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Comparative analysis of demographic, clinical, biochemical, and predictors of mortality in COVID-19 and NON-COVID-19 ARDS patients

A retrospective cohort study

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Abstract

The COVID-19 pandemic has brought a significant increase in the incidence of acute respiratory distress syndrome (ARDS). This retrospective study aims to compare the differences in demographic, clinical, and biochemical variables and predictive factors in 2 situations of ARDS cause (COVID-19 vs NON-COVID-19) in patients admitted to the intensive care unit. The Mann–Whitney rank-sum test was performed for quantitative variables, and Fisher exact test for qualitative variables. 115 patients with ARDS were enrolled (53 patients with COVID-19 ARDS and 62 NON-COVID-19 ARDS). The COVID-19 ARDS group consisted of 33 male patients (66.2%), whereas the NON-COVID-19 ARDS group had 25 male patients (40.3%) ($P = .0248$). The median and interquartile age difference of the COVID-19 ARDS group was 64.0 [52.0–69.5], and non-COVID-19 ARDS was 49.0 [34.0–63.0] ($P = .0011$). Body mass index, simplified acute physiology score, sequential organ failure assessment, and intensive care unit length of stay, with *P*-values of .0061, .0002, .0003, and <.0001, respectively (COVID-19 vs NON-COVID-19 ARDS). Diabetes, arterial hypertension, venous thrombosis, and chronic obstructive pulmonary disease had values of <.0001, .0234, .0358, and .0001, respectively. On the other hand, the NON-COVID-19 ARDS group had a greater need for dialysis ($P = .0109$). The stepwise logistic regression showed that relevant clinical, and demographic characteristics associated with ARDS due to COVID-19, such as male gender, diabetes, chronic obstructive pulmonary disease, and body mass index, were independent prognostic factors of severity in patients with COVID-19 ARDS, compared to NON-COVID-19 ARDS. The overall mortality rate was 62.9% for COVID-19 ARDS and 77.4% for the non-COVID-19 ARDS group ($P = .2950$). Ventilatory parameters of COVID-19 ARDS and NON-COVID-19 ARDS were similar.

Abbreviations: ACE 2 = angiotensin-converting enzyme, ARDS = acute respiratory distress syndrome, BMI = body mass index, COPD = chronic obstructive pulmonary disease, ICUs = intensive care units, LOS = length of stay, SAPS 3 = simplified acute physiology score, SOFA = sequential organ failure assessment, OR = odds ratio.

Keywords: acute respiratory distress syndrome, COVID-19, ICU setting, outcome, predictors

1. Introduction

Acute respiratory distress syndrome (ARDS) was first described by Ashbaugh et al[1] in 1967. ARDS emerges mainly from situations such as sepsis, trauma, and massive blood transfusions, among other causes. These authors pointed out several pulmonary disorders such as alveolar-capillary membrane injury, and increased capillary permeability leading to a pronounced edema and hypoxemia, with bilateral micro and macronodular images not symmetrical to chest radiography, creating a condition of noncardiogenic pulmonary edema. Despite the apparent improvement of medical care and mechanical ventilation techniques seen in the past 5 decades, ADRS is still a primary concern of health authorities because of its mortality of 40%.[2]

The COVID-19 pandemic has been responsible for an even greater increase in ADRS cases, causing a never-before-seen demand situation in intensive care units (ICUs), posing an unprecedented challenge in the history of global health systems. The pathogen responsible for causing severe pneumonia and refractory hypoxia was identified in late December 2020 in China, as coronavirus 2 (SARS-CoV-2). However, some authors

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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assumed that the ARDS presented by patients with COVID-19 was considered atypical and, therefore, different from those of ARDS caused by other causes.[3–6]

This retrospective study aims to compare demographic, clinical, biochemical, and predictors of mortality in patients with ARDS (COVID-19 vs NON-COVID-19) of patients admitted to the ICU.

2. Methods

2.1. Study design and setting

This retrospective study was carried out in the ICU of Clinics Hospital of Ribeirão Preto Medical School, University of São Paulo, Brazil. This tertiary ICU admits critically ill adults, such as clinical cases, surgical or COVID-19 patients. The study protocol was approved by the Research Ethics Committee of the Clinics Hospital of Ribeirão Preto Medical School, University of São Paulo (CAAE: 3711922.3.0000.5440).

2.2. Patients and collected variables

All patients admitted to the adult ICU diagnosed with ARDS from February 2015 to June 2021 were evaluated. ARDS patients were divided into 2 groups: COVID-19 ARDS and NON-COVID-19 ARDS. Subsequently, a search of the medical records was carried out using the hospital registry, and, data were collected regarding demographics (age, sex, height, weight, and body mass index [BMI]), length of hospital and ICU stay, clinical outcome (discharge or death), laboratory tests (arterial blood gases, serum lactate, leukogram, and C-reactive protein), aggravating factors (obesity, diabetes mellitus, chronic obstructive pulmonary disease [COPD], use of vasopressors, hemodialysis, blood transfusion), and ventilatory parameters (FiO_2 = fraction of oxygen in inspired air, PAO_2 = alveolar oxygen pressure, $D(A\text{-}a)O_2$ = alveolar-arterial oxygen difference. Data were also collected for the calculation of prognostic indices and physiological variables during the first 24 hours after the patient´s admission. Therefore, diagnostic data on arrival at ICU, comorbidities, and clinical characteristics have been documented. Clinical and physiological variables, as well as the simplified acute physiology score (SAPS 3),[7] sequential [sepsis-related] and organ failure assessment (SOFA)[8] were recorded.

2.3. Statistical analysis

Comparisons of demographic and clinical data of the ARDS patients (COVID-19 and NON-COVID-19) were carried out using the test for two independent samples (rank-sum) of Mann–Whitney for quantitative variables and Fisher exact test for qualitative variables. All variables were presented as median and interquartile range or as the number (percentage) in tables.

The collected data were submitted to two logistic regression models. One to assess clinical-demographic characteristics present at ICU admission and potentially associated with ARDS due to COVID-19, compared to other patients with ARDS. The other was to assess the impact of COVID-19 on ICU mortality due to ARDS, modulating it to other potential risk factors or predictors. The logistic regression model used was treated with the stepwise strategy. Thus, the crude odds ratio (OR) was calculated, and then the variables without statistically significant association were removed, leaving only the adjusted OR, with its respective 95% confidence intervals and *P*-values. Finally, to estimate and interpret ICU survival and hospital survival time, Kaplan–Meier curves were performed for the 2 groups of ARDS patients (COVID-19 and NON-COVID-19). To compare these 2 survival curves, a nonparametric log-rank classification test was used. The significance level was set at $P < .05$. All these statistical analyses were performed using the MedCalc v.14 software (Ostend, Belgium) and the STATA SE v. 14 software (STATA Corp, College Station, TX). The sample size was performed by convenience sampling.

3. Results

One hundred and fifteen patients were retrospectively studied. Of these patients, 53 were in the COVID-19 ARDS group, and 62 were in the NON-COVID-19 ARDS group. They consisted of 33 male patients (66.2%)/20 females and 25 males (40.3%)/37 females, respectively ($P = .248$). The median and interquartile age difference (in years) of the COVID-19 ARDS group was 64.0 [52.0–69.5], and non-COVID-19 ARDS was 49.0 [34.0–63.0] ($P = .0011$). The BMI for the COVID-19 ARDS group was 30.4 [26.3–25.1], and for the NON-COVID-19 ARDS group was 26.3 [22.8–31.2] ($P = .0061$). The SOFA was 9 [6.0–13.0] and 12.0 [9.0–14] ($P = .0002$), while the SAPS 3 was 67.5 [56.0–74.0] and 81.0 [62.2–95.0] ($P = .0003$), for the COVID-19 ARDS and NON-COVID-19 ARDS groups, respectively.

The length of stay (LOS) in the ICU was 16.0 [11.0–30.2] for COVID-19 ARDS and NON-COVID-19 ARDS was 8.0 [4.0–14.0] ($P < .0001$), while the hospital LOS was 29.0 [14.7–40.2] for COVID-19 ARDS and NON-COVID-19 ARDS was 22.5 [10.0–40.0] ($P = .2232$). The overall mortality rate was 62.9% and 77.4% ($P = .2950$) for the COVID-19 ARDS and NON-COVID-19 ARDS groups, respectively. It should be noted that, except the length of hospital stay and the overall mortality rate, the comparisons between the other variables were all significant. However, the duration (in days) of mechanical ventilation was not different for the comparison between the groups.

However, when comparing surviving (S) and non-surviving (NS) patients of the COVID-19 ARDS (SxNS) and NON-COVID-19 ARDS (SxNS) subgroups, statistical differences in the length of hospital stay ($P = 0060$) are observed for the COVID-19 ARDS (SxNS) subgroup. On the other hand, the NON-COVID-19 ARDS (SxNS) subgroups presented numerous variables with statistically significant differences, such as age ($P = .0197$), SOFA ($P = .0014$), SAPS 3 ($P < .0001$), ICU ($P = .0063$), and hospital ($P = .0308$) LOS. Demographic and clinical characteristics are listed in Table 1. The main clinical conditions that led to hospitalization in the ICU of patients with NON-COVID ARDS were predominantly lung infections, present in 58.1% of patients. The remaining diagnoses for both groups, corresponding to the criteria for case-mix admission in the ICU, included major clinical or surgical system disorders such as gastrointestinal (14.5%), bloodstream (12.9%), urologic (8.1%), dermatologic (4.8), and others (1.6%).

Concerning the biochemical and respiratory parameters of total patients (n = 115) and survivors (S) and non-survivors (NS) with ARDS caused by COVID-19 and NON-COVID-19 admitted to the ICU, the only statistical difference observed was the pH between patients with NON-COVID ARDS (SxNS) ($P = .0242$), but without evident clinical expression (Table 2).

Table 3 shows a statistical difference for diabetes, COPD, systemic arterial hypertension, and deep vein thrombosis were predominant in patients with ARDS COVID-19, $P < .0001$, $P = .0001$, $P = .0234$, and $P = .0358$, respectively. In contrast, patients with non-COVID-19 ARDS were more dialyzed than patients with ARDS-COVID ($P = .0109$). The comparison of comorbidities between the subgroups of surviving (S) and non-surviving COVID-19 ARDS (NS) patients was not statistically different. In the NON-COVID-19 ARDS subgroup, non-surviving patients had a higher dialysis indication than surviving patients ($P = .0160$).

In comparing of the 2 survival curves, the log-rank test was performed to determine the occurrence of differences in the survival distribution for the 2 groups of patients. The distribution of survival time for these patients, considering the LOS in

the ICU for the 2 groups of patients, was statistically different ($P = .0011$) (Fig. 1). On the contrary, the hospital survival time for the 2 groups did not differ ($P = .2280$) (Fig. 2).

The crude logistic regression model that sought to assess the impact of COVID-19, and the various clinical and demographic characteristics on the risk of death in the ICU, presented *P* values without discrimination of statistical significance. In addition, the OR of the variables with age and SAPS 3, which were borderline, were selected for the logistic regression model using the stepwise method, thus showing a statistically significant OR (Table 4).

The same logistic regression procedure was used to assess the clinical and demographic characteristics of ARDS due to COVID-19, compared to other patients with ARDS. Table 5 shows the various variables, with male gender, diabetes, COPD, and BMI standing out in significance. These variables were isolated to the logistic regression model using the stepwise method, which presented a statistically significant OR.

4. Discussion

The COVID-19 pandemic was responsible for a considerable increase in the flow of hospitalizations for severe acute respiratory failure in ICUs. Due to the peculiar nature of some clinical characteristics, some authors initially assumed that the pulmonary involvement of ARDS in COVID-19 might be different from that described in other clinical cases. The issue that COVID-19 presented with ARDS with atypical pathophysiology generated the idea of the need for a different approach, which is very controversial and, perhaps, currently discontinued.[3,6,9]

Table 1

Demographic and clinical characteristics of patients with respiratory distress syndrome caused by COVID-19 and Non-COVID-19 admitted to the ICU.

Patients (n = 115)	COVID-19 ARDS (n = 53)	NON-COVID-19 ARDS (n = 62)	P*	COVID-19 ARDS S (n = 17)	COVID-19 ARDS NS (n = 36)	P†	NON-COVID-19 ARDS S (n = 23)	NON-COVID-19 ARDS NS (n = 39)	P†
Gender M (%)/F	33 (66.2)/20	25 (40.3)/37	0.0248	12 (70.5)/5	21 (58.3)/15	0.5457	8 (34.8)	17 (43.6)	0.5958
Age (year)	64.0 [52.0–69.5]	49.0 [34.0–63.0]	0.0011	59.0 [42.6–69.0]	65.5 [56.0–71.0]	0.1850	37.0 [27.0–56.5]	51.0 [40.2–70.0]	0.0197
BMC (kg/m^2)	30.4 [26.3–25.1]	26.3 [22.8–31.2]	0.0061	31.1 [27.3–37.0]	28.9 [26.3–34.9]	0.5260	26.3 [24.0–31.2]	26.0 [21.5–31.3]	0.5484
SOFA escore	9.0 [6.0–11]	12.0 [9.0–14.0]	0.0002	10.0 [8.0–12.0]	9.0 [5.0–11.0]	0.1270	9.0 [6.0–11.7]	12.0 [11.0–15.0]	0.0014
SAPS 3 escore	67.5 [56.0–74.0]	81.0 [62.2–95.0]	0.0003	71.0 [56.2–73.5]	67.0 [56.0–74.5]	0.2364	61.5 [47.0–80.0]	91.0 [73.7–96.2]	<0.0001
ICU LOS (days)	16 [11.0–30.2]	8.0 [4.0–14.0]	<0.0001	25.0 [11.7–32.0]	14.5 [10.5–29.0]	0.2222	13.0 [5.0–19.7]	6.0 [3.2–2.5]	0.0063
Hospital LOS(days)	29.0 [14.7–40.2]	22.5 [10.0–40.0]	0.2232	34.0 [26.2–70.7]	20.5 [13.0–34.0]	0.0060	28.0 [18.7–49.0]	19.0 [9.2–33.5]	0.0308
MV (days)†	15.0 [9.0–29.2]	10.0 [3.0–28.0]	0.1612	19.0 [11.7–29.2]	14.0 [7.0–27.5]	0.2566	15.0 [2.25–30.0]	10 [4.25–25.0]	0.9360
ICU mortality n (%)	36 (67.9)	39 (62.9)	0.6948	–	–	–	–	–	–
Hospital mortality n (%)	36 (67.9)	48 (77.4)	0.2950	–	–	–	–	–	–

Values expressed as % (sex, mortality) and median [interquartile range].

ARDS = acute respiratory distress syndrome, ICUs = intensive care units, LOS = length of stay, SAPS 3 = simplified acute physiology score, SOFA = sequential organ failure assessment.

*P = Comparison between total COVID-19 and NON-COVID-19 ARDS cases.

†P = Comparison between survivors (S) and non-survivors (NS) of COVID-19 and NON-COVID-19 ARDS cases.

Table 2

Biochemical and respiratory parameters of total patients and, survivors (S) and non-survivors (NS) with ARDS COVID-19 and NON-COVID-19 admitted to the ICU.

Parameter	ARDS COVID (n = 53)	ARDS NON-COVID (n = 62)	P*	ARDS COVID S (n = 17)	ARDS COVID NS (n = 36)	P†	ARDS NON-COVID S (n = 23)	ARDS NON-COVID NS (n = 39)	P†
pH	7.32 [7.26–7.39]	7.34 [7.25–7.40]	0.8883	7.23 [7.22–7.39]	7.28 [7.26–7.40]	0.7894	7.39 [7.30–7.41]	7.32 [7.21–7.38]	0.0242
PaO_2 (mm Hg)	78.7 [67.0–87.4]	84.7 [71.6–105.3]	0.0781	79.4 [67.0–87.7]	78.5 [67.4–87.5]	0.9848	87.9 [69.7–131.2]	84.3 [71.6–98.9]	0.4934
$PaCO_2$ (mm Hg)	41.5 [36.5–53.6]	42.6 [34.7–46.4]	0.4504	41.5 [36.9–50.5]	42.0 [36.5–55.0]	0.8339	36.3 [33.3–45.6]	44.2 [37.1–46.6]	0.1352
HCO_3	22.5 [19.0–25.3]	21.8 [17.9–25.6]	0.2135	21.3 [19.4–23.2]	24.1 [18.6–26.7]	0.2732	22.3 [18.2–26.9]	21.4 [17.9–24.4]	0.3472
Lactate (mmol/L)	2.25 [1.64–2.71]	2.20 [1.65–3.86]	0.5285	2.1 [1.9–2.5]	2.3 [1.6–2.7]	0.9052	2.2 [1.7–2.9]	2.2 [1.6–5.5]	0.8342
CPR (mg/L)	12.8 [5.9–25.6]	17.3 [7.7–27.9]	0.3229	20.4 [4.9–26.7]	12.7 [7.0–24.8]	0.6073	10.9 [4.1–24.7]	21.8 [13.5–28.2]	0.0642
FiO_2	0.55 [0.40–0.80]	0.50 [0.40–0.70]	0.3441	0.55 [0.40–0.72]	0.52 [0.40–0.90]	0.6377	0.45 [0.40–0.60]	0.55 [0.40–0.81]	0.2907
PaO_2/FiO_2	144 [96–192]	179 [105–233]	0.1250	142 [101–191]	159 [89–192]	0.9294	201 [104–299]	165 [105–215]	0.1618
PAO_2 (mm Hg)	291 [225–478]	272 [214–431]	0.3810	328 [213–442]	287 [226–507]	0.5952	254 [206–346]	302 [215–482]	0.4144
$D(A\text{-}a)O_2$ (mm Hg)	210 [144–386]	180 [120–308]	0.2783	250 [147–362]	201 [143–427]	0.9647	135.9 [116–280]	186 [126–377]	0.2818

Values expressed as median [interquartile range].

ARDS = acute respiratory distress syndrome, CRP = C-reactive protein, $D(A\text{-}a)O_2$ = alveolar-arterial difference of oxygen, FiO_2 = fraction of oxygen in inspired air, HCO_3 = bicarbonate in arterial blood, $PaCO_2$ = partial pressure of carbon dioxide in arterial blood, PaO_2 = partial pressure of oxygen in arterial blood, PAO_2 = alveolar pressure of oxygen.

*P = Comparison between total COVID and NON-COVID ARDS cases.

†P = Comparison between survivors (S) and non-survivors (NS) of COVID and NON-COVID ARDS cases.

Table 3

Comorbidities and interventions of total patients and, survivors (S) and non-survivors (NS) with ARDS COVID-19 and NON-COVID-19 admitted to the ICU.

Comorbidity/ Intervention	ARDS COVID-19 (n = 53)	ARDS NON- COVID-19 (n = 62)	P*	ARDS COVID-19 S (n = 17)	ARDS COVID-19 NS (n = 36)	P†	ARDS NON-COVID-19 S (n = 23)	ARDS NON-COVID-19 NS (n = 39)	P†
Diabetes	30 (56.6)	10 (16.1)	<0.0001	9 (52.9)	21 (58.3)	0.7720	3 (13.0)	7 (17.9)	0.7312
Arterial hypertension	36 (56.6)	21 (33.3)	0.0234	10 (58.8)	20 (55.5)	0.9999	4 (17.4)	17 (43.5)	0.0517
Venous thrombosis	12 (22.6)	5 (8.0)	0.0358	5 (29.4)	7 (19.4)	0.4900	2 (8.7)	3 (7.7)	0.9999
COPD	23 (43.4)	7 (11.3)	0.0001	7 (41.1)	16 (44.4)	0.9999	2 (8.7)	5 (12.8)	0.9999
Vasopressors	32 (60.3)	47 (75.8)	0.1061	10 (58.8)	22 (61.1)	0.9999	14 (60.8)	33 (84.6)	0.0631
Dialysis	8 (15.0)	23 (37.0)	0.0109	2 (11.7)	6 (16.6)	0.9999	4 (17.4)	19 (48.7)	0.0160
Blood transfusions	10 (18.8)	13 (20.9)	0.8189	2 (11.7)	8 (22.2)	0.4711	2 (8.7)	11 (28.2)	0.1662

Values expressed in n%.

ARDS = acute respiratory distress syndrome, COPD = chronic obstructive pulmonary disease.

*P = *P*-value for comparison between total COVID-ARDS and NON-COVID cases.

†P = *P*-value for comparison between survivors (S) and non-survivors (NS) of COVID-19 and NON-COVID-19 ARDS cases.

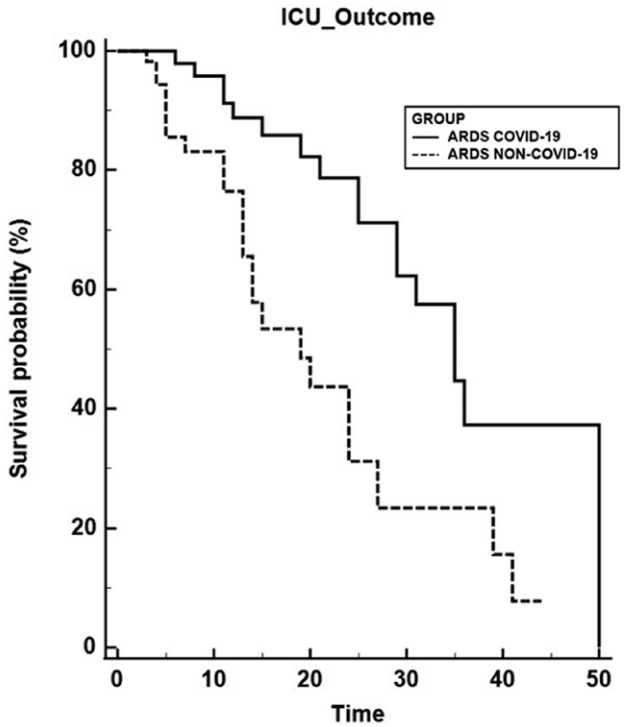

Figure 1. Survival curves for ICU length of stay (LOS) of patients with ARDS COVID-19 and NON-COVID-19.

Meyer et al[10] demonstrate similar mortality for both sexes of patients with NON-COVID-19 ARDS, also showing a tendency for males to develop ARDS more easily and worse outcome in groups of women with severe ARDS due to longer duration of disease associated with the opposite sex. Subsequently, Pollard et al[11] demonstrate data from the US, where females had a lower prevalence of ARDS cases due to COVID-19. Klein and Flanagan[12] justified these findings by associating the susceptibility of viral infections (such as COVID-19) to the male sex through regulatory responses of genes and polymorphisms observed on the Y chromosome.

Age and BMI were higher in the COVID-19 ARDS group when compared to the NON-COVID-19 ARDS group. Buffon et al,[13] in a study analyzing 150 medical records of individuals with COVID-19, verified a mean age of 59 years (SD ± 14.2) and BMI of 31 (SD ± 6.8), data similar to those found in the present study. Wu et al,[14] when analyzing 201 individuals with ARDS due to COVID-19, suggest that susceptibility of the elderly to evolve with worse clinical outcomes is due to the immunological decline resulting from aging.

Demeulemeester et al[15] discussed the predisposition of obese patients to develop ARDS in COVID-19 due to the chronic inflammatory process observed in these individuals and the angiotensin-converting enzyme (ACE 2) produced by adipocytes, facilitating viral storage in these cells. The data for SOFA and SAPS 3 are conflicting in the literature, justified by the complexity of NON-COVID-19 patients previously admitted to the ICU. Zheng et al[16] showed the good performance of the SOFA for organ dysfunction and mortality in individuals with ARDS due to COVID-19 since the disease progresses with multiple organ failure. A multicenter analysis by Lázaro et al,[17] including 767 individuals with COVID-19 between the first and second waves, found that SAPS 3 had satisfactory performance for the probability of death in these individuals. However, Kurtz et al[18] recommend caution and improvement in the calibration of the SAPS 3 before its application in COVID-19.

Hodgson et al[19] found longer hospitalization time (in days) in the ICU and ward in the ARDS group due to COVID-19 in their study, data similar to our findings. According to these authors, the profile of patients associated with more extended periods of mechanical ventilation use justifies the prolongation of hospitalization compared to non-COVID-19 ARDS. Di Mitri et al[20] have also discussed the literature associating the prolongation of patients with ARDS COVID-19 hospitalization to protocols such as RT-PCR negative test for discharge criteria. There was no statistically significant difference between both groups regarding ICU and hospital mortality, which is consistent with the study by Hsieh et al,[21] where they also found no difference in mortality. Huppert et al[22] described pneumonia (whether bacterial or viral) as the leading triggering cause of ARDS from other causes, similar to the present study in which pulmonary focus sepsis was the main predisposing to the clinical evolution of NON-COVID-19 ARDS.

Ismaiel and Henzler[23] pointed out that protective ventilation associated with permissive hypercapnia leads to better outcomes. It was observed a lower risk of lung injury through reduced mechanical stress, local inflammatory response, and lung cell apoptosis. Thus, the authors observed a slight acid-base alteration in surviving individuals with non-COVID-19 ARDS compared to non-survivors. Brault et al[24] compared a group of 63 patients, 24 patients with ARDS caused by COVID-19 versus 39 patients with NON-COVID-19 ARDS. This study did not show significant differences between several ventilatory parameters, such as the PaO_2/FiO_2 ratio, PEEP level (≥10 mm

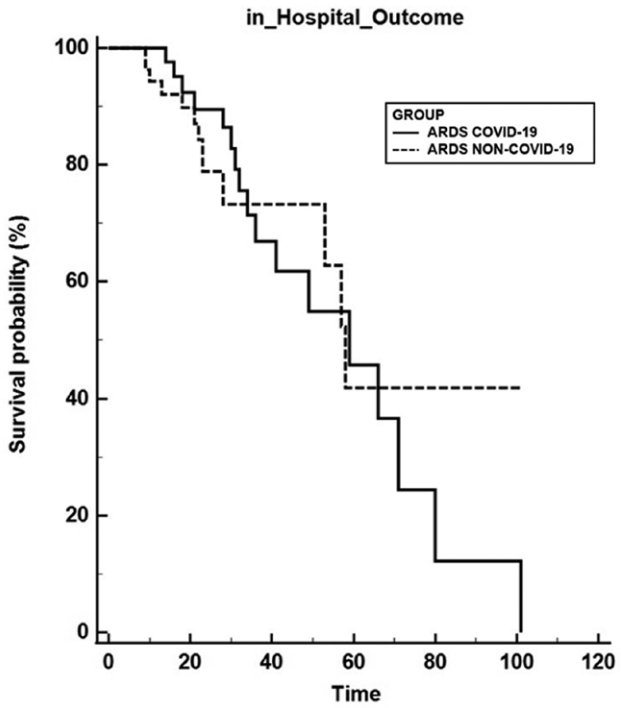

Figure 2. Survival curves for the length of hospital stay (LOS) of patients with ARDS COVID-19 and NON-COVID-19.

Table 4

Crude logistic regression model, evaluating the impact of COVID-19 and other clinical-demographic characteristics on the risk of ICU death (A). Logistic regression model using the "stepwise" method, evaluating the impact of COVID-19 and other clinical-demographic characteristics on the risk of death in the ICU (B).

ICU outcome	Odds ratio	CI (95%)	*P* value
A			
COVID-19	1.8038	0.6470–5.0246	.259
Male gender	0.9541	0.3831–2.3762	.920
Age	1.0203	0.9930–1.0485	.146
SAPS 3	1.0270	0.9998–1.0550	.051
Thrombosis	0.5751	0.1672–1.9770	.380
Vasopressors	1.3644	0.5216–3.5684	.526
Dialysis	2.3207	0.7150–7.5326	.161
Blood transfusions	2.5989	0.7356–9.1809	.138
B			
Age	1.0257	1.0014–1.0506	.037
SAPS 3	1.0319	1.0085–1.0559	.007

ICUs = intensive care units, SAPS 3 = simplified acute physiology score.

Hg), oxygenation response in the prone position and, ICU mortality. In addition, the results of the present study revealed that the 2 groups did not differ between measures of respiratory mechanics such as plateau pressure, driving pressure, and lung compliance, which agrees with other similar studies published in the literature.[25,26]

In line with these investigations, Asar et al[27] studied 17 patients diagnosed with COVID-19 and 16 patients with other causes of ARDS. All patients were on mechanical ventilation and were monitored with a Swan-Ganz catheter during the first week of hospitalization. This study did not observe significant differences between the groups of patients regarding the

Table 5

Crude logistic regression model evaluating clinical and demographic characteristics associated with ARDS due to COVID-19, compared to other patients with ARDS (A). Logistic regression model adjusted by the "stepwise" method evaluating clinical and demographic characteristics associated with ARDS due to COVID-19 compared to other patients with ARDS (B).

COVID-19	Odds ratio	CI (95%)	*P* value
A			
Male gender	2.8744	1.0621–7.7790	.038
Age	1.0291	0.9940–1.0655	.104
Diabetes	5.7267	1.8192–18.0273	.003
COPD	3.2035	0.9997–10.2655	.050
Arterial hypertension	0.6326	0.1716–2.3316	.492
BMI	1.1044	1.0308–1.1833	.005
B			
Male gender	2.7474	1.0417–7.2461	.041
Diabetes	6.0802	2.2146–16.6925	<.001
COPD	4.0153	1.2955–12.4446	.016
BMI	1.0955	1.0275–1.1682	.005

ARDS = acute respiratory distress syndrome, BMI = body mass index, COPD = chronic obstructive pulmonary disease.

respiratory and hemodynamic parameters measured. Therefore, patients infected with the SARS-CoV-2 virus have a very varied spectrum of clinical signs, ranging from asymptomatic cases to severe cases of acute respiratory failure and ARDS. Sjoding et al[28] retrospectively compared a cohort of 130 mechanically ventilated patients with severe COVID-19 versus 382 patients with NON-COVID-19 ARDS. The findings of this investigation showed a difference in 28-day mortality of 30 and 38%, for patients with COVID-19 ARDS versus NON-COVID-19 ARDS, respectively. However, the authors did not find significant clinical differences or differences between some biological markers of systemic inflammation, such as lymphocyte count.

Bain et al[29] studied 27 patients with ARDS due to COVID-19 and ARDS due to viruses (n = 17), bacteria (n = 21), and culture-negative (n = 30). The authors observed a similarity between COVID-19 ARDS and other causes of ARDS. However, patients with COVID-19 ARDS had a longer duration of mechanical ventilation. In cases of ARDS due to COVID-19 and viral ARDS, IL-6 and lung minute volume were lower than ARDS of bacterial causes and culture-negative. Notwithstanding these differences, the treatment or evolution of ARDS should be not affected. Tomazini et al[30] compared lung mechanics between 229 patients with ARDS due to COVID-19 and 1010 patients with NON-COVID-19 ARDS. This study showed that patients with NON-COVID-19 ARDS had a higher PEEP value, a lower tidal volume, and a lower lung static compliance. The 2 groups had no statistical difference in 28-day mortality and duration of mechanical ventilation. Zhang et al[31] conducted a multicenter study comparing lung injury in 90 COVID-19 patients versus 130 NON-COVID-19 patients. These authors observed an increase in C-reactive protein, LDH and a decrease in troponin and procalcitonin in COVID-19 cases. Multivariate analysis indicated in this cohort that age, fever, prothrombin time, procalcitonin, $PaCO_2$, and oxyhemoglobin are independent risk factors associated with COVID-19.

With regard to comorbidities, diabetes, COPD, and BMI were present in the majority of individuals with COVID-19 ARDS, and logistic regression were statistically significant as an independent risk factor. Landstra et al[32] corroborate this finding in their study by demonstrating that diabetes is associated with complications and deaths from several diseases, including those of the respiratory tract, associating immune dysfunction with

low interleukin production, decreased chemotaxis, phagocytic activity, and immobilized polymorphonuclear leukocytes. Arterial hypertension was also commonly observed in individuals with ARDS due to COVID-19, and significant values in the regression determining a possible independent factor for the development of ARDS. However, according to Shibata et al[33] there is also inconclusiveness about hypertension, unlike diabetes, as a risk factor for severe cases or deaths from COVID-19. A study conducted by Fang et al[34] considered the hypothesis that drugs used to treat hypertension and diabetes containing ACE inhibitors and angiotensin 2 receptor blockers would increase the concentration of ACE2, facilitating COVID-19 infection. Among the previous comorbidities analyzed in the present study, COPD was predominantly present in the COVID-19 ARDS group. Singh et al[35] suggested, in their study, the presence of high ACE2 expressions in COPD lung cells and that associated with this, there is a profile of preexisting comorbidities in these individuals, such as diabetes, increased BMI, and recurrent respiratory tract infections, which may worsen the clinical findings.

The hospital mortality in the present study did not show a statistically significant difference when comparing both groups (COVID-19 ARDS vs NON-COVID ARDS), however there is a difference observed in the Kaplan–Meier curve concerning time × survival in the ICU. It was reported consistency in the literature on the homogeneity of mortality of COVID-19 versus NON-COVID-19 individuals compared between hospital LOS and associate it with worse outcomes in NON-COVID-19 patients when analyzing the time × survival curve due to immunosuppression-related aspects commonly seen in patients with ARDS from other causes.[21] A systematic review and meta-analysis conducted by Mahamat-Saleh et al[36] are in agreement with our findings related to logistic regression in which hypertension, diabetes, and increased BMI showed that they present a higher risk (OR = 1.42, 1.54, 2.68 respectively) for COVID-19 mortality. These findings coincide with our results, where we found a higher risk in individuals with comorbidities.

This investigation has some limitations. This study was conducted in a single center, which prevented the extension of the results to other populations and generalizations. In addition, the protocol design was observational and retrospective. Thus, the group of patients with COVID-19 ARDS was studied in a different period than patients with NON-COVID-19 ARDS, with possible variability in data collection and different medical practices (e.g., pronation, more used during COVID-19). However, through this study, we would like to convey a message to anesthesiologists and intensivists, indicating the importance of epidemiological comparative studies between COVID-19 and NON-COVID-19 ARDS.

5. Conclusions

Even with the limitation of the sample studied, it was possible to demonstrate statistically significant differences between the 2 groups in characteristics such as age, gender, BMI, and LOS in the ICU. SOFA and SAPS 3 also showed a different behavior, having been higher in the NON-COVID-19 ARDS group. Also, many clinical and ventilatory parameters of COVID-19 ARDS were similar when compared to the group of patients with ARDS NON-COVID-19, not justifying individualizations or changes in the use of established protocols for treating ARDS. Relevant clinical-demographic characteristics associated with ARDS due to COVID-19, such as male gender, diabetes, COPD, and BMI, were independent predictors of severity in patients with ARDS COVID-19, compared to other patients with ARDS. In addition, the outcome was similar in both groups. However, due to the limited number of patients included in the present investigation, further studies, preferably multicenter with a larger cohort, are needed to reinforce these findings.

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