Prone position in intubated patients with acute respiratory failure due to COVID-19 in an ICU in the state of São Paulo

Postura prona em pacientes intubados com insuficiência respiratória aguda por COVID-19 em uma UTI do estado de São Paulo

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Abstract

Introduction: The severity of acute respiratory distress syndrome (ARDS) caused by COVID-19 can vary and be influenced by comorbidities. The position is a treatment strategy for critically ill patients; however, it is unclear what the physiological response is and which patients benefit. **Objective:** To determine whether the prone position (PP) and the length of stay in the intensive care unit (ICU) are associated with the time of orotracheal intubation (OTI) and with the death rate in patients on mechanical ventilation with moderate to severe ARDS. **Methods:** An observational, longitudinal, retrospective study was carried out in a tertiary public hospital in the city of São Paulo. Data were collected from the medical records of all patients diagnosed with COVID-19, with a positive PCR, admitted to the ICU and intubated, from April 2020 to July 2021. Pearson's chi-square and Fischer's exact tests were used to compare sample data, and distributions in the two groups were compared using the Mann-Whitney test. **Results:** There was no statistically significant difference for ICU length of stay, OTI time and death rate between patients who were prone versus non-prone [13 (4.0 – 23.0) vs. 13.5 (7.2 – 17.0), p = 0.453; 12 (3.0 – 13.0) vs. 10 (6.0 -15.5), p = 0.772; 71 vs. 68%, p = 0.817, respectively]. **Conclusion:** This study did not demonstrate an association between PP and days of OTI, days of hospitalization and mortality in patients with severe hypoxemia.

Keywords: COVID-19. Prone position. Respiratory distress syndrome. SARS-CoV-2.

Resumo

Introdução: *A gravidade da síndrome do desconforto respiratório agudo (SDRA) ocasionada pela COVID-19 pode variar e ser influenciada por comorbidades presentes. A postura prona é estratégia de tratamento para pacientes graves, no entanto, não está claro qual é a resposta fisiológica e quais pacientes se beneficiam.* ***Objetivo:*** *Verificar se existe associação da postura prona (PP) com o tempo de internação em unidade de terapia intensiva (UTI), tempo de intubação orotraqueal (IOT) e taxa de óbito em pacientes em ventilação mecânica com SDRA de moderada a grave.* ***Métodos:*** *Trata-se de um estudo observacional, longitudinal e retrospectivo, realizado em hospital público terciário no município de São Paulo. Foram coletados dados dos prontuários de todos os pacientes com diagnóstico de COVID-19, com PCR positivo, internados na UTI e intubados, no período de abril de 2020 a julho de 2021. Os testes qui-quadrado de Pearson e exato de Fischer foram utilizados para comparar dados da amostra, e as distribuições nos dois grupos foram comparadas por meio do teste de Mann-Whitney.* ***Resultados:*** *Não houve diferença estatisticamente significante para o tempo de internação na UTI, tempo de IOT e taxa de óbito entre os pacientes que foram pronados versus os não pronados [13 (4,0 – 23,0) vs. 13 (7,2 – 17,0), p = 0,453; 12 (3,0 – 13,0) vs. 10 (6,0 - 15,5), p = 0,772; 71% vs. 68%, p = 0,817, respectivamente].* ***Conclusão:*** *Este estudo não demonstrou associação da PP com os dias de IOT, dias de internação na UTI e mortalidade em pacientes com hipoxemia grave.*

Palavras-chave: *COVID-19. Decúbito ventral. Síndrome do desconforto respiratório. SARS-CoV-2.*

Introduction

The COVID-19 pandemic, a disease caused by the SARS-CoV-2 virus, brought major challenges in terms of care, as a considerable proportion of patients developed severe respiratory failure and required mechanical ventilation, meeting the criteria for acute respiratory distress syndrome (ARDS),[1] with notable pulmonary edema, profound hypoxemia, multiple organ failure and high associated mortality rate.[2,3]

The severity of respiratory failure varies and can be influenced by the individual's comorbidities. Conditions that increase the risk of worsening include moderate to severe asthma, chronic lung disease, severe heart disease, immunocompromised state, chronic kidney disease requiring dialysis, diabetes, liver disease, severe obesity and advanced age.[1]

By definition, four clinical criteria must be met to establish the diagnosis of ARDS: time – acute onset, new event or worsening of respiratory symptoms; chest imaging (bilateral opacities) not completely explained by pleural effusions, lobar or lung collapse, or nodules; origin of edema – respiratory failure not explained by heart failure or volume overload; and oxygenation: arterial oxygen partial pressure/inspired oxygen fraction (PaO_2/FIO_2) and positive end-expiratory pressure (PEEP) classified as mild (201 – 300 mmhg ≥ 5 cm H_2O), moderate (201 – 300 mmhg ≥ 5 cm H_2O) and severe (101 – 200 mmhg ≥ 5 cm H_2O).[4]

What is known about ARDS is that inflammatory edema leads to varying degrees of lung collapse, resulting in ventilation/perfusion (V/Q) ratio mismatch, including a significant shunt fraction. However, in ARDS secondary to COVID-19, pulmonary microthrombi are suspected, resulting in different levels of dead space and ineffective ventilation, worsening the hypoxemia condition.[5]

In patients with severe ARDS, one strategy to consider is the use of the prone position (PP), which consists of providing ventilatory support with the patient lying in the prone position. It is considered an additional therapy for improving oxygenation attributed to the redistribution of perfusion, more homogeneous ventilation, improved gas exchange by inducing alveolar recruitment, improved postural drainage to remove secretions and better chest wall compliance.[6,7] There is little incidence of complications (around three per thousand patients/day), but when they occur they can be fatal, as in cases of extubation and central catheter avulsion.[8]

There are no absolute contraindications for using PP, but there are some situations that may make it difficult, such as severe hemodynamic instability, presence of drains in the anterior region of the chest or abdomen, cerebral edema or intracranial hypertension, recent sternotomy, presence of vertebro-medullary injuries, cardiogenic pulmonary edema, alveolar hemorrhage, recent abdominal surgeries, pregnant women, extreme obesity, extensive skin lesions and abdominal compartment syndrome.[9]

In recent years, several studies have demonstrated significant benefits of PP on the survival of patients with ARDS,[10] as its physiological effects correspond to the improvement between ventilation and perfusion, but the studies have not related physiological changes to clinical results, especially in patients who had severe COVID-19.[11]

In this study, we sought to understand whether there is an association between PP and the length of stay in the ICU, time of orotracheal intubation (OTI) and death rate in patients on mechanical ventilation with moderate to severe ARDS. It is important to understand whether PP can be a complementary therapeutic intervention for more seriously ill patients.

Methods

An observational, longitudinal, retrospective study was conducted through the analysis of medical records of patients admitted to an adult intensive care unit (ICU) and diagnosed with COVID-19, from April 2020 to July 2021, in a tertiary public hospital in the city of São Paulo. Data collection was carried out at the hospital after acceptance by the Research Ethics Committee under Approval No. 4,747,582 of the proposing institution (Pontifical Catholic University of São Paulo) and under No. 4,871,871 of the co-participating institution (Hospital Dr. José Soares Hungria).

Data from patients who met the inclusion criteria were included: diagnosis of COVID-19, with positive PCR (polymerase chain reaction); admitted to the ICU in the above-mentioned period; intubated with moderate or severe ARDS, with $FiO_2 \geq 60\%$ and/or inability to maintain a PaO_2/FiO_2 ratio ≥ 150 mmHg in the first 48 hours of diagnosis; and with protective mechanical ventilation (distension pressure ≤15 cm H_2O) and pH < 7.2. Excluded were patients with hemodynamic instability with elevated vasopressors, severe acute arrhythmias, intracranial hypertension, spinal instability, recent sternotomy/cardiac surgery and peritoneostomy.

The information taken from the medical records included age, sex, comorbidities, lung involvement based on the computed tomography report, the use of the prone position, days spent in the ICU, days of OTI and score for APACHE II (Acute Physiology and Chronic Health Disease Classification System II). The protocol used for the length of stay in PP was 16 hours, with a 12-hour interval between one PP and another. After the improvement in the PaO_2/FiO_2 ratio, maintaining >150 mmHg, the patient was made supine.

For statistical analysis, patients were classified according to whether or not PP was used during their ICU stay. Pearson's chi-square test or Fischer's exact test was used to compare the distributions of sex, comorbidities and lung involvement between the groups that underwent PP or not. For age, APACHE II score, days spent in the ICU and days of OTI, the values of descriptive statistics were calculated. Their distributions in the two groups were compared using the Mann-Whitney test. The significance level adopted was 5%, and the free software R version 4.0.2 (www.r-project.org) was used in the analyses.

Results

The sample consisted of 43 patients of both sexes, of which 22 underwent proning and 21 did not. Table 1 presents the frequency distribution of the demographic and clinical characteristics of patients according to whether or not PP was used during their ICU stay. Descriptive statistics values for ICU hospitalization days, OTI days and death rates, according to whether or not PP was used, are described in Table 2. The distributions of ICU hospitalization days and OTI days, according to PP use, can be seen in Figure 1.

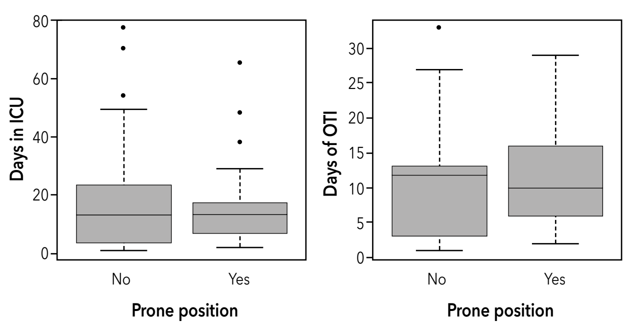

Figure 1 - Boxplots for days in intensive care unit (ICU) and for days of orotracheal intubation (OTI) according to whether or not the prone position was used.

Discussion

The results of an observational, longitudinal, retrospective study that evaluated the potential benefits of PP in COVID-19 patients with moderate to severe ARDS are described. This study demonstrated that 63% of patients had lung involvement between 50 and 70%, a condition considered serious and thus a predictor of increased risk for mortality.[11]

Table 1 - Frequency distribution (n and %) or summary measures of demographic and clinical characteristics according to group

Variable	Prone position		Total (n = 43)	p-value
	No (n = 21)	Yes (n = 22)		
Age (years)*	50.0 (39 - 71)	59.5 (55 - 66)	59.0 (48 - 70)	0.207
Sex (male)**	12 (57.1)	15 (68.2)	27 (62.8)	0.454
Lung involvement (%)**				
< 25	5 (23.8)	2 (9.1)	7 (16.3)	0.424
25 - 50	3 (14.3)	2 (9.1)	5 (11.6)	
50 - 70	12 (57.1)	15 (68.2)	27 (62.8)	
> 70	1 (4.8)	3 (13.6)	4 (9.3)	
Comorbidities**				
Diabetes mellitus	4 (19.0)	13 (59.1)	17 (39.5)	**0.007**
Hypertension	8 (38.1)	14 (63.6)	22 (51.2)	0.094
Obesity	2 (9.5)	10 (45.5)	12 (27.9)	**0.009**
Some of the above*	9 (42.9)	18 (81.8)	27 (62.8)	**0.008**
APACHE II*	15.0 (13.0 - 19.0)	11.5 (9.0 - 16.5)	15.0 (10.0 - 18.5)	**0.011**

Note: *Median (first quartile - third quartile). **n (%). APACHE II = Acute Physiology and Chronic Health Disease Classification System II. Values in bold are statistically significant.

Table 2 - Summary of days spent in intensive care unit (ICU), days of orotracheal intubation (OTI) and death according to whether or not the prone position was used

Variable	Prone position		Total (n = 43)	p-value
	No (n = 21)	Yes (n = 22)		
Days of OTI*	12 (3.0 - 13.0)	10 (6.0 - 15.5)	10 (4.5 - 15.0)	0.772
Days in ICU*	13 (4.0 - 23.0)	13 (7.2 – 17.0)	13 (7.0 - 21.5)	0.453
Death**	15 (71.4)	15 (68.2)	30 (69.8)	0.817

Note: *Median (first quartile - third quartile). **n (%).

A semiquantitative score was used to classify the extent of lung involvement, such as more or less dense consolidations on chest tomography, and those who displayed involvement above 51% were considered severe.[11]

Our results demonstrated that patients admitted to the ICU were predominantly male, of advanced age, with at least one reported comorbidity. These data corroborate a systematic review and meta-analysis published by Ng et al.,[12] where comorbidities were analyzed in patients with ARDS secondary to COVID-19. The authors found a higher incidence in severe and fatal cases, with those who were older and with pre-existing comorbidities including hypertension, obesity and diabetes being the most prevalent. Such data are in line with what was identified in the present study, where 51.2% of patients were hypertensive, 39.5% diabetic and 27.9% obese. Most patients who underwent proning were hypertensive. A previous study demonstrated that the risk of mortality increased 2.1 times in patients with hypertension, indicating a significant effect on mortality in patients with ARDS secondary to COVID-19.[12]

Patients who underwent PP remained hospitalized in the ICU one day less than patients who were not prone, but without showing statistical significance. Regarding intubation time and death rate, there was similarly no significant difference between patients who were put in prone position and those who were not. Therefore, it was not possible to associate PP with the length of hospital stay, days of OTI and occurrence of death. Patients who underwent PP during hospitalization had lower APACHE II score values than those who were not put in prone position, demonstrating that they had less clinical severity.

Of the 43 patients who were intubated in the ICU and mechanically ventilated, 30 (70%) died, data that reveal a high mortality rate and corroborate the first publications from Wuhan, China, where mortality rates ranged from 86 to 97% among patients who required mechanical ventilation.[13] In the United Kingdom, 67% of those who received mechanical ventilation died, and reports from smaller cohorts in the United States indicated that 71 to 75% of those patients who received invasive mechanical ventilation died.[14,15]

It is certain that PP ventilation can improve oxygenation in critically ill patients with COVID-19; however, it is not clear whether it can reduce mortality.[16-18] In a cohort study with more than 6,000 patients admitted to the ICU with COVID-19, approximately half were treated with protective mechanical ventilation in PP, but no association was found between the early use of PP and survival in patients on mechanical ventilation with severe hypoxemia.[19]

In the present study, it was found that PP was not an effective therapeutic strategy for reducing mortality in critically ill patients, given that it may be related to the small sample size of the PP group and the greater number of patients with comorbidities in the prone patient group, worsening the prognosis.

Some limitations should be noted in this study. This was a study carried out in a single center and in an environment with limited resources, both in terms of infrastructure and technology and qualified labor. Although patients had intensive care needs, they were often treated by professionals without adequate experience, as the pandemic period forced hospitals to act on an emergency basis and many professionals were hired to meet the demand in the hospital's ICUs. The decision to start or stop the intervention was left to the team responsible for the treatment. If the staff was consulted about PP and if the patient had moderate to severe ARDS and met criteria for PP, it was considered that they could benefit from intervention in addition to protective mechanical ventilation. The results of this study should not be generalized to the entire population with ARDS resulting from other causes. The mortality rate was high (70%) and perhaps if other advanced interventions had been used alongside PP, such as extracorporeal membrane oxygenation or additional attention and care from an experienced multidisciplinary team, another outcome could have been obtained.

The present study demonstrated that the use of PP was not associated with OTI days, days spent in the ICU and patient mortality. As this was a retrospective study, the patient selection criteria did not allow controlling comorbidities, and it was evident that patients who underwent proning had higher rates of comorbidities, such as hypertension, diabetes and obesity.

It is important to highlight that the data in the medical records were structured correctly, which allowed them to be removed and the impact of PP to be assessed. The results of this study can help determine the criteria of patients who would be eligible for the adoption of PP in future studies, highlighting that PP is considered a precursor and beneficial therapy in ARDS for causes other than COVID-19.

Conclusion

This study did not demonstrate an association between PP and days of OTI, days of hospitalization and mortality in patients with severe hypoxemia; however, patients who were prone had higher rates of comorbidities, such as hypertension, diabetes and obesity. Although PP was not associated with the outcomes studied, it is important to highlight that it is a precursor and beneficial therapy in ARDS due to other causes.

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Authors' contributions

FPLS and EBG carried out data collection and prepared the article. RE conceived and designed the study and performed the analysis and interpretation of the data. LFM and JSB contributed to the preparation and review and editing of the manuscript. All authors approved of the final version.

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