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Original Article

Prone positioning in the COVID-19 pandemic: Real-world data from southern Brazil

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ABSTRACT

Introduction: The COVID-19 pandemic rapidly overcrowded hospitals and overwhelmed every aspect of the healthcare systems worldwide, presenting unprecedented challenges for physicians on the front lines managing the increasing number of patients with acute respiratory distress syndrome (ARDS) necessitating respiratory support. The aim of this study was comparing data from patients with COVID-19 submitted to the supine and prone position during the acute phase of ARDS. **Methods**: In this prospective cohort study demographic and clinical data from 1,545 patients with a positive RT-PCR test for SARS-CoV-2, were evaluated. **Results**: The prone position group was 69.1% male, 58 years old (interquartile range [IQR]:46.0-69.0), 45.1% were admitted to ICU, and 36.4% had ≥50% pulmonary involvement. The profile of patients who required oxygen-therapy was: 91.0% for catheter oxygen, 49.5% for Hudson mask, 36.5% for non-invasive mechanical ventilation (NIMV), and 26.2% for IMV. These patients had a median of 58 years old (IQR: 46.0-69.0), length of stay (LOS) of 11 days (IQR: 7-21), and case-mix of 3.6542 (IQR: 1.7522-5.1284). The clinical variables more prevalent in prone patients were ICU admission, pressure injury, CT graduation ≥50%, LOS, case-mix, dyspnea, oxygen-therapy, corticosteroid, convalescent plasma, vasopressor, and C-Reactive Protein. **Conclusion**: The results demonstrate differences between the groups regarding their medical history and severity of the current illness, which probably had a great influence on therapeutic decisions and long-term outcomes of these patients.

Keywords: *COVID-19; Acute Respiratory Distress Syndrome; prone position; SARS-COV-2.*

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INTRODUCTION

The COVID-19 pandemic rapidly overcrowded hospitals and overwhelmed every aspect of the healthcare systems worldwide, presenting unprecedented challenges for physicians on the front lines managing the increasing number of patients with acute respiratory distress syndrome (ARDS) necessitating respiratory support[1]. The strain on intensive care unit (ICU) resources forced clinicians to limit the use of mechanical ventilation by seeking novel therapeutic strategies[1-2].

Before 2019, prone positioning was widely adopted as a standard practice due to improvements in oxygenation and a reduction in mortality among mechanically ventilated patients with moderate to severe ARDS[2-4]. At that time, the evidence for prone positioning in awake (non-ventilated) patients was scarce and came mostly from small case series but similarities underlying the mechanisms leading to improvement in oxygenation and the great shortage of ICU beds made physicians adopt this technique in emergency and ward patients, even though there was no hard evidence to support it[5-7].

As the pandemic unfolded, widespread use of the prone position in awake patients proved itself feasible and safe[8-10] but data on its benefits on avoiding intubation[11,12] and mortality[12,13] were unclear and under-sampled. This study comes on to aggregate knowledge to this body of evidence and presents long-term data on patients submitted to an awake prone position during the acute phase of ARDS caused by SARS-COV-2 infection. Therefore, the objective of this study was to compare data from patients with COVID-19 submitted to the supine and prone position during the acute phase of ARDS.

METHODS

This prospective cohort study was carried out in Brazil, in the city of Porto Alegre, State of Rio Grande do Sul (RS), at private hospital. All participants signed an informed consent form and this study was approved by the Institutional Review Board of the National Health Council of Brazil (approval number 4.497.118; date: 4 January 2021; title: National multicenter hospital registry of patients with disease caused by SARS-COV-2). This study was ethically conducted according to Helsinki Declaration of 1975. We identified COVID-19 hospitalizations and performed a retrospective review of patient data. We reviewed 1,545 patients with a positive RT-PCR test for SARS-CoV-2, aged 18 years or older with initial hospitalization because of coronavirus disease between March 2020 and September 2021. 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 images and classified as typical (ground-glass opacity) or atypical[14].

Oxygen supplementation was defined based on the maximum level of respiratory support documented during the hospital stay, in order to capture the highest severity of respiratory compromise encountered by each patient. Prone positioning may have been implemented either prior to or following the period of greatest respiratory deterioration. In the present study, mortality refers to all-cause in-hospital mortality. This definition includes any death occurring during hospitalization, regardless of the direct or indirect cause. For example, patients admitted with COVID-19 who subsequently died due to a secondary bacterial infection were classified under all-cause mortality.

The variable “casemix” refers to the resource utilization weight assigned to each patient based on the Brazilian Hospital Admission System classification, which accounts for clinical complexity, comorbidities, procedures performed, and length of stay. The vital signs presented in the manuscript refer to the first recorded values following study inclusion, that is, upon hospital admission. This criterion was chosen to ensure consistency across patient records. Patient-reported outcome measures (PROMs) according to International Consortium for Health Outcomes Measurement (ICHOM) were evaluated at 7, 14, 30, 60, and 180 days after hospital discharge for functional status and quality of life, social functioning, and symptoms (https://connect.ichom.org/wp-content/uploads/2020/10/FINAL-C19-Reference-Guide-20201007.pdf). These variables were collected by telephone contact, in three attempts.

Kolmogorov-Smirnov with Lilliefors correction and Shapiro-Wilk tests were performed to evaluate the normality of the continuous data. Quantitative variables were presented as median followed by the interquartile range (IQRs). The Mann-Whitney test was used to compare possible differences between these variables and supine and prone groups. The Kruskal-Wallis test followed by the Tukey posthoc test was used to compare the median percentages of PROMs between the 7, 14, 30, 60, and 180-day follow-ups. Categorical variables are reported as numbers (percentage), and Pearson’s chi-square or Fisher’s exact tests as appropriate were used for study comparisons. Poisson regression was applied to assess the most prevalent variables in patients with prone. Independent variables included in the Poisson regression model were selected based on clinical relevance and evidence from the literature, rather than solely on statistical significance in univariate analyses. This approach was adopted to ensure comprehensive adjustment for potential confounding factors. The Prevalence Ratio (PR) with 95% Confidence Interval (95%CI) was applied. *p*-values ≤ 0.05 for all tests were considered significant. SPSS, Version 25.0 for Windows (SPSS Inc., Chicago, IL, USA), and R software (R Foundation for Statistical Computing, Vienna, Austria; <http://www.R-project.org>) were used for data analysis.

RESULTS AND DISCUSSION

This study included 1,545 COVID-19 patients, with 35.9% submitted to prone positioning. The prone position group was 69.1% male, with 35.5% being ≥65 years and 98.4% self-declared white skin color. Of these patients 31.2% had no comorbidities, 10.5% had cardiac disease, 39.4% had hypertension, 11.2% had pulmonary disease, 18.8% had diabetes, 2.5% had kidney disease, 2.0% had liver disease, 2.3% had a prior stroke, 3.2% had another central nervous system (CNS) disease, 7.0% had cancer, 2.0% had arthritis, 45.1% were admitted in ICU, 12.1% had organ damage by COVID-19 infection, 94.7% had typical COVID-19 computerized tomography (CT) findings, 36.4% had ≥50% pulmonary involvement on CT, and 3.6% were readmitted. All patients were questioned about their symptoms upon admission and 55.4% had fever, 53.1% had cough, 4.7% had sore throat, 29.2% had difficulty breathing, 8.7% had diarrhea, 9.2% had nausea, 11.0% had headache, 2.5% runny nose, 44.2% asthenia, 67.0% dyspnea, 20.2% myalgia. Male patients, no comorbidities, ICU admission, pressure lesions, death, typical COVID-19 CT finding, ≥50% pulmonary involvement on CT, cough, asthenia, and dyspnea were variables statistically ($p \leq 0.05$) more frequent in patients submitted to awake prone positioning than patients that were not. However, patients ≥65 years old, with cardiac disease, kidney disease, cancer, readmission, and death were variables statistically ($p \leq 0.05$) more frequent in patients that remained supine (**Table 1**).

Table 1: Demographic and clinical characterization of patients diagnosed with COVID-19 between March 2020 and September 2021 stratified by supine and prone positioning

Variables	*Supine (n=991)*		*Prone (n=554)*		*p*-value
	n	*%*	*n*	*%*	
Male	569	57.4	383	69.1	**<0.01**
Age ≥65 years old	470	42.4	197	35.5	**<0.01**
White skin color	881	98.2	480	98.4	0.84
Comorbidities					
Without comorbidities	253	25.5	173	31.2	**0.01**
Cardiac disease	153	15.4	58	10.5	**<0.01**
Hipertension	439	44.3	218	39.4	0.06
Pulmonar disease	125	12.6	62	11.2	0.41
Diabetes	200	20.2	104	18.8	0.50
Kidney disease	56	5.7	14	2.5	**<0.01**
Liver disease	21	2.1	11	2.0	0.86
Stroke problems	38	3.8	13	2.3	0.11
CNS disease	86	8.7	18	3.2	**<0.01**
Cancer	101	10.2	39	7.0	**0.04**
Arthritis	27	2.7	11	2.0	0.36
Clinical features					
ICU admission	253	25.7	247	45.1	**<0.01**
Pressure injury	53	5.6	74	13.7	**<0.01**
Overall death	276	27.8	125	22.5	**0.03**
Death by COVID-19	126	12.7	58	10.4	0.59
Readmission	81	8.1	20	3.6	**<0.01**
Organ damage	23	7.2	19	12.1	0.08
Typical COVID-19 CT finding	801	84.6	518	94.7	**<0.01**
CT graduation ≥50%	230	27.3	195	36.4	**<0.01**
Symptoms					
Fever	505	51.0	307	55.4	0.09
Cough	471	47.5	294	53.1	**0.04**
Sore throat	42	4.2	26	4.7	0.67
Difficulty breathing	241	24.3	162	29.2	**0.03**
Diarrhea	91	9.2	48	8.7	0.73
Nausea	94	9.5	51	9.2	0.85
Headache	122	12.3	61	11.0	0.44
Runny nose	32	3.2	14	2.5	0.43
Adynamia	381	38.4	245	44.2	**0.03**
Dyspnea	551	55.6	371	67.0	**<0.01**
Myalgia	187	18.9	112	20.2	0.52

CNS: Central Nervous System; ICU: Intensive Care Unit; CT: Computed tomography.
In bold, significant *p*-values are highlighted.

Oxygen supplementation and medications used were evaluated. The profile of patients with awake prone positioning who required oxygen therapy was: 91.0% for catheter oxygen, 49.5% for Hudson mask, 36.5% for non-invasive mechanical ventilation, and 26.2% for invasive mechanical ventilation. All these methods were statistically more frequent in prone patients ($p \leq 0.05$). Of these patients, 0.2% used oseltamivir, 44.6% azithromycin, 70.2% other antibiotics, 96.4% corticosteroids, 3.6% hydroxychloroquine, 8.7% convalescent plasma, 5.4% tocilizumab, 21.3% vasopressors, and 47.8% anticoagulants. The use of azithromycin, corticosteroids, convalescent plasma, and vasopressors were statistically ($p \leq 0.05$) more frequent in patients submitted to prone positioning than patients that were not (**Table 2**).

Table 2: Oxygen therapy and medications of patients diagnosed with COVID-19 between March 2020 and September 2021 stratified by supine and prone positioning

Variables	*Supine (n=991)*		*Prone (n=554)*		*p*-value
	n	*%*	*n*	*%*	
Oxygen therapy					
Catheter oxygen	728	73.5	504	91.0	**<0.01**
Hudson mask	266	26.8	274	49.5	**<0.01**
Invasive mechanical ventilation	180	18.2	145	26.2	**<0.01**
Non-invasive mechanical ventilation	296	29.9	202	36.5	**<0.01**
Medications					
Oseltamivir	2	0.2	1	0.2	0.99
Azithromycin	366	36.9	247	44.6	**<0.01**
Antibiotics other than azithromycin	659	66.5	389	70.2	0.13
Corticosteroid	872	88.0	534	96.4	**<0.01**
Hydroxychloroquine	23	2.3	20	3.6	0.14
Convalescent plasma	25	2.5	48	8.7	**<0.01**
Tocilizumab	40	4.0	30	5.4	0.21
Vasopressor	132	13.3	118	21.3	**<0.01**
Anticoagulant	451	45.5	265	47.8	0.38

In bold, significant *p*-values are highlighted.

Transitions to higher levels of oxygen support during hospitalization were observed in both prone and supine groups, reflecting the progression of respiratory failure in a subset of patients. Although specific temporal sequences were not the primary focus of this study, the data indicate that patients in the prone group more frequently required advanced respiratory support modalities, including non-invasive mechanical ventilation (36.5%) and invasive mechanical ventilation (26.2%). This contrasts with lower utilization rates of these modalities in the supine group, suggesting that the prone group presented with greater disease severity. These differences likely influenced both the choice of respiratory management strategies and the clinical outcomes observed.

Patients with awake prone positioning had a median of 58 years old (IQR: 46.0 - 69.0), length of stay (LOS) of 11 days (IQR: 7 - 21), length of stay in ICU of 11 days (IQR: 7 - 22), ventilation time of 8 days (IQR: 5 - 15), and case-mix of 3.6542 (IQR: 1.7522 - 5.1284). Upon arrival, patients had a systolic blood pressure of 123 mmHg (IQR: 113 - 135), diastolic blood pressure of 72.0 mmHg (IQR: 64 - 81), axillary temperature of 37.1ºC (IQR: 36.4 - 37.8), heart rate of 94 (IQR: 83 - 105), and respiratory frequency of 20 (IQR: 19 - 22). Age, length of stay, and case-mix were statistically ($p \leq 0.05$) higher in patients with awake prone positioning than in patients without this positioning (**Table 3**). The median LOS in patients with awake prone positioning was 11 days vs 8 days in patients without this positioning ($p \leq 0.05$). LOS in pronated patients admitted to the ICU was 11 days vs 12 days in patients without this positioning ($p = 0.74$). Additionally, total ventilation time in patients submitted to awake prone positioning was 8 days vs 7 days in patients without this positioning ($p = 0.72$).

PROMs were evaluated at 7, 14, 30, 60, and 180 days after hospital discharge and there was a significant improvement ($p <0.01$) in the evaluation of the general sample (1,545 patients) over time, especially after 30 days of follow-ups in all domains

evaluated (functional status and quality of life, social functioning, and symptoms). However, when comparing patients who underwent the prone position with those who did not, there were no significant differences (p >0.05) between these groups for all domains evaluated (**Figure 1**).

Table 3: Quantitative variables of patients diagnosed with COVID-19 between March 2020 and September 2021 stratified by supine and prone positioning

Variables		Percentile 25	Median	Percentile 75	*p*-value
Age (years)	**supine**	48.0	63.0	76.0	**<0.01**
	prone	46.0	58.0	69.0	
Lenght of stay (days)	**supine**	5.0	8.0	15.0	**<0.01**
	prone	7.0	11.0	21.0	
Lenght of stay in ICU (days)	**supine**	5.0	12.0	26.0	0.74
	prone	7.0	11.0	22.0	
Ventilation time (days)	**supine**	4.0	7.0	14.0	0.72
	prone	5.0	8.0	15.0	
Casemix	**supine**	1.2955	1.7524	2.0158	**<0.01**
	prone	1.7522	3.6542	5.1284	
Systolic blood pressure (mmHg)	**supine**	111.0	124.0	137.0	0.36
	prone	113.0	123.0	135.0	
Diastolic blood pressure (mmHg)	**supine**	62.0	72.0	81.0	0.22
	prone	64.0	72.0	81.0	
Axillary temperature (ºC)	**supine**	36.2	36.8	37.6	0.15
	prone	36.4	37.1	37.8	
Heart rate	**supine**	80.0	92.0	105.0	0.12
	prone	83.0	94.0	105.0	
Respiratory frequency	**supine**	19.0	24.0	26.0	0.21
	prone	19.0	20.0	22.0	

In bold, significant *p*-values are highlighted.

Laboratory tests were evaluated, and patients with prone positioning had median of 46.0 million/mm3 erythrocytes (IQR: 42.0 - 50.0), hemoglobin of 13.9 g/dL (IQR: 12.5 - 14.9), hematocrit of 40.2% (IQR: 36.9 - 42.7), leukocytes of 8,350 per mm^3 (IQR: 5,790 - 11,120), platelets of 207,000 per mm^3 (IQR: 160,000 - 258,000), D-Dimer of 735,0 µg FEU/L (IQR: 490.5 - 1,116.5), troponin of 8.0 ng/mL (IQR: 6.0 - 12.0), lactate dehydrogenase of 354.0 U/L (IQR: 291.0 - 457.0), C-reactive protein (CRP) of 93.0 ug/L (IQR: 50.0 - 153.0), natriuretic peptide of 450.0 pg/ml (IQR: 160.0 - 1,660.0), total bilirubin of 4.0 mg/dL (IQR: 3.0 -5.0), creatinine of 10.0 mg/dL (IQR: 8.0 - 11.0), sodium of 136.5 mEq/L (IQR: 134.0 - 139.0), pH of 7.2 (IQR: 7.2 - 7.7), PaO2 of 71.0 mmHg (IQR: 62.0 - 78.0), PaCO2 of 37.0 mmHg (IQR: 32.0 - 39.0), HCO3 of 25.0 mEq/L (IQR: 21.0 - 26.0), base excess of 11.0 mEq/L (IQR: -4.0 - 25.0), and O2 saturation of 92.0% (IQR: 91.0 - 97.0). Leukocytes, platelets, d-dimer, and CRP were higher ($p \leq 0.05$) in patients with prone positioning than in patients without this positioning. However, the natriuretic peptide was statistically ($p \leq 0.05$) higher in patients without prone positioning (**Table 4**).

Table 4: Laboratory tests variables of patients diagnosed with COVID-19 between March 2020 and September 2021 stratified by supine and prone positioning

Variables		Percentile 25	Median	Percentile 75	*p*-value
Erythrocytes (million/mm3)	**supine**	41.0	45.0	49.0	0.51
	prone	42.0	46.0	50.0	
Hemoglobin (g/dL)	**supine**	12.3	13.5	14.6	0.12
	prone	12.5	13.9	14.9	

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Table 4: Continuation.

Variables		Percentile 25	Median	Percentile 75	*p*-value
Hematocrit (%)	**supine**	35.8	39.4	42.3	0.15
	prone	36.9	40.2	42.7	
Leukocytes (units per mm^3)	**supine**	5,310	7,250	9,870	**0.01**
	prone	5,790	8,350	11,120	
Platelets (units per mm^3)	**supine**	151,000	189,000	242,000	**0.02**
	prone	160,000	207,000	258,000	
D-Dimer (µg FEU/L)	**supine**	490.0	761.0	1,219.0	**0.01**
	prone	490.5	735.0	1,116.5	
Troponin (ng/mL)	**supine**	7.0	10.0	19.0	0.21
	prone	6.0	8.0	12.0	
Lactate dehydrogenase (U/L)	**supine**	269.0	336.0	427.0	0.08
	prone	291.0	354.0	457.0	
C-reactive protein (ug/L)	**supine**	34.0	78.0	136.0	**<0.01**
	prone	50.0	93.0	153.0	
Natriuretic peptide (pg/ml)	**supine**	160.0	600.0	1,540.0	**<0.01**
	prone	160.0	450.0	1,660.0	
Total bilirubin (mg/dL)	**supine**	3.0	4.0	5.0	0.99
	prone	3.0	4.0	5.0	
Creatinine (mg/dL)	**supine**	8.0	10.0	12.0	0.75
	prone	8.0	10.0	11.0	
Sodium (mEq/L)	**supine**	134.0	136.0	139.0	0.25
	prone	134.0	136.5	139.0	
ph	**supine**	7.4	7.5	7.5	0.45
	prone	7.4	7.2	7.7	
PaO2 (mmHg)	**supine**	64.0	71.0	82.0	0.41
	prone	62.0	69.0	78.0	
PaCO2 (mmHg)	**supine**	32.0	35.0	38.0	0.48
	prone	32.0	37.0	39.0	
HCO3 (mEq/l)	**supine**	22.0	24.0	25.0	0.87
	prone	21.0	25.0	26.0	
Base Excess (mEq/l)	**supine**	-10.0	8.0	23.0	0.21
	prone	-4.0	11.0	25.0	
O_2 saturation (%)	**supine**	92.0	94.0	96.0	0.28
	prone	91.0	92.0	97.0	

In bold, significant *p*-values are highlighted.

In the multivariable analysis by Poisson regression, the variables independently associated with prone positioning: male sex (PR: 1.64; 95%CI: 1.31–2.05; $p < 0.01$), age ≥65 years old (PR: 0.71; 95%CI: 0.59–0.87; $p < 0.01$), not having comorbidities (PR: 1.32; 95%CI: 1.05–1.66; $p = 0.01$), cardiac disease (PR: 0.65; 95%CI: 0.46–0.88; $p < 0.01$), kidney disease (PR: 0.43; 95%CI: 0.23–0.78; $p < 0.01$), CNS disease (PR: 0.35; 95%CI: 0.21–0.59; $p < 0.01$), ICU admission (PR: 2.37; 95%CI: 1.90–2.96; $p < 0.01$), pressure injury (PR: 2.67; 95%CI: 1.84–3.87; $p < 0.01$), readmission (PR: 2.05; 95%CI: 1.03–3.15; $p = 0.03$), typical COVID-19 CT finding (PR: 3.25; 95%CI: 2.15–4.92; $p < 0.01$), CT graduation ≥50% (PR: 1.52; 95%CI: 1.21–1.92; $p < 0.01$), longer LOS (PR: 1.81; 95%CI: 1.61–2.15; $p < 0.01$), case-mix (PR: 3.88; 95%CI: 2.33–5.21; $p < 0.01$), dyspnea (PR: 1.62; 95%CI: 1.30–2.01; $p < 0.01$), catheter

oxygen (PR: 3.58; 95%CI: 2.71–5.15; p <0.01), Hudson mask (PR: 2.61; 95%CI: 2.12–3.47; p <0.01), invasive mechanical ventilation (PR: 1.44; 95% CI: 1.15–2.84; p <0.01), non-invasive mechanical ventilation (PR: 2.33; 95%CI: 1.87–3.58; p <0.01), use of corticosteroid (PR: 2.54; 95%CI: 1.54–6.97; p <0.01), use of convalescent plasma (PR: 2.88; 95%CI: 2.01–8.15; p <0.01), use of vasopressor (PR: 1.76; 95%CI: 1.33–2.31; p <0.01), and higher CRP (PR: 1.81; 95%CI: 1.42–2.28; p <0.01) (**Table 5**).

Table 5: Multivariable associations of factors (demographic, comorbidities, clinical features, symptoms, oxygen therapy, and medications) for prone positioning in patients diagnosed with COVID-19 between March 2020 and September 2021

Variables	Prevalence Ratio	Lower CI95%	Upper CI95%	*p*-value
Male	**1.64**	**1.31**	**2.05**	**<0.01**
Age ≥65 years old	**0.71**	**0.59**	**0.87**	**<0.01**
White skin color	1.09	0.46	2.56	0.84
Comorbidities				
Without comorbidities	**1.32**	**1.05**	**1.66**	**0.01**
Cardiac disease	**0.65**	**0.46**	**0.88**	**<0.01**
Hypertension	0.82	0.66	1.01	0.07
Pulmonary disease	0.87	0.63	1.20	0.81
Diabetes	0.91	0.70	1.19	0.50
Kidney disease	**0.43**	**0.23**	**0.78**	**<0.01**
Liver disease	0.94	0.44	1.95	0.86
Stroke problems	0.60	0.31	1.14	0.08
CNS disease	**0.35**	**0.21**	**0.59**	**<0.01**
Cancer	0.66	0.45	1.05	0.08
Arthritis	0.72	0.35	1.47	0.37
Clinical features				
ICU admission	**2.37**	**1.90**	**2.96**	**<0.01**
Pressure injury	**2.67**	**1.84**	**3.87**	**<0.01**
Overall death	0.77	0.56	1.02	0.15
Death by COVID-19	1.24	0.49	3.13	0.69
Readmission	2.05	1.03	3.15	**0.03**
Organ damage	1.76	0.95	3.35	0.09
Typical COVID-19 CT finding	**3.25**	**2.15**	**4.92**	**<0.01**
CT graduation ≥50%	**1.52**	**1.21**	**1.92**	**<0.01**
Length of stay (scale)	**1.81**	**1.61**	**2.15**	**<0.01**
Casemix	**3.88**	**2.33**	**5.21**	**<0.01**
Symptoms				
Fever	1.19	0.97	1.47	0.15
Cough	1.24	0.94	1.54	0.06
Sore throat	1.11	0.67	1.83	0.67
Diarrhea	0.94	0.65	1.35	0.73
Nausea	0.96	0.67	1.38	0.85

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Table 5: Continuation.

Variables	Prevalence Ratio	Lower CI95%	Upper CI95%	*p*-value
Headache	0.88	0.63	1.22	0.44
Runny nose	0.77	0.41	1.46	0.48
Adynamia	1.26	0.99	1.57	0.07
Dyspnea	**1.62**	**1.30**	**2.01**	**<0.01**
Myalgia	1.08	0.84	1.41	0.55
Oxygen therapy				
Catheter oxygen	**3.58**	**2.71**	**5.15**	**<0.01**
Hudson mask	**2.61**	**2.12**	**3.47**	**<0.01**
Invasive mechanical ventilation	**1.44**	**1.15**	**2.84**	**<0.01**
Non-invasive mechanical ventilation	**2.33**	**1.87**	**3.58**	**<0.01**
Drugs treatments				
Azithromycin	1.37	0.96	1.70	0.09
Corticosteroid	**2.54**	**1.54**	**6.97**	**<0.01**
Convalescent plasma	**2.88**	**2.01**	**8.15**	**<0.01**
Vasopressor	**1.76**	**1.33**	**2.31**	**<0.01**
Laboratory tests				
Hemoglobin (scale)	1.08	0.71	1.18	0.14
Hematocrit (scale)	1.12	0.66	1.12	0.11
Leukocytes (scale)	1.50	0.98	1.68	0.08
Platelets (scale)	1.42	0.95	1.58	0.09
Ddimers (scale)	0.74	0.63	1.28	0.21
Lactate dehydrogenase (scale)	1.15	0.84	1.74	0.19
C-reactive protein (scale)	**1.81**	**1.42**	**2.28**	**<0.01**
Natriuretic peptide (scale)	**0.88**	**0.70**	**1.35**	**0.15**
PROMs (overall)				
Funcional status and quality of life (scale)	0.98	0.74	1.59	0.57
Social functioning (scale)	0.96	0.71	1.77	0.63
Symptoms (scale)	1.08	0.81	1.94	0.54

CNS: Central Nervous System; ICU: Intensive Care Unit; CT: Computed tomography.

In bold, significant *p*-values are highlighted. PROMs: Patient reported outcome measures.

Our paper was able to clinically delineate a prospective cohort of consecutive patients treated at a private hospital in southern Brazil during the hardest period of the pandemic, clearly demonstrating the propensity of the staff to indicate the prone position, in the context of severe ARDS due to COVID-19, in previously less comorbid and more acutely ill patients. In addition, the study showed the tendency of physicians to pronate more patients who had imaging changes suggestive of COVID-19 to the detriment of other causes of respiratory failure. No decrease in intubation or mortality rates was observed.

While prone positioning is already a very well-established maneuver, with robust evidence in ventilated patients[4], the practice of pronating awake patients is relatively new and has gained much of its popularity during the COVID-19 pandemic, although it is less supported by methodologically sound studies and is still under active investigation. From a physiological standpoint, prone positioning

plays a major role in reducing ventilation/perfusion mismatch, intrapulmonary shunt, and recruiting aerated lung regions[15], but its impact on clinical outcomes, intubation, and survival rates in patients with COVID-19 remains controversial. Most of the early research denotes that prone positioning may improve short-term oxygenation levels with no severe complications, but some studies have shown neutral results in the long run[11,16].

In our study, the baseline clinical variables most associated with the decision to pronate the patients were younger age (<65 years), absence of comorbidities (heart, kidney, or neurological disease), complaint of dyspnea, and the need for any type of oxygen supplementation or non-invasive ventilation. All these characteristics are by the empirical experience of symptomatic relief of dyspnea by pronating awake patients and the greater ease and safety of performing such a maneuver in younger and less comorbid patients since any restriction of movement or additional difficulty in quickly returning to the supine position would put them at potential risk.

It is also not strange that, from a biochemical point of view, patients submitted to prone positioning had higher values of C-reactive protein, D-dimer, and total leukocytes and lower values of pro-BNP. This directly translates to the idea that patients chosen by physicians to be pronated had fewer underlying cardiac comorbidities, had respiratory failure most probably caused by the viral disease (not fluid overload), and were considerably more inflamed than their non-pronated peers.

Some indirect measures of disease severity assessed after patient discharge, such as total length of stay, ICU admission, pressure ulcers, more than 50% involvement of lung parenchyma on chest CT, use of vasopressors, need for mechanical ventilation and case-mix value were also significantly higher in pronated patients than in those maintained in a supine position. All these findings are also congruent in pointing out the fact that, despite being fundamentally healthier in the baseline, patients that were chosen to be pronated were more severely affected by the acute disease. This disparity between premorbid status and severity of acute illness may also explain, at least in part, the lack of significant differences found in ICU length of stay, time in mechanical ventilation, and mortality rates, since in another study[1,17] some of those variables were associated with high in-hospital lethality.

After discharge, all patients were followed for up to 6 months, during which time some long-term outcomes were measured. A higher rate of unplanned hospital readmission was found in the group that was not pronated, a difference that was adjusted, losing statistical significance in the multivariate model. One explanation for this finding is that readmission rates are possibly more associated with age, the number of comorbidities, and the degree of previous dependence (which continue to be present after initial discharge) than with the intensity of the acute illness. On the other hand, there were no differences between groups regarding reported PROMs of quality of life, social interaction, residual symptomatology, and functional status. A consistent and equivalent improvement was noted in all domains for both groups over time, which may have occurred due to a selection bias, considering the greater propensity for engagement and response of those patients who, despite being more seriously ill, had a better outcome and responded to our calls.

This study has some limitations. First, the study population was restricted to a convenience sample of a single private center, where care practices adopted at the time may have influenced decisions to pronate, intubate, admit to the ICU, or even prescribe a certain antibiotic or another type of therapy, bearing in mind that the period in question was one of collective learning and constant changes. Second, in addition to the indication - or not - of pronating the patient, it was also up to the attending physician to determine the moment, duration, and frequency with which the patient would be pronated, with no protocol to guide these decisions. In the present study, prone positioning may have been implemented either prior to or following the period of greatest respiratory deterioration. However, given the retrospective design of the study, it was not possible to consistently determine the precise temporal relationship between proning and the nadir of oxygenation for all patients. Additionally, due to limitations in the retrospective data, it was not possible to consistently determine the exact duration of ventilation in the prone versus supine position.Despite being an observational study, which carries all the known biases of this type of study, this is one of the largest cohorts already described on the matter, with subjects being followed prospectively up to 6 months of discharge.

In conclusion, there was no difference in mortality, readmissions, or PROMs at 6 months between patients who underwent prone positioning and those who did not. The clinical characterization of the sample demonstrates clear differences between the groups regarding their medical history and severity of the current illness, which probably had a great influence on therapeutic decisions and the long-term outcomes of these patients. These data demonstrate the need for a standardized protocol and clearer selection criteria for patients undergoing prone positioning in future studies so that its long-term effects can be better evaluated.

REFERENCES

1. Wolf JM, Petek H, Maccari JG, Nasi LA. COVID-19 pandemic in Southern Brazil: Hospitalizations, intensive care unit admissions, lethality rates, and length of stay between March 2020 and April 2022. J Med Virol. 2022;94(10):4839-49.

2. Abroug F, Ouanes-Besbes L, Elatrous S, Brochard L. The effect of prone positioning in acute respiratory distress syndrome or acute lung injury: a meta-analysis: areas of uncertainty and recommendations for research. Intensive Care Med. 2008;34(6):1002-11.

3. Sud S, Friedrich JO, Taccone P, Polli F, Adhikari NK, Latini R, et al. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. Intensive Care Med. 2010;36(4):585-99

4. Guérin C, Reignier J, Richard J-C, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159-68.

5. Scaravilli V, Grasselli G, Castagna L, Zanella A, Isgrò S, Lucchini A, et al. Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: A retrospective study. J Crit Care. 2015;30(6):1390-4.

6. Valter C, Christensen A, Tollund C, Schønemann N. Response to the prone position in spontaneously breathing patients with hypoxemic respiratory failure. Acta Anaesthesiol Scand. 2003;47:416-8.

7. Bellone A, Basile A. Prone positioning in severe acute hypoxemic respiratory failure in the emergency ward. Emerg Care J. 2018;14:22-3.

8. Coppo A, Bellani G, Winterton D, Di Pierro M, Soria A, Faverio P, et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. Lancet Respir Med. 2020;8(8):765-74.

9. Tonelli R, Pisani L, Tabbì L, Comellini V, Prediletto I, Fantini R, et al. Early awake proning in critical and severe COVID-19 patients undergoing noninvasive respiratory support: A retrospective multicenter cohort study. Pulmonology. 2022;28(3):181-92.

10. Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. Crit Care. 2020;24(1):28.

11. Ferrando C, Mellado-Artigas R, Gea A, Arruti E, Aldecoa C, Adalia R, et al. Awake prone positioning does not reduce the risk of intubation in COVID-19 treated with high-flow nasal oxygen therapy: a multicenter, adjusted cohort study. Crit Care. 2020;24(1):597.

12. Chong WH, Saha BK, Tan CK. Clinical Outcomes of Routine Awake Prone Positioning in COVID-19 Patients: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Prague Med Rep. 2022;123(3):140-65.

13. Chen L, Zhang Y, Li Y, Song C, Lin F, Pan P. The Application of Awake-Prone Positioning Among Non-intubated Patients With COVID-19-Related ARDS: A Narrative Review. Front Med (Lausanne). 2022;9:817689.

14. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol. 2020;30(8):4381-9.

15. Pelosi P, Brazzi L, Gattinoni L. Prone position in acute respiratory distress syndrome. Eur Respir J. 2002;20(4):1017-28.

16. Elharrar X, Trigui Y, Dols A-M, Touchon F, Martinez S, Prud'homme E, Papazian L. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. JAMA. 2020;323(22):2336-8.

17. Wolf JM, Petek H, Gasparetto Maccari J, Nasi LA. Hospital mortality rates between 2015 and 2022: a comparison between the pre-pandemic and pandemic period shows that COVID-19 is a critical health problem. Clin Biomed Res. 2023;43(1):9-13.

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