

# Characteristics and outcomes of COVID-19 patients assisted by intensivists and nonintensivists

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## SUMMARY

**OBJECTIVE:** The aim of this study was to assess the outcomes of critically ill patients with COVID-19 in an intensive care unit seen by a care team formed by intensive and nonintensive physicians and treatment guided by processes and protocols linked to the “choosing wisely” concept, comparing them with similar data recently published.

**METHODS:** An observational cohort including adult patients with COVID-19 admitted to the intensive care unit of Hospital Independência between August 2020 and August 2021. Inclusion criteria were 18 years of age or older and there were no exclusion criteria.

**RESULTS:** The study included 449 patients, of which 64.1% were referred from the ward, 21.6% from emergency rooms, and 14.2% from another hospital (continuity of attendance). The overall mortality was 48.5%, occurring mainly in the elderly and/or those undergoing mechanical ventilation. We did not find any associations between different strata of body mass index and mortality. In the multivariate analysis, the time elapsed between the onset of symptoms and hospital admission, mechanical ventilation, C-reactive protein value at the end of the first week in the intensive care unit, and renal failure were independently associated with mortality. Vaccinated people comprised 8.8% of the sample, with no differences in mortality among the different vaccines, and 13.4% of patients underwent palliative treatment.

**CONCLUSIONS:** Patients admitted for acute respiratory syndrome due to SARS-CoV-2 are severe and have a high mortality rate, mainly if submitted to invasive mechanical ventilation. The emergence of acute renal failure marks an especially severe subgroup with increased mortality. Processes and protocols linked to the “choosing-wisely” concept seemed to significantly benefit our intensive care unit since it had a large contingent of nonspecialist physicians.

**KEYWORDS:** Critical care. COVID-19. Mechanical ventilation.

## INTRODUCTION

Severe acute respiratory syndrome by Coronavirus 2 (SARS-CoV-2), which belongs to the Coronaviridae family, is responsible for the current Coronavirus 2019 (COVID-19) outbreak and has been devastating worldwide<sup>1,2</sup>. This infection constitutes a flu-like illness similar to severe acute respiratory syndrome by coronavirus (SARS-CoV) and Middle East respiratory syndrome by coronavirus (MERS-CoV), which occurred in 2002 and 2012, respectively. It has a broad spectrum of signs and symptoms so that most infections (80%) are mild, and 6–10% will require transfer to the intensive care unit (ICU)<sup>3-5</sup>.

Critically ill patients who are transferred to the ICU usually develop ventilatory failure and the need for noninvasive or invasive ventilatory support, in addition to multiorgan dysfunctions, secondary to a combination of exacerbated inflammatory and thrombogenic activity<sup>1</sup>. The mortality of critically ill patients due to COVID-19 is high, with reports ranging

between 50 and 90%<sup>6</sup>. An observational study found that mortality in Brazil varied by region (higher in the north and northeast) and changed with aspects related to the need for invasive ventilatory support or age<sup>7</sup>.

This study aims to describe the epidemiological profile, clinical behavior, and outcomes of critically ill patients seen by a care team formed by intensive and nonintensive physicians, comparing them with similar data recently published.

## METHODS

### Design and patients

This observational study included adult patients with COVID-19 admitted to the ICU of Hospital Independência. Inclusion criteria were 18 years of age or older. There were no exclusion criteria. The Research Ethics Committee approved the study at our institution.

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## Institutional protocol for the treatment of critically ill patients with COVID-19

Patients admitted to the ICU undergo the institutional protocol for the treatment of critically ill patients with COVID-19, which is summarized as follows:

- a) Noninvasive ventilatory support if feasible (noninvasive ventilation, high-flow oxygen cannula); self-prone position.
- b) Invasive ventilatory support in the event of failure or when (a) is not feasible. Preferentially adjusted volume-controlled regimen within current ventilation assumptions for patients with acute respiratory distress syndrome – protective ventilation strategy; prone ventilation in refractory hypoxemia.
- c) Hemodynamic support according to the institution's usual protocol: a fluid challenge in patients with dysoxia and volume responders (pulse pressure variation – delta PP, ultrasound indicators); use of vasopressors (noradrenaline and/or vasopressin).
- d) Use of antimicrobial drugs only if the bacterial infection diagnosis is confirmed or if there is a strong possibility of associated bacterial contamination.
- e) Preferentially enteral and early nutritional support (started within the first 24–48 h after hemodynamic stability, caloric and protein target adjusted for the first 3 and 7 days).
- f) Nonuse of “labeled” drugs as early therapy for COVID (e.g., chloroquine, ivermectin, azithromycin, and zinc).
- g) Use of dexamethasone 6 mg daily for 10 days.
- h) Anticoagulation in cases of vascular thrombosis.
- i) Daily rounds with an intensive care specialist.

## Data and collection tools

Data collection took place over 13 months (August 2020 to August 2021). Data were obtained by consulting medical records. The information collected was recorded in an electronic spreadsheet: age, gender, morbidities (e.g., hypertension, diabetes, heart disease, lung disease, and cancer), duration of mechanical ventilation (MV), length of stay in the ICU and hospital, body mass index (BMI), SAPs-3 score, and outcome (hospital discharge or death). Morbidities were assumed to be present based on data from medical records with a demonstration or confirmatory tests that allowed the diagnosis to be confirmed.

## Statistical analysis

Sample for convenience. Descriptive analysis used frequencies and percentages, means and standard deviations (SDs), or

medians and interquartile ranges (IQRs). Comparisons were performed using  $\chi^2$  or Fisher's exact tests for qualitative variables and using t-tests or nonparametric Wilcoxon tests for quantitative variables. Binary logistic regression models were used to compare in-hospital courses and clinical outcomes between the groups. The number of independent variables followed the rule of including one variable for every 10 results. A p-value <0.05 was considered statistically significant. Data were analyzed using the statistical software package Microsoft Excel version 16.5, StatPlus version v7, and IMB SPSS-23.0.

## RESULTS

Data were collected between August 2020 and August 2021 and totaled 449 patients. The admissions came from 64.1% by referral from the ward, 21.6% by referral from emergencies or emergency care units in the state of Rio Grande do Sul (UPA), and 14.2% by referral from another hospital (continuity of attendance). When previously admitted to the ward and later transferred to the ICU, the average transfer time was 1 [0–2] day. Table 1 summarizes the epidemiological profile of the sample, stratified for mortality.

The standardized mortality ratio (SMR), using the prediction of mortality from the score of the SAPS-3 score, was 1.25 (if we consider the hospital mortality of the patient admitted to the ICU, we have an SMR of 1.3). The time (in days) elapsed between the onset of symptoms and hospitalization and the time to perform tracheotomy between our patients and patients transferred from another institution for continuity of care in our ICU did not show a significant difference (9 [7–12] vs. 9.5 [6.75–12];  $p=0.705$  and 22 [18–27] vs. 23 [19–27];  $p=0.923$ , respectively). As for invasive ventilatory support, we observed that when we stratified patients by age (over and under 60 years), mortality was found to be 81.1 and 51.4%. Mortality was even higher in older ventilated patients. Individuals who were invasively ventilated and aged 75 years and 80 years or older had mortality rates of 97.5 and 100%, respectively. Table 2 compares the observed mortality of different age groups in this study with reports from other studies.

We found no association between different BMI strata (less than 20 kg/m<sup>2</sup>, between 20 and 30 kg/m<sup>2</sup>, between 30 and 40 kg/m<sup>2</sup>, and greater than 40 kg/m<sup>2</sup>;  $p=0.458$ ) and outcomes. Patients with a BMI of <20 kg/m<sup>2</sup> represented 1.8% of the population, between 20 and 30 kg/m<sup>2</sup> enrolled 48.3%, and greater than 30 kg/m<sup>2</sup> comprised 49.9% of patients. All patients received oral/enteral nutritional support following the institutional protocol (we did not observe cases of parenteral nutrition).

**Table 1.** Epidemiological profile of critically ill patients with COVID-19.

	All 449	Outcomes		p-value
		Survival 231 (51.45%)	Nonsurvival 218 (48.55%)	
Age (years)	60 [50–70]	56 [45–73]	65 [56–73]	<0.001
Male (%)	52.11	51.71	48.29	0.907
Time between OS and H (days)	9 [7–12]	10 [8–11]	9 [7–11]	0.001
Time between H and ICU (days)	1 [0–2]	1 [0–2]	1 [0–2]	0.531
Previous morbidities				
Diabetes mellitus (%)	28.5	46.9	53.1	0.220
Arterial hypertension (%)	52.6	44.1	55.9	0.001
Ischemic heart disease (%)	8.2	37.8	62.9	0.083
Cardiac insufficiency (%)	3.6	37.5	62.5	0.255
Chronic kidney failure (%)	4.5	50	50	0.894
Cancer (%)	4.0	27.8	72.2	0.042
AIDS (%)	2.2	60	40	0.584
COPD (%)	7.6	17.6	82.4	<0.001
Asthma (%)	5.8	53.8	46.2	0.800
Absence of known morbidities (%)	28.7	59.6	40.4	0.001
SAPS-3	53 [47–61]	50 [47–66]	58 [52–66]	<0.001
BMI (kg/m <sup>2</sup> )	29.8 [26.1–34.2]	30.3 [26.3–33.4]	29.3 [25.6–33.4]	0.114
CRP initial (mg/dL)	19 [7.2–26.5]	17.8 [6.15–28.4]	20.8 [9.5–28.4]	0.004
CRP final (mg/dL)	7.2 [3.9–21.3]	4.5 [2.3–27.67]	15 [6.2–27.6]	<0.001
CRP variation (%)	-45.9 [-78.4–9.5]	-72.1 [-86.6–32.6]	-20.6 [-66–32.6]	<0.001
Mechanical ventilation (%)	68.5	32.9	67.1	<0.001
Time to MV (days)	13 [8–20]	13 [9–18]	13 [7–18]	0.152
Tracheotomy (total %)	15.4	50.3	49.7	0.896
Tracheotomy at IND (%)	8.4	48.6	51.4	0.744
Time to tracheotomy (days)	22 [18–28.5]	21 [18–27]	22.5 [18.2–27]	0.505
Acute kidney failure (%)	41.4	22	78	<0.001
Hemodialysis (%)	22.3	16	84	<0.001
CCI (%)	34	46.8	56.2	0.002
Vaccinated (2 doses %)*	8.8	39.3	60.7	0.190
Palliative care (%)	13.4	10	90	<0.001
ICU LOS (days)	11 [6–18]	9 [6–19]	14 [8–19]	<0.001
Hospital LOS (days)	17 [11–24]	18 [12–22]	16 [10–22]	<0.001

OS: onset of symptoms; H: hospitalization; ICU: intensive care unit; AIDS: acquired immunodeficiency syndrome; COPD: chronic obstructive pulmonary disease; SAPS-3: Simplified Acute Physiology Score 3; BMI: body mass index; CRP: C-reactive protein (Initial and final PCR over the first week); MV: mechanical ventilation; IND: Hospital Independência; CCI: chronic critical illness; LOS: length of stay. \*Related to hospitalization after vaccination campaign (28 vaccinated out 319 admissions).

A multivariate model was constructed using the univariate analyses most significantly associated with mortality (Table 3).

Regarding admissions of previously vaccinated patients, we have 6.2% (28 patients) fully vaccinated, if we consider the entire collection period. If we consider the admissions that

took place after the start of vaccination, the percentage rises to 8.8%. The partially vaccinated group totaled 16 patients, corresponding to 3.5 and 5%, respectively, of the total number of patients admitted during the entire collection period or only after the start of vaccination. Of those fully vaccinated,

**Table 2.** Comparative mortality data with other studies.

	Ranzani (Ref 7)		Al Mutair (Ref 12)	IND
	Brazil	South (Brazil)		
MV	47.8	54.3	29.0	33.7
Deaths in the ICU	59.0	55.5	41.8	46.4
Deaths in MV	79.7	72.2	65.3	67.3
Deaths in MV <60 years	67.8	54.6		51.4
Deaths in MV ≥60 years	87.3	82.1		81.1
Age <60 years	41.6	35.8		34.8
Age ≥60 years	71.7	68.6		61.1

Data are reported in percentages. IND: Hospital Independência; MV: mechanical ventilation; ICU: intensive care unit.

**Table 3.** Multivariate analysis of parameters associated with mortality.

	RR (95%CI)	p-value
Age	1.013 (0.967–1.061)	0.578
SAPS-3	1.099 (1.017–1.188)	0.016
Time between OS and H	0.887 (0.794–0.991)	0.034
Mechanical ventilation	36.489 (2.645–503.385)	0.007
CRP initial	0.997 (0.992–1.001)	0.219
CRP final	1.010 (1.004–1.016)	<0.001
CRP variation percentage	0.934 (0.809–1.080)	0.361
Arterial hypertension	0.380 (0.085–1.701)	0.206
COPD	7.792 (0.582–104.262)	0.120
Absence of known morbidities	0.331 (0.074–1.469)	0.146
Acute kidney failure	7.516 (2.969–19.024)	<0.001
Critical chronic illness	0.634 (0.245–1.642)	0.348

RR: relative risk; CI: confidence interval; SAPS-3: Simplified Acute Physiology Score 3; OS: onset of symptoms; H: hospitalization; CRP: C-reactive protein (in the beginning and at the end of first week); COPD: chronic obstructive pulmonary disease.

89.3% received CoronaVac, 7.1% AstraZeneca, and 3.5% Pfizer. The age of patients who received CoronaVac was higher but not statistically significant compared to those vaccinated with AstraZeneca (73 [66–77] years vs. 68 [62.5–77] years;  $p=0.713$  – only one patient vaccinated with Pfizer, 56 years old). Mortality in this group was 60.7%, all CoronaVac (non-significant difference,  $p=0.055$ ). Analyzing the partially vaccinated in the same way, we observed that 37.5% received one dose of CoronaVac, and 62.5% received one AstraZeneca dose. Their ages also did not vary significantly (CoronaVac 58.5 [43–62.5] years; AstraZeneca 55 [48.75–62.5];  $p=0.872$ ). Mortality in this group was 31.2%, 20% of whom received

the CoronaVac vaccine, and 80% AstraZeneca (nonsignificant difference,  $p=0.329$ ).

Our team defined a palliative treatment strategy for 13.4% of patients. Mortality in the ICU was 80% and in-hospital was 90%.

## DISCUSSION

Due to the pandemic caused by SARS-CoV-2 and unlike other hospitals in the city, we set up an inexperienced medical group of nonspecialists in intensive care medicine. To this end, we review our protocols and guide decisions within the recommendations of “choosing wisely”<sup>8-10</sup>, in addition to highlighting medical leadership specialized in intensive care medicine and aligned with these recommendations.

Our retrospective cohort showed that 71.3% of patients admitted by COVID-19 to our ICU had some prior morbidity and that this was significantly associated with mortality (58.9%;  $p=0.001$ ). The morbidities that were significantly associated with death were arterial hypertension and chronic obstructive pulmonary disease. Obesity (BMI ≥30 kg/m<sup>2</sup>) was prevalent, representing 59.9% of the enrolled population.

According to our study, mortality in the ICU was 46.4% and in-hospital was 48.5%. The SMR demonstrated an excess of mortality in the order of 30%. However, SAPS-3 seems to underestimate the mortality of critically ill patients with COVID-19, with the need to calibrate the tool to parameterize outcomes in this context<sup>11</sup>. The SAPS-3 score probably should receive a calibration for COVID-19.

In the univariate analyses, the time elapsed between the onset of symptoms caused by SARS-CoV-2 infection, older age, SAPS-3 mortality score, highest C-reactive protein (CRP) (in the beginning and at the end of first week), renal failure, high blood pressure, cancer, and chronic obstructive pulmonary disease were significantly associated with mortality. Except for the behavior of CRP and the occurrence of renal failure, our data agree with the study by Al Mutair et al<sup>12</sup>. They carried out a similar analysis in Asia. Also, in agreement with this study, we could not demonstrate that BMI strata are associated with mortality (which surprised us). Regarding CRP, we understand that this biomarker that measures inflammation was much more related to the secondary infectious complications in the course of patients than viral pneumonia per se, because, as suggested by the increased time lag between symptom onset and hospital admission (Table 1), the possibility of previous asymptomatic hypoxia<sup>13</sup> cannot be disregarded, so that the CRP measurement in the first week of ICU stay is probably no longer related to the viral infection at this time. Thus, the variation in CRP in the

first 7–10 days says much more about the control of the secondary bacterial infection than the control of the virus disease itself. The disagreement regarding the impact of renal failure and the need for renal replacement therapy between our study and the Asian cohort must be due to different epidemiological contexts. Other studies have linked renal dysfunction to worse outcomes in critically ill patients<sup>14,15</sup>.

The association between older age and the need for invasive MV seemed essential to determine death, especially in individuals aged over 60 years. These data do not differ from the Brazilian case series that included more than 250,000 patients<sup>7</sup>, demonstrating the devastating consequences of severe coronavirus pneumonia in the elderly.

In the multivariate analysis, the time elapsed between symptom onset and hospital admission, MV, CRP value at the end of the first week in the ICU, and renal failure were independently associated with mortality, notably the need for invasive ventilatory and renal support. These data can support us in the elaboration of an earlier prognosis for critically ill patients with COVID-19. Chronic critical illness (CCI), according to our expectations, had a high incidence in our ICU. We defined CCI according to consensus published over the past decade<sup>16-18</sup>, mainly based on prolonged dependence on MV (longer than 14 days), associated with evident muscle weakness acquired in the ICU. As expected, it constituted a fragile population, manifesting the usual range of signs/symptoms that characterize the syndrome.

Our study failed to identify the clear superiority of one vaccine over another among those hospitalized after vaccination. It is important to emphasize that the number of vaccination constituted a small portion of our total population, making us analyze the data with extreme caution.

The choice for palliative treatment resulted from the assessment of the multidisciplinary care group when there was agreement that therapeutic tenacity generated futility from a certain point onward and would increase dyspnea and the suffering of the patient and their families. In this context, two worlds were always associated, CCI and the need for palliative

treatment. At this moment, the decision-making process was done in the best interest of the patients. Advance directives were respected, although it is an uncommon condition in our reality<sup>19</sup>.

Our study has limitations. It is an observational study, and as such, we cannot determine causality. Our study was carried out in a single center so that generalizations should not be made without caution and contextualization. We did not analyze aspects potentially related to organizing pneumonia because we do not have images of all patients with this suspicion. In addition, the patients did not undergo a formal organizing pneumonia protocol.

## CONCLUSIONS

Patients admitted for acute respiratory syndrome due to SARS-CoV-2 are severe and have a high mortality rate, mainly if submitted to invasive MV. The emergence of acute renal failure marks an especially severe subgroup with increased mortality. Our results are similar to the best results published to date and demonstrate that the consolidation of processes and application of protocols linked to the “choosing-wisely” concept seemed to significantly benefit our ICU since a large contingent of non-specialist physicians.

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## AUTHORS' CONTRIBUTIONS

**SHL:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **DCL:** Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **GC:** Formal analysis, Writing – original draft, Writing – review & editing.

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