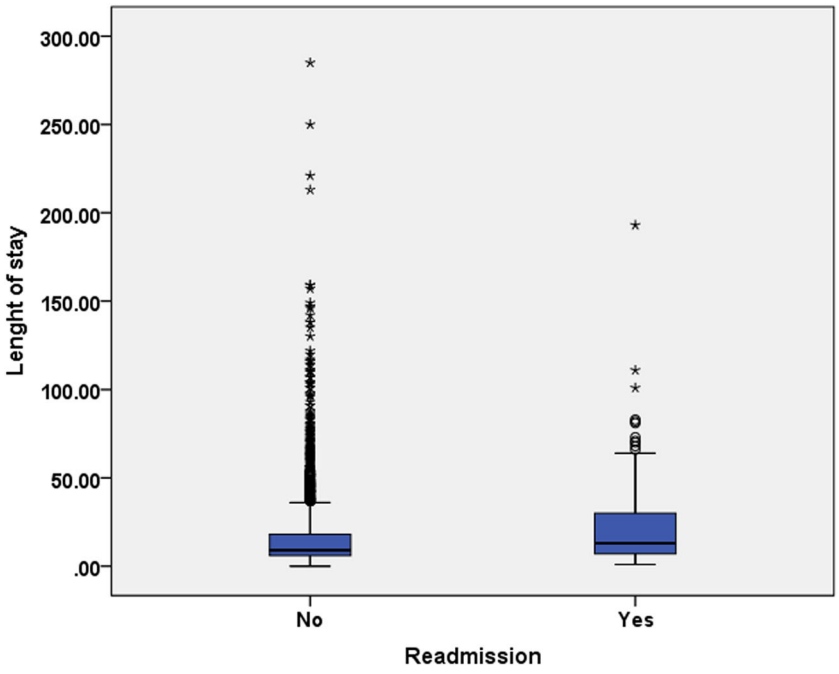

FIGURE 3 Length of stay in patients who were not readmitted and readmitted for unplanned causes.

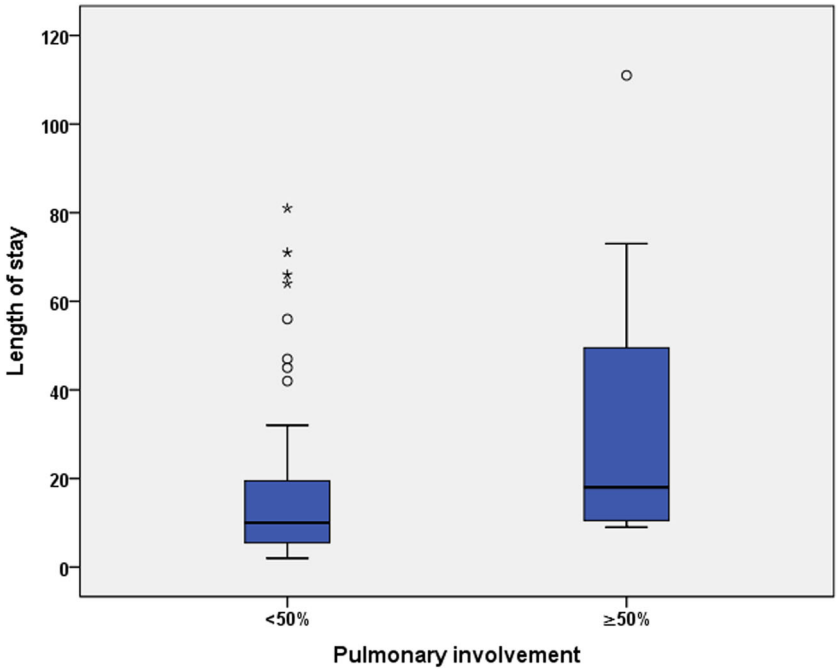

FIGURE 4 Length of stay in patients with pulmonary involvement (<50%) and (≥50%).

cough, fever, and dyspnea were more frequently detected and these findings are similar to other reports.[3–5]

Most of the patients readmitted showed chest CT typical for SARS-CoV-2 infection, with bilateral pulmonary involvement and ground-glass opacities. This clinical aspect is very characteristic of the disease and has been reported in a specific report of the World Health Organization.[11] Approximately half of readmitted patients required ICU treatment, with pulmonary involvement (≥50%), LOS, days between discharge/first readmission, and use of oxygen therapy significantly higher than patients who did not need the ICU. In multivariate analysis, longer LOS, longer days between discharge/first readmission, and pulmonary involvement (≥50%) were independently associated with ICU admission. These clinical characteristics of patients most severely affected by SARS-CoV-2 were also reported in studies carried out from China,[9] Italy,[2] United Kingdom,[12] and the United States.[3–6,13]

Patients who returned presented a median of 25.5 days of days between discharge/first readmission, with 40.5% of these requiring

TABLE 3 Multivariable associations of risk factors with ICU admission among COVID-19 patients.

Variables	Wald Chi-square	Prevalence ratio	Lower CI 95%	Higher CI 95%	*p* Values
Sex (female)	0.29	1.19	0.63	2.26	0.59
Age (scale)	0.08	1.12	0.53	2.35	0.77
Length of stay (scale)	5.61	3.46	1.24	5.67	**<0.01**
Days between discharge/first readmission (scale)	4.67	2.21	1.15	5.88	**<0.01**
Pulmonary involvement (≥50%)	4.32	1.59	1.11	3.54	**<0.01**
Comorbidities (≥2)	2.68	1.55	0.88	3.09	0.15
Oxygen catheter	0.53	1.37	0.59	3.17	0.47
Hudson mask	0.24	0.84	0.41	1.71	0.63
Noninvasive ventilation	2.67	1.83	0.89	3.78	0.10
High flow oxygen	1.67	1.55	0.80	3.01	0.20
Invasive mechanical ventilation	2.23	1.82	0.83	4.00	0.14

Note: Significant *p* values are highlighted in bold.

Abbreviations: CI, confidence interval; ICU, intensive care unit.

ICU admission. There was a higher prevalence of LOS, days between discharge/first readmission, pulmonary involvement (≥50%), and oxygen therapies applied in ICU patients. Second, respiratory distress, accounting for half of all symptoms on return, was the most common cause for returning to the hospital and LOS was higher in patients with pulmonary involvement (≥50%). These findings may offer implications for the postdischarge care of patients hospitalized with COVID-19, and if verified, could inform resource allocation.[12,14,15]

COVID-19 represents a massive challenge for health care systems and the ICUs in Brazil and throughout the world. A high number of patients required intensive care at the same time leading to an elevated risk of collapsing the health care systems. Until effective and specific treatments are available, supportive care is a key factor for critically ill patients. Providing this care at a high-quality level for the high volume of patients to treat is the main challenge for all health care systems worldwide.

Interestingly, we note that patients who returned to the hospital had higher LOS. Despite administrative prioritization to reduce LOS and readmissions, studies about COVID-19 have suggested these two outcomes may be directly related.[2,5,6] Reducing LOS during the COVID-19 pandemic has also been emphasized to preserve resources and limit exposure. Further, we observed returning patients were more likely to have required ICU stay during the LOS. ICU stay serves as a marker of illness severity and thereby may caution medical staff to ensure clinical stability before discharge.[16] Whether continued in-hospital observation translates into longer LOS for improvement in respiratory profile impacts readmission context and exposure risk warrants further investigation.[12,17,18]

This study has some limitations. First, the study population only included patients within the Rio Grande do Sul state. Second, the data were collected from the electronic health record database. This precluded the level of detail possible with a manual medical record review. The absence of data on patients who remained hospitalized at the final study date may have biased the findings.

The main reasons for readmission for COVID-19 treatment were a respiratory, gastroenterological, renal, and cardiac disease. Factors such as the patient's LOS, days between discharge/first readmission, and pulmonary involvement (≥50%) were independently associated with ICU admission. These factors can be used as predictors to assess the probability of the patient being admitted to the ICU and having a worse prognosis. Also, patients >80 years admitted to the ICU had higher rates of thrombosis, bacterial infection, and readmission for respiratory reasons. In conclusion, the clinical knowledge of factors related to readmission after COVID-19 hospitalization provides the possibility to give more attention to important points in the outpatient follow-up and soon perceive risk factors and symptoms that the patient might have that led to a new hospitalization. Further research about this issue and also investing in the creation of clinics that focus on the care of patients after COVID-19 would expand the comprehension of the disease and the safety of the patients.

AUTHOR CONTRIBUTIONS

Sarah G. Peixoto, Jonas M. Wolf, Andressa B. Glaeser, Juçara G. Maccari, and Luiz A. Nasi designed the study. Jonas M. Wolf performed the statistical analyses. Sarah G. Peixoto, Jonas M. Wolf, Andressa B. Glaeser, Juçara G. Maccari, and Luiz A. Nasi wrote the first draft of the manuscript and contributed to the literature review

and discussion of results. All authors contributed to and have approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

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

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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