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Clinical characteristics and results of discharge and death of critically ill adults with COVID-19: a retrospective observational cohort study

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ABSTRACT. Invasive mechanical ventilation (IMV) as a supportive care can be vital for maintaining the respiratory function of those who develop severe respiratory failure and acute respiratory distress syndrome related to coronavirus disease 2019 (COVID-19). Observational retrospective cohort study with a quantitative approach carried out with data from an official electronic platform for recording in two public hospitals in the state of Paraíba patients with confirmed cases of SARS-CoV-2. To describe clinical characteristics of critically ill patients with COVID-19 and associate the outcome with discharge and death. The sample consisted of 81 patients with COVID-19 admitted between March and December 2020. Demographic, clinical, respiratory support, oxygen therapy, adjuvant measures, length of stay in the intensive care unit (ICU) and survival were collected. Data were tabulated in Excel software and spent in SPSS software, version 26.0, using descriptive and inferential statistics. Revealed that the average age of participants was 61.6 years; 58.0% of the individuals were male, 88.9% had comorbidities, 87.7% were admitted to the ICU and IMV was used in 56.8%. Age over 60 years and use of IMV support are highly associated with patient death. Age between 18 and 59 years and the use of oxygen therapy are associated with discharge. Patients with COVID-19 who evolved critically and required IMV were associated with increased mortality. Mortality was higher in older patients, with need for ICU, comorbidities and with a lower PaO2/FiO2 ratio.

Keywords: COVID-19; invasive mechanical ventilation; acute respiratory failure; mortality risk fator.

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Introduction

SARS-CoV 2 is a β-Coronavirus considered the etiological agent of coronavirus disease 2019 (COVID-19). It was identified primarily in Wuhan, China, in December 2019 and quickly spread to several countries. The World Health Organization (WHO) declared it a global pandemic on March 11, 2020. Currently, the numbers of infected patients and deaths continue to rise. As of June 22, 2022, there were 536 million confirmed cases, with 6.3 million deaths worldwide (World Health Organization [WHO], 2022; Petrilliet al., 2020).

As for its presentation, COVID-19 may have several clinical outcomes: asymptomatic or mild symptoms in most individuals. A small part of those infected developed critical illness and there were worse outcomes in those with a more advanced age and who present comorbidities. Patients who advance severely develop dyspnea and hypoxemia usually within a week after the onset of the disease, which may progress quickly to acute respiratory distress syndrome (ARDS) and organ failure (Wu et al., 2020).

Invasive mechanical ventilation (IMV) as a supportive care can be vital for maintaining the respiratory function of those who develop severe respiratory failure and ARDS related to COVID-19. However, the use of this support may be associated with a greater lung damage, such as the development of mechanical ventilation-induced lung injury (VILI), contributing to worsening the prognosis and to the mortality of these patients. In addition, providing adequate ventilation for this type of patient has been a challenge considering the limitations of physical, human, and training resources during the pandemic (Gupta, Alkandari, Mohammed, Tobar,& Abdelmohsen, 2020; Dondorp, Hayat, Arya, Beane & Schultz, 2020). In this study, we

aimed todescribe the clinical characteristics of critically ill patients with confirmed COVID-19 and to associate the outcome with discharge and death.

Material and methods

Study design

This is a retrospective observational cochort study with a quantitative approach carried out in two public hospitals in the state of Paraíba, Brazil, between October 2020 and January 2021. The medical records of patients with a diagnosis confirmed by laboratory examination were included and the medical records with insufficient data records were excluded. The sample consisted of the 81 medical records of randomly selected patients with COVID-19 who were hospitalized between March and December 2020.

The research was carried out considering the ethical aspects contained in the Resolution no. 466/12 of the National Health Council/Ministry of Health and is in accordance with the Declaration of Helsinki. The study was approved by the Research Ethics Committee of University Hospital Lauro Wanderley under opinion no. 4.455.533.

Settings

Data related to sociodemographic aspects, including age and gender, and to clinical aspects that included the classification of the severity of COVID-19, changes shown in the computed tomography (CT) of the chest, respiratory machines used during the analysis were analyzed, namely oxygen therapy, noninvasive ventilation (NIV) and IMV, as well as other types of care, such as prone position, which is performed using concomitant invasive ventilatory support.

To determine the severity of COVID-19, the classification proposed by the WHO (2020) was used, which classifies the disease according to the clinical presentation into four stages: Mild: symptomatic patients who meet the case definition for COVID-19 without evidence of hypoxia or pneumonia; Moderate: when there are clinical signs of pneumonia (fever, cough, dyspnea, tachypnea) with SPO2 ⩾ 90% in room air; Severe: clinical signs of pneumonia plus some of the following: respiratory rate ⩾ 30 breaths/min or oxygen saturation <90% in room air. Critical: the condition meets the criteria for ARDS, septicemia, septic shock, or organ failure that require intensive care (World Health Organization [WHO], 2021).

Statistical analysis

The data were tabulated in the software Excel and analyzed using the software SPSS, version 26.0. The analysis was performed using descriptive statistics (absolute and relative frequency, and central tendency and dispersion) and inferential statistics (Pearson's Chi-square test, Fisher's exact test, Student t test; Mann-Whitney test). For all analyses, the significance value was 5% ($p<0.05$). Nonparametric tests were performed in cases where the data did not show a normal distribution according to the results of the Kolmogorov-Smirnov test.

Results

Participants' characteristics

Figure 1 shows the flow chart of the collection of medical records, showing the identification of 415 medical records based on the admission record of patients with COVID-19 in the two hospitals. However, 163 medical records were unavailable for consultation in the filing sector, totaling 252 medical records available. Of these, 66 medical records were available at hospital 1, 26 of which were excluded because they did not present sufficient data of interest to this study, thus totaling 40 medical records of this hospital included in the analysis. In hospital 2 there were 186 medical records available, 15 of which were excluded for not having sufficient data and 130 were not accessed, totaling 41 medical records of this hospital analyzed. This study thus evaluates 81 medical records.

Descriptive data

Table 1 shows the characterization of the sample. It is possible to verify a predominance of male individuals of 58.0% (n=47). The mean age of the participants was 61.6 years (SD=16.0). 60.5% (n=49) of them were aged over 60 years. As for the severity of COVID-19, most participants were critical, corresponding to 84.0% (n=68) of the sample.

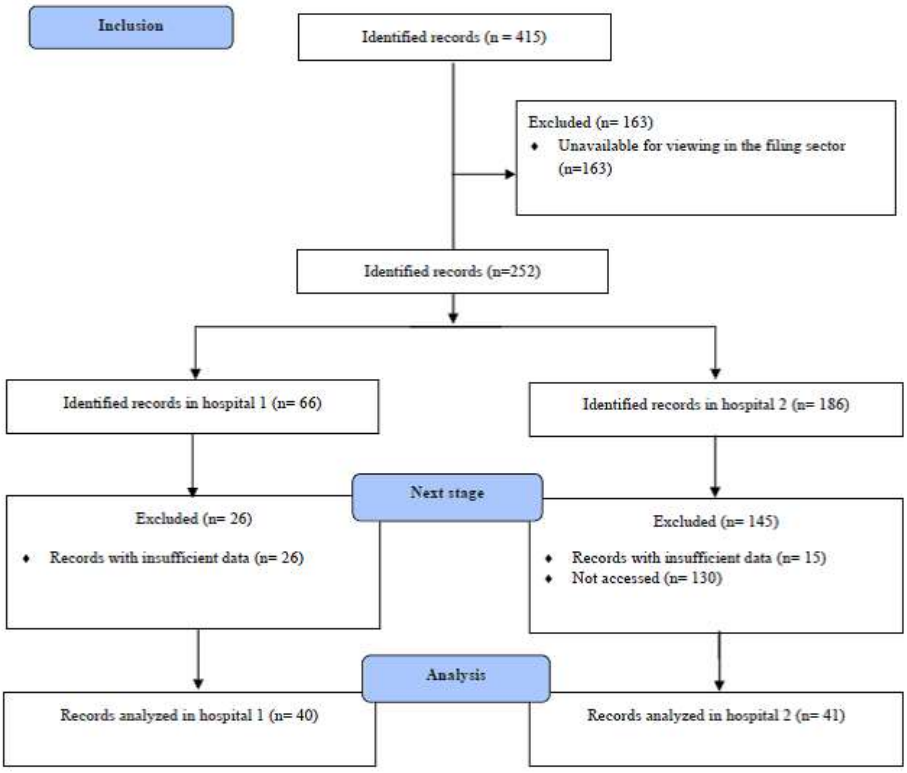

Figure 1. Flow chart for the collection of medical records.

Table 1. Characterization of the studied sample.

	Variable	N	%
Gender	Female	34	42.0
	Male	47	58.0
Age	18-60 years	32	39.5
	Over 60 years	49	60.5
	Mild	1	1.2
	Moderate	7	8.6
Gravity of COVID-19	Severe	5	6.2
	Critical	68	84.0
	Hypertension	46	63.9
Comorbidity	Diabetes	32	44.4
	Obesity	12	16.7
	COPD	12	16.7
	Vascular disease	13	18.1
	Chronic kidney disease	12	16.7
	Less than 25%	7	8.6
Extension of pulmonary involvement on CT (%)	Between 25 and 50%	20	24.7
	Higher than 50%	34	42.0
	Oxygen therapy	28	34.6
Respiratory support	NIV	7	8.6
	IMV	46	56.8
	No support	7	8.6
Outcome	Death	48	59.3
	Discharge	33	40.7

Legend: COPD: Chronic obstructive pulmonary disease; CT: computed tomography; NIV: Non-invasive ventilation; IMV: Invasive mechanical ventilation; Results expressed by n (%).

Of all participants, 88.9% (n=72) had at least one comorbidity, of which 63.9% (n=46) were hypertensive, 44.4% (n=32) were diabetic, 16.7% (n = 12) were obese, 18.1% (n=13) had vascular disease, 16.7% (n=12) had chronic obstructive pulmonary disease (COPD), 16.7% (n=12) had chronic kidney disease, and 6.9% (n=5) had neurological disease.

Of the patients who underwent chest CT (75.3%; n=61), 42.0% (n=34) had more than 50% impairment of the lung parenchyma, 24.7% (n=20) had 25-50% of impairment, and 8.6% (n=7) had less than 25% of damage.

In chest CT, ground-glass opacities occurred in 82.7% of cases (n=67), septal thickening in 48.1% (n=39), and bilateral involvement in 71.6% (n=58), predominating the lower lobes in 45.7% (n=37) and the posterior region (32.1%; n=26), with consolidations in 64.2% (n=52), peripheral distribution in 54.3% (n=44), and multifocal distribution in 46.9% (n=38).

Considering the respiratory support used, only oxygen therapy was used in 34.6% (n=28) of cases, NIV in 8.6% (n=7), IMV in 56.8% (n=46), and no respiratory support in 8.6% (n=7). Patients who underwent oxygen therapy recorded a mean number of days using the support of 10.2 days and the mean of the highest oxygen concentration used during hospitalization was 9.0 l/min, administered through a nasal cannula in 82.1% (n=23) of these cases and by reservoir masks in 64.3% (n=18). The mean age for those who used only oxygen therapy was 56.8 years and the mean of the lowest PaO2/FiO2 ratio was 149.3 mmHg.

For those who underwent NIV, the mean number of days in intermittent use of the support was 3.8 days, and all those who used this support were intubated. The mean age for this group was 55.8 years and the mean for the PaO2/FiO2 ratio was 70.5 mmHg. The mean of the total days on IMV was 12.0 days, with 68.2% (n=30) being ventilated predominantly in pressure-controlled ventilation (PCV) mode, 29.5% (n=13) predominantly on volume-controlled control (VCV), and 2.3% (n=1) predominantly in pressure support ventilation (PSV). Also for these patients, the mean of the highest positive pressure end-expiratory pressure (PEEP) during hospitalization was 12.4 cm H2O. The alveolar recruitment maneuver was used in 24.7% (n=20) of the cases and the prone position in 23.9% (n=11) of cases. The mean age for those who used only IMV was 64.8 years and the mean of the lowest PaO2/FiO2 ratio was 95.2 mmHg.

The most frequent complications among this population were ARDS in 72.1% (n=49) of cases, acute kidney injury (AKI) in 38.2% (n=26), and sepsis in 27.9% (n=19) of patients. Of all individuals, 87.7% (n = 71) were admitted to the intensive care unit (ICU). The mean number of days in the ICU was 10.0 days, while the mean number of days in the hospital was 16.9 days. As for the outcomes, death predominated in 59.3% (n=48) of the sample and discharge in 40.7% (n=33).

Table 2 shows the association between sociodemographic and clinical variables and the patients' outcomes of discharge and death, showing an association between the patients' age and the outcomes (p value=0.006). The highest number of deaths were among patients 60 years or older and the most frequent number of discharges were among patients aged between 18 and 59 years.

There was also an association between ICU admission and the outcomes discharge and death (p<0.001), with a higher frequency of deaths among patients admitted to the ICU compared to patients admitted to the ward, where discharge was the most frequent outcome. There was no association between the existence of comorbidities and the outcomes analyzed (p=0.731).

Table 2. Associations of sociodemographic and clinical variables with the outcomes discharge and death.

Sociodemographic and clinical variable		Death n (%)	Discharge n (%)	P value
Age	Between 18 and 59 years	13 (40.6)	19 (59.4)	0.006*
	60 or older	35 (71.4)	14 (28.6)	
Place of hospitalization	ICU	48 (67.6)	23 (32.4)	<0.001**
	Ward	0 (0.0)	10 (100)	
Comorbidity	Yes	42 (58.3)	30 (41.7)	0.731**
	No	6 (66.7)	3 (33.3)	
PaO2/FiO2	<100 mmHg	32 (76.2)	10 (23.8)	0.012 **
	⩾100 to ⩽200 mmHg	12 (50.0)	12 (50.0)	
	>200 to ⩽300 mmHg	2 (28.6)	5 (71.4)	
Oxygen therapy	Yes	6 (21.4)	22 (78.6)	<0.001*
	No	42 (79.2)	11(20.8)	
Use of NIV	Yes	5 (71.4)	2 (28.6)	0.695**
	No	43 (58.1)	31 (41.9)	
Use of IMV	Yes	41 (89.1)	5 (10.9)	<0.001*
	No	7 (20.0)	28 (80.0)	

ICU: Intensive care unit; PaO2/FiO2: Arterial oxygen partial pressure/Inspired oxygen fraction; *Pearson's Chi-square test; **Fisher's exact test.

There was an association between the PaO2/FiO2 ratio and the outcomes (p=0.012), by which patients with a ratio <100 mmHg died more frequently compared to patients with a ratio between ⩾100 and ⩽200 mmHg and between >200 and ⩽300 mmHg. Discharge was more frequent among patients with a ratio between >200 and ⩽300 mmHg compared to patients with a ratio between ⩾100 and ⩽200 mmHg and <100 mmHg.

In this sample, there was also an association between oxygen therapy and outcomes (p<0.001). Patients who underwent only oxygen therapy had a higher frequency of discharge compared to patients who did not use only this support; death was more frequent among the latter. There was no association between NIV and outcomes (p=0.695).

There was also an association between IMV and outcomes (p<0.001): patients who used IMV showed a higher frequency of deaths than those who did not use this support. Discharge was the most frequent outcome for patients who did not use IMV.

Analyzing the association of outcomes with other life supports, there was an association between the use of alveolar recruitment maneuver and outcomes (p=0.007). Death was more frequent among patients who used the maneuver compared to patients who did not use it. An association was also found for the prone position and outcomes (p=0.002). Death was the most frequent outcome among patients who in prone position compared to patients who were not put into the prone position.

Figure 2 shows the receiver operating characteristics curve (ROC) for the relation between IMV and death, showing a sensitivity of 85.4% and a specificity of 15.2% with an area under the curve of 0.85 ROC (95% CI = 0.76-0.94; p<0.001).

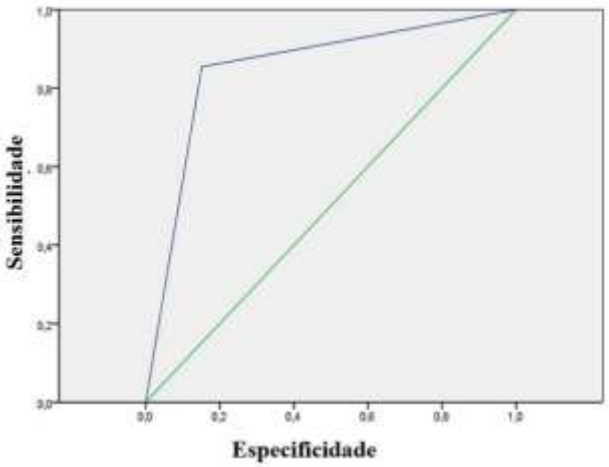

Figure 2. ROC curve based on the relation between IMV and death.

Figure 3 shows the ROC for the relation between oxygen therapy and discharge, showing a sensitivity of 66.7% and a specificity of 12.5% with an area under the curve of 0.77 ROC (95% CI = 0.66-0.88; p<0.001).

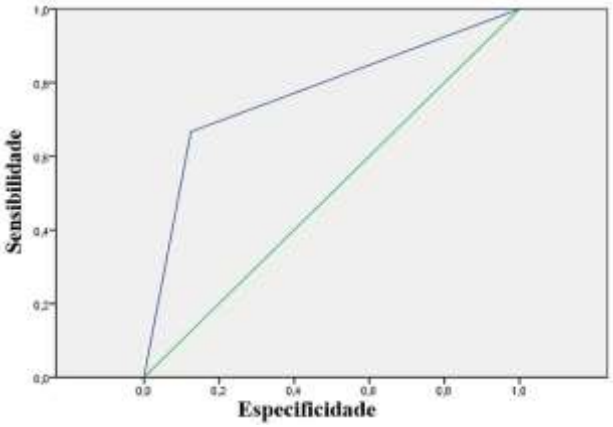

Figure 3. ROC curve based on the relation between oxygen therapy and patient discharge.

Discussion

Considering the current situation in the context of COVID-19, there are still few studies that assess the clinical characteristics of critically ill patients with confirmed COVID-19 and associate the outcome with discharge and death of patients affected by COVID-19 in Brazil. In the present study, data from 81 patients with COVID-19 showed high mortality for patients who needed IMV.

Critical patients who required ICU admission predominated in this sample, with a mortality rate of 59.3% among the individuals analyzed. Accordingly, Ranzani, Bastos, Gelli, Marchesi, Baião, Hamacher, and Bozza, (2021) in a retrospective study with 250.000 patients with COVID-19 recorded in the epidemiological surveillance information system in Brazil, identified a concentration of high mortality rates in the Northeast region compared to the South region of Brazil. The authors reported a high number of patients requiring ICU admission and invasive mechanical ventilatory support (Ranzani et al., 2021).

In our study, most individuals were male with a mean age of 61.6 years. Grasselli et al. (2020) reported similar results in a cohort study with 3.988 critically ill patients infected by SARS-CoV-2 in Italy. The authors found a mean age of 63.0 years among patients analyzed and a predominance of male individuals (Grasselli et al, 2020).

With this in mind, studies reported the impacts of gender on the outcomes of COVID-19. Gebhard, Regitz-Zagrosek, Neuhauser, Morgan, and Klein, (2020), in a systematic review, showed that the number of men hospitalized in the ICU can be three to four times higher than that of women, thus configuring a risk factor of greater severity and mortality by COVID-19 (Gebhard, et al., 2020). Aspects such as differences in baseline immunological abilities and high rates of smoking and alcohol intake among men may contribute to the development of comorbidities. Lower rates of hand washing and delay in seeking health care are pointed out as possible causal factors (Jin et al., 2020; Takahashi et al., 2020).

In our study, there was a higher mortality among individuals aged 60 years or older. These results are consistent with those pointed out in the multicenter, retrospective study that Zhou et al. (2020) developed with 191 hospitalized patients (Zhou et al., 2020). Advanced age was an independent risk factor for mortality by COVID-19. Although the mechanisms by which this occurs are not yet clear, factors such as the reduction in pulmonary compliance in these individuals, marked innate responses, low cellular and humoral immune functions, and the increased risk of developing comorbidities are pointed out as possible explanations for such a scenario (Wang, & Wang, 2021).

Most individuals in our study had comorbidities (88.9%). Hypertension was the most frequent, followed by diabetes, vascular disease, obesity, COPD, and chronic kidney disease. These findings corroborate the results of Jain and Yuan's meta-analysis. The authors found a greater number of individuals with comorbidities in severe groups who needed to be admitted to the ICU. Among them, the most frequent were hypertension, diabetes, and cardiovascular diseases (Jain, & Yuan, 2020).

Another result we found is the higher mortality rate of patients who had a PaO2/FiO2 ratio below 100 mmHg. On this, Dhont, Derom, Van Braeckel, Depuydt, and Lambrecht, (2020) state that COVID-19 may cause changes in the ventilation/perfusion ratio (V/Q) driven by a hypercoagulable state. Thus, the formation of intravascular microthrombi, the deviation of arterial blood flow to unventilated alveoli, the loss of hypoxic vasoconstriction, and the impaired diffusion capacity could be associated with the severe hypoxemia these patients presented and could explain the presence of significant changes in gas exchange without an initial impairment of pulmonary mechanics, as observed in some cases (Dhont et al., 2020).

However, it is possible that these patients evolve rapidly with a high respiratory work, increases in minute volume at the expense of high transpulmonary pressures driven by a hypermetabolic and hyperinflammatory state, which contribute to the development of self-inflicted lung injury (P-SILI), leading to worse pulmonary mechanics and the need for IMV. At this stage, patients may present characteristics typical of ARDS (Camporota, Vasques, Sanderson, Barrett & Gattinoni 2020).

Accordingly, ARDS was reported in this study as a complication in 72.1% of the cases. Chen et al. (2020) also found similar results when they analyzed 1,590 patients with COVID-19 in China. ARDS was the most frequent complication, followed by secondary infection and septic shock (Chen et al., 2020).

As for the use of respiratory supports, in our sample there was a high mortality of patients who underwent IMV, with a sensitivity of 85.4% and a specificity of 15.2% for the relation between IMV and death. Ranzani et al. (2021) reported similar results in a retrospective study conducted in Brazil, in which the authors showed that 45.205 patients with COVID-19 required IMV and the mortality rate was 80% among them (Ranzani et al., 2021). However, these data contrast with the low mortality rates reported by studies developed in other countries, such as that developed by Fusco et al. (2021) in the United States, which confirmed through a database record of 29.383 patients a mortality rate of 53.8% among patients who used IMV (Fusco et al., 2021). In another study developed by Karagiannidis et al. (2020) in Germany, the authors analyzed resources used by hospitalized patients due to COVID-19 and evidenced a mortality rate of 53% in a population of 1.318 patients who used IMV (Karagiannidis et al., 2020).

In a context of pandemic, the higher burden on the health system in regions that have few resources may contribute to the worse outcomes of critically ill patients. In addition, a substantial attention has been paid to the availability of resources, such as ICU beds and mechanical ventilators, and less attention has been paid to the training of health professionals to support clinical practice, early identification of severe cases, and management of patients on IMV (Ranzani et al., 2021).

Bastos et al. (2020) analyzed a population of 88 patients with COVID-19 in the southern region of Brazil and found that age above or equal to 65 years was an independent risk factor for IMV. This result is in agreement with that found in our study, according to which patients who used invasive mechanical ventilatory support had a mean age of 68.8 years (Bastos et al., 2020).

In contrast, there was a low frequency in the use of NIV in our study, and all patients who used it evolved to a later need for IMV. It is assumed that the failure to use this support may be related to the severe oxygen deficit shown by patients who underwent this type of therapy and that the low adherence to the NIV in a hypoxic manner by professionals can be explained by the recommendations related to the risks of contamination during its use spread since the beginning of the pandemic. Regarding this situation, the WHO 1 recommended a cautious use of this device in view of the aerosol dispersion capacity. The institution must have additional protective care for health teams, in addition to strict patient monitoring, paying attention to the early recognition of failure in the use of the life support (World Health Organization [WHO], 2021).

In addition, Mukhtar, Lotfy, Hasanin, El-Hefnawy, and El Adawy, (2020) reported higher rates of use and success of NIV. The authors analyzed 55 patients with COVID-19 and reported that 39 of them used NIV, with a 77% success rate among them (Mukhtar et al., 2020). In another recent study with a cohort of 61 patients with COVID-19 who underwent NIV, the success rate was 72.1%. It is noteworthy, however, that patients who failed to use NIV were older; they also presented higher respiratory rates and D-dimer levels (Avdeev et al., 2021).

On the other hand, in this study, patients who needed only oxygen therapy had a better outcome and a higher frequency of discharge, showing a sensitivity of 66.7% and specificity of 12.5% for the relation between oxygen therapy and discharge. It is assumed that the higher frequency of discharge in this group may be related to a less severe oxygen deficit compared to patients who used other life supports, in addition to the lower mean age of these patients. These data corroborate the study of Myers, Parodi, Escobar, and Liu, (2020) who, among 264 patients admitted to the ward, 54.9% received oxygen supplementation and the result was a lower mortality (6.3%) among them (Myers et al., 2020).

In our study, the mean number of days undergoing supplemental oxygen therapy was ten days, which is higher than that found by Daher et al. (2021) In a retrospective study with 57 patients admitted to the ward receiving oxygen supplementation, the authors reported that the therapy lasted an average of eight days (Daher et al., 2021). Such data may provide information for the planning of care capacity of patients with COVID-19 who need supplemental oxygen therapy.

We emphasize here that this study had limitations, especially the small sample size, the study design, and the unavailability of a large number of physical records for consultation due to the context of transmissibility of the SARS-CoV-2. It is also worth mentioning limitations regarding the recording of information on obesity or patients' weight data in the medical records analyzed here.

Conclusion

With our findings, we can conclude that patients with COVID-19 who progressed critically in need of IMV support is associated with an increased mortality. Mortality was higher in older patients, needing to go to the ICU, with comorbidities and with a lower PaO2 / FiO2 ratio. Studies with larger samples are needed to assess whether these characteristics are actually present in other populations of patients with COVID-19 in Brazil and to identify aspects related to the use of IMV support, which may contribute to the worst outcomes of these patients.

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