

## **Difference in Days of Mechanical Ventilation in Prone Position Less than 48 Hours Compared to More than 48 Hours in Critical Patients with Sdra and Covid-19**

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### **ABSTRACT**

**Introduction:** The COVID 19 pandemic has come to change paradigms in terms of ventilatory support measures worldwide, prone ventilation was shown to decrease mortality in patients with ARDS.

**Objective:** To identify the difference in days of mechanical ventilation of patients with respiratory failure by COVID-19 in the Intensive Care Unit with prone position for  $\leq 48$  hours compared to  $>48$  hours.

**Material and methods:** We evaluated all patients admitted to the Intensive Care Unit of UMAE Hospital No. 1 de Especialidades del Bajío, who required mechanical ventilation and prone position for refractory acute respiratory failure due to SARS-CoV-2 infection, we identified those in prone position for  $\leq 48$  hours versus  $> 48$  hours (h), and we evaluated the difference in days of mechanical ventilation between the two groups, concluding who maintained more days of mechanical ventilation.

**Results:** Statistical significance was found only for the following variables: days of mechanical ventilation ( $p < 0.001$ ), days of ICU stay ( $p = 0.04$ ), time in prone position ( $p = 0.001$ ) and PaO<sub>2</sub>/FiO<sub>2</sub> ratio after maintaining prone position ( $p < 0.001$ ).

**Conclusion:** The improvement in the oxygenation index in prone position  $>48$  h is greater compared to those who remained  $\leq 48$  h, however, the time (days) under mechanical ventilation was less in the  $\leq 48$  h group; complications had no impact on the time in prone position.

**KEYWORDS:** SARS-CoV-2, ARDS, prone position, days of mechanical ventilation.

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### **INTRODUCTION**

The Coronaviridae (CoV) family has 6 phenotypes that infect humans, but 4 were identified that develop respiratory distress syndrome (1). On January 3, 2020, the new coronavirus 2019 (2019-nCoV) was identified in bronchoalveolar lavage fluid samples. (2) In Mexico, 568,621

total cases have been identified with 61,450 deaths due to COVID 19 (3).

The most commonly used serological test for diagnosis is PCR (Polymerase Chain Reaction), which identifies the RNA of the virus (4). According to studies published in the journal Radiology, computed tomography of the thorax can be a more

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reliable, practical and fast method to diagnose and evaluate COVID-19 in comparison with the PCR test, a sensitivity of 98% has been identified in comparison with that of the PCR of 71% (5).

### SEVERE RESPIRATORY DISEASE SECONDARY TO SARS-CoV-2

The latest definition for ARDS was made in Europe as the Berlin criteria define ARDS: presence of a known clinical lesion or new respiratory symptoms in less than 7 days with acute hypoxemia ( $\text{PaO}_2 / \text{FiO}_2 \leq 300$  mmHg), in a patient with a positive end-expiratory pressure (PEEP) of at least 5 cmH<sub>2</sub>O, and bilateral opacities not explained by heart failure or volume overload, patients carrying COVID 19 have demonstrated a different pattern of behavior that does not comply as pure ARDS phenotype. (6)

Shang et al. (2020) in the study entitled "Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China" makes recommendation for the use of prone positioning in patients with severe COVID-19 with a Grade 1+ (strong recommendation), where prone positioning was found to have beneficial effects on oxygenation. Currently, the duration of prone sessions is still not standardized; the PROSEVA study recommends an average of 17 h for pronation (7).

Ayzac L, et al. in a prospective, single-center study published in the Annals of Critical Medicine where they included all patients in prone position from June 2016 and January 2018 in an Intensive Care unit and performed a more focused justification. They observed beneficial effects in patients who continued in prone position after 16 h and at least up to 24 h, with objective evidence-based recommendations. A beneficial effect was observed which continued to increase after at least 24 h (7).

This study makes it reasonable to continuously leave patients in prone position until the general improvement of their condition allows to stop sedation and resume spontaneous ventilation instead of repeating the sessions. It would probably be better to extend the sessions. The beneficial effect is related to the duration in prone position, not to the maneuver itself.

We conducted this study to determine the benefit of the patient belonging to the target population remaining > 48 hours or less time, and whether that period is a determinant in the days of mechanical ventilation.

### MATERIAL AND METHODS

The study was conducted in the Intensive Care Unit (ICU) of Instituto Mexicano del Seguro Social, Unidad Médica de Alta Especialidad, Hospital de Especialidades No. 1, Centro Médico Nacional del Bajío (IMSS, UMAE HE No. 1 CMN del Bajío) León, Guanajuato. Mexico. This is an observational, comparative, analytical, retrospective study.

The primary objective was to identify the difference in days of mechanical ventilation of patients with respiratory failure by COVID-19 in the Intensive Care Unit with prone position for  $\leq 48$  hours compared to more than 48 hours.

On admission, all patients with a diagnosis of acute respiratory distress syndrome with SARS-CoV-2 infection and a positive PCR test who were admitted to the Intensive Care Unit of UMAE HE No.1 Bajío and required mechanical ventilation and prone position were evaluated according to selection, exclusion and elimination criteria; those in prone position for  $\leq 48$  hours were identified, as well as patients with > 48 hours, and the number of days of mechanical ventilation required by these patients were subsequently counted, respectively. A checklist was made according to the file sent to the bioethics committee, all the patients were entered into a database in which groups were organized according to general and specific objectives, as well as secondary ones, and a statistical analysis was performed. We identified which patients of the two groups maintained more days of mechanical ventilation in order to determine which strategy in relation to prone time had more relevance in relation to days of mechanical ventilation.

The sample calculation was obtained based on the results published by Jochmans et al. Ann. Intensive Care (2020) of the average number of days of prone position, considering an average of 24 hours, with a bilateral approach, significance level of 5 %, with alpha risk 0.05, Beta 0.20, resulting in 51 subjects in both groups, the common standard deviation was assumed to be 4 with a minimum difference to be detected of 2. The estimated number of lost cases was 0.10.

### Statistical management of the data

The exploratory analysis was determined by means of the skewness and kurtosis values of the continuous quantitative variables, whether they had normal distribution or not (Kolmogorov-Smirnoff test).

Continuous quantitative variables with normal distribution were presented as mean and standard deviation (median and percentiles, otherwise). Qualitative variables were expressed as frequencies or proportions.

Data obtained from the groups of patients who were prone for  $\leq 48$  h and those who remained in the prone position for >48 h were pooled, followed up and the days of mechanical ventilation recorded; the results were analyzed using the SPSS statistical package. Comparison of the groups for qualitative variables was performed using  $\chi^2$  (or Fisher's exact test as appropriate) and for quantitative variables with qualitative variables using Student's t test. For the comparison of quantitative variables, the t test for related samples or the Wilcoxon test was used, depending on the distribution found. Comparison of means of two or more groups was performed by ANOVA analysis or the Kruskal-Wallis test according to the reported distribution; post hoc analysis was performed with Tukey's test.

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Quantitative variables were correlated by Pearson's or Spearman's correlation coefficient according to the type of distribution of the variables. For all inferential statistical analyses, values of  $p < 0.05$  were considered significant.

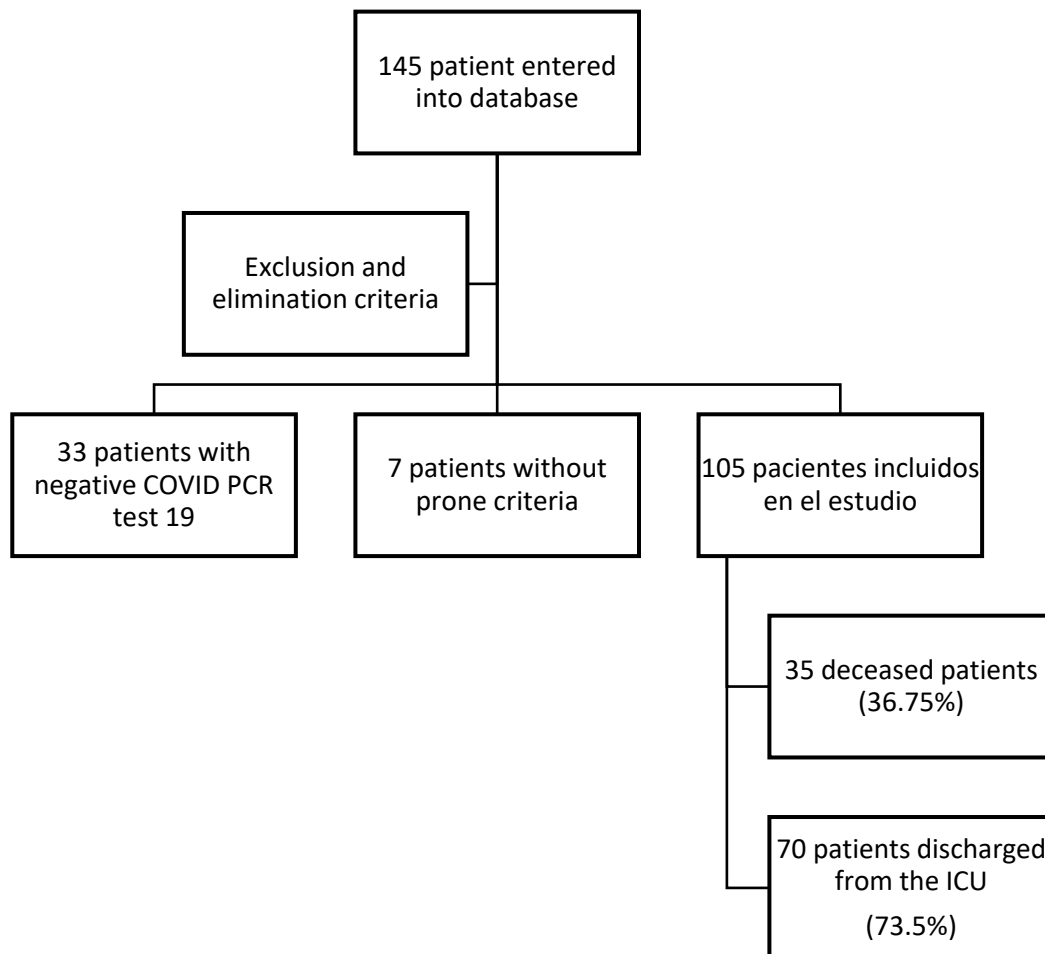
### Ethical considerations

In the study, no actions were carried out that would have entailed an added risk to those inherent to the procedures used for the diagnosis or treatment of the condition such as cabinet studies, paraclinical studies, which were explained and subsequently authorized by the patient.

Once the protocol was authorized by the Hospital's research committee with registration number R-2020-1001-129, written authorization

### RESULTS

145 patients were admitted to the ICU of IMSS, UMAE HE No. 1 CMN del Bajío, León, Guanajuato, Mexico however, when applying the selection criteria, a sample of 105 patients was obtained (Figure 1).



**Fig.1 out of 145 patients registered in the census of the intensive care unit UMAE T1 CMN El Bajío de León Guanajuato a sample of 105 patients was obtained after application of the selection criteria**

Within the demographic and clinical characteristics of the study population (Table 1) it was observed that the mean age of the subjects was 52.64 years (13.91); 69 women (66.3%) and 35 men (33.7%); with respect to anthropometry the body mass index was reported with a mean of 31.23 (5.31) kg/m<sup>2</sup>. The presence of smoking in the patients was 39 (37.5%). The comorbidities of the patients the frequencies are diabetes mellitus type 2: 41(39.4%), systemic arterial hypertension 39

(37.5%), COPD 15 (14.4%), immunocompromised 4 (3.8%). The mean length of stay in the ICU was 9.93 (13.91), the prone position time of the patients was 63.1 h (38.13), the PaO<sub>2</sub>/FiO<sub>2</sub> ratio before prone (pre) 101.42 (48.11) and PaO<sub>2</sub>/FiO<sub>2</sub> after prone (post) 240.35 (82.09). Among the side effects of prone position, tracheostomy 36 (34.6%) and facial edema 10 (9.6%) were reported.

**Table 1. Demographic and clinical characteristics of the study population**

	n= 104
Age	52.64 (13.91)
Gender	
Male	69 (66.3%)
Female	35 (33.7%)
Comorbidities	
Diabetes Mellitus type 2	41 (39.4 %)
Hypertension	39 (37.5%)
COPD	15 (14.4%)
Inmunocompromised	4 (3.8%)
Smoking	39 (37.5 %)
Antropometric measures	
Weight	85.37 ( 15.73)
BMI	31.23 (5.31)
Days of mechanical ventilation	9.13 (5.29)
Intensive Care Unit days	9.93 (13.91)
Prone position (hours)	63.15 (38.13)
PaO <sub>2</sub> /FiO <sub>2</sub> before prone position	101.42 (48.11)
PaO <sub>2</sub> /FiO <sub>2</sub> after prone position	240.35 (82.09)
Prone position side effects	
Tracheostomy	36 (34.6%)
Facial edema	10 (9.6%)

*Values not represented as percentages refer to means (SD).*

Subsequently, the population was categorized into two groups according to the time they remained in prone position  $\leq 48$  hours (n=51) and  $> 48$  hours (n=53), the demographic characteristics of both groups are described in (Table 2), reporting statistical significance only for the variable BMI (p= 0.042), days of mechanical ventilation (p=  $<0.001$ ), days of ICU stay (p=0.04), time in prone position (p=0.001) and PaO<sub>2</sub>/FiO<sub>2</sub> ratio after maintaining prone position (p= $<0.001$ ).

No statistical significance was reported in the PaO<sub>2</sub>/FiO<sub>2</sub> ratio before prone position with a mean in the  $\leq 48$ -hour group

of 99.3 (33.3) and  $> 48$  hours of 103.46 (59.23) with a p=0.661.

**Table 2. Table by groups of ≤ 48 hours and > 48 hours (prone position)**

	≤ 48 hours (n51)	> 48 hours (n53)	p- value
Age	51.29 (13.197)	53.94 (14.585)	p= 0.497 <sup>a</sup>
Gender n (%)			
Male	33 (64.7%)	36 (67.9%)	p= 0.836
Female	18 (35.35%)	17 (32.1%)	
Deceased n (%)	19 (37.3%)	16 (30.2%)	p=0.535
Comorbidities			
Diabetes Mellitus 2	19 (37.3 %)	22 (41.5%)	p=0.692
Hypertension	15 (29.4%)	24 (45.3%)	p=0.109
Inmunocompromised	3 (5.9 %)	1 (1.9%)	p=0.358
Smoking	16 (31.4%)	23 (43.4%)	p=0.229
COPD	6 (11.85%)	9 (17.0%)	p=0.579
Intensive Care Unit days	8.2 (5.26)	11.6 (6.54)	p= <u>0.004</u> <sup>a,c</sup>
Patient weight	86.91 (17.33)	83.9 (14.02)	p=0.332
BMI	32.31 (5.47)	30.2 (4.99)	p=0.042
Mechanical ventilation (days)	5.96 (4.28)	12.9 (4.2)	p= <u>&lt;0.001</u> <sup>a,c</sup>
PaO <sub>2</sub> /FiO <sub>2</sub> before prone position	99.3 (33.33)	103.46 (59.23)	p=0.661
Prone position (hours)	30.39 (14.3)	94.68 (24.95)	p= <u>0.001</u> <sup>a,c</sup>
PaO <sub>2</sub> /FIO <sub>2</sub> after prone position	201.43 (74.35)	277.79 (71.54)	p= <u>&lt;0.001</u> <sup>a,c</sup>

*Values not represented as percentages refer to means (SD).*

<sup>a</sup> *t test*

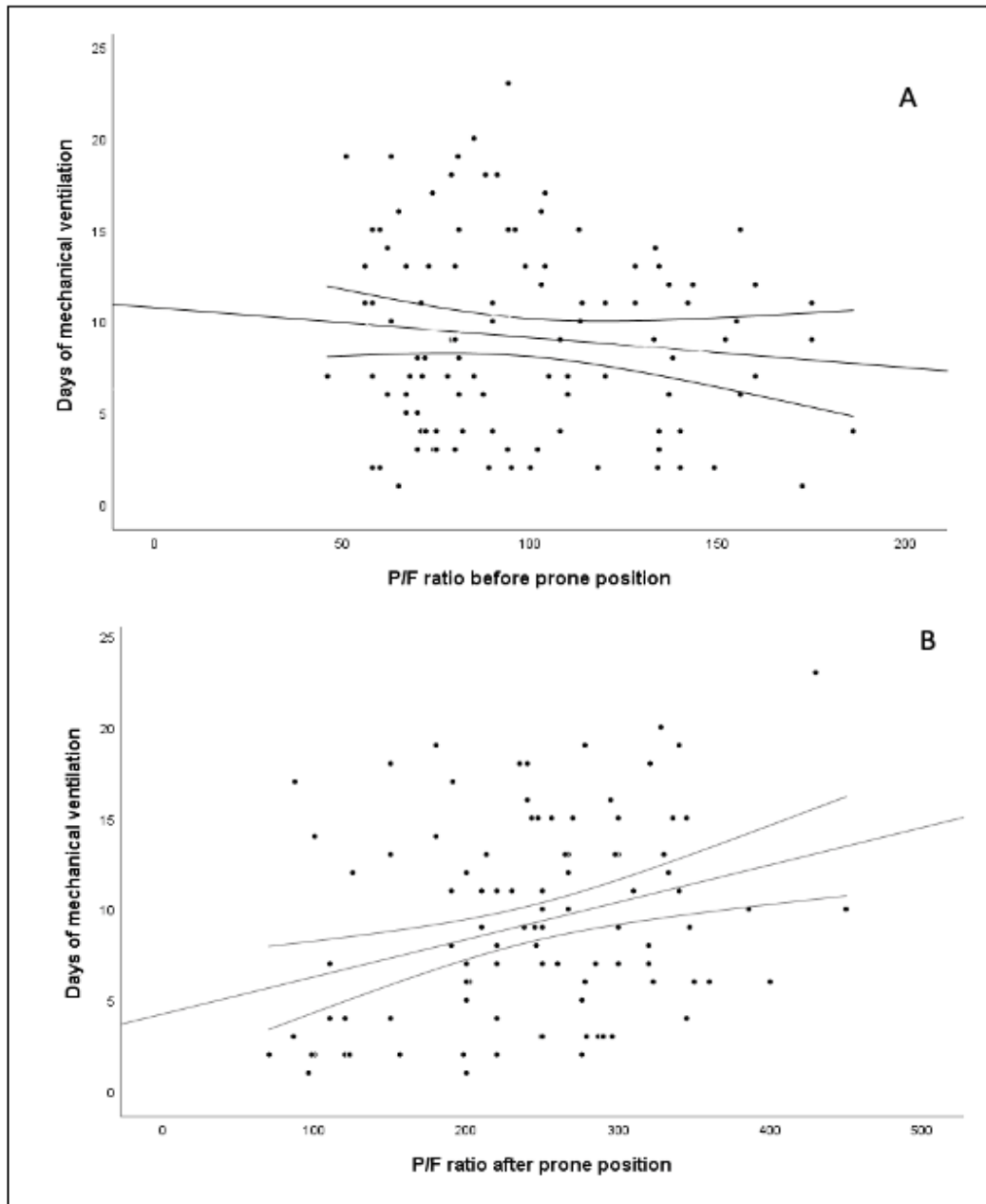
<sup>b</sup> *chi square test*

<sup>c</sup> *statistical significance for p-value*

Then the correlation between the oxygenation indexes with the time spent by the patients in prone position was performed. It was reported as follows: PaO<sub>2</sub>/FiO<sub>2</sub> ratio pre with time in prone, r = - 0.047 p= 0.633; PaO<sub>2</sub>/FiO<sub>2</sub>post ratio with time in prone, r = 0.411 p= <0.001.

As well as the oxygenation indexes with the days of mechanical ventilation, we found the following, correlation between PaO<sub>2</sub>/FiO<sub>2</sub> ratio before prone position with days of mechanical ventilation with r = -0.062 p=0.532 and PaO<sub>2</sub>/FiO<sub>2</sub> after prone position with days of mechanical ventilation with r = 0.315 p=0.001. (Figure 2).

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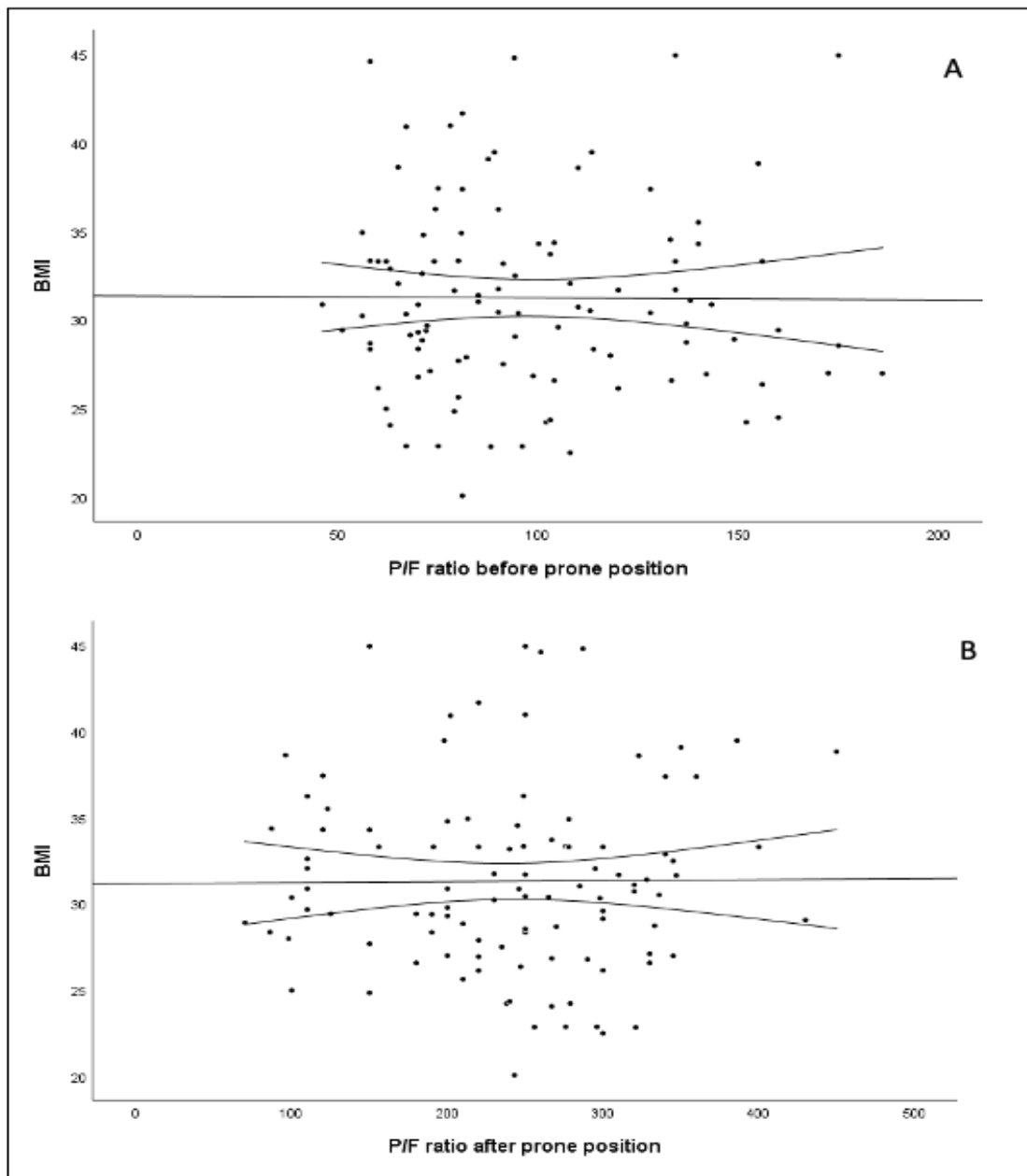


**Fig. 2 Correlation between oxygenation index with days of mechanical ventilation: 2A. PaO<sub>2</sub>/FiO<sub>2</sub> before prone position with days of mechanical ventilation (r = - 0.062, p=0.532) 2B. PaO<sub>2</sub> /FiO<sub>2</sub> after prone position with days of mechanical ventilation (r = 0.315, p=0.001).**

Oxygenation indexes were also related to anthropometric measures such as body mass indexes reporting PaO<sub>2</sub>/FiO<sub>2</sub>

before prone position / BMI r= 0.08, p=0.411 PaO<sub>2</sub>/FiO<sub>2</sub> after prone position/ BMI r=0.004, p=0.971. (Figure 3).

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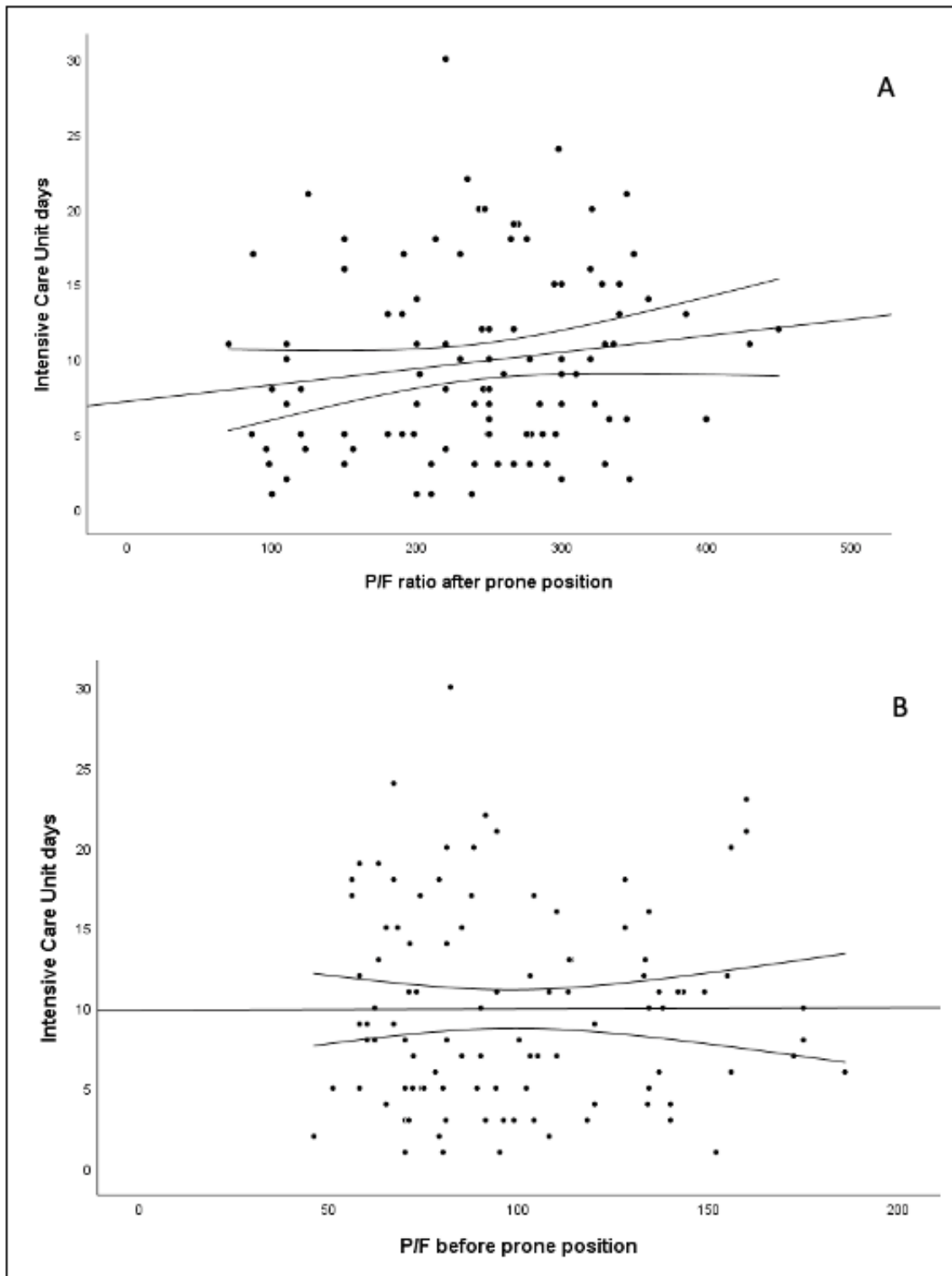


**Fig. 3 Correlation between oxygenation index with anthropometric measures such as body mass index: 3A. PaO<sub>2</sub>/FiO<sub>2</sub> before prone position / BMI (r= 0.08, p=0.411) 3B. PaO<sub>2</sub>/FiO<sub>2</sub> after prone position / BMI (r=0.004, p=0.971).**

Oxygenation indexes were also related to Intensive Care Unit days, reporting the following: PaO<sub>2</sub>/FiO<sub>2</sub> before prone

position / ICU days (r= 0.023, p=0.818), PaO<sub>2</sub>/FiO<sub>2</sub> after prone position/ ICU days (r=0.154, p=0.118) (Figure 4).

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**Fig 4. Correlation between oxygenation index with Intensive Care Unit days reported as follows: 4A. PaO<sub>2</sub>/FiO<sub>2</sub> before prone position / ICU days (r= 0.023, p=0.818); 4B. PaO<sub>2</sub>/FiO<sub>2</sub> after prone position / ICU days of stay (r=0.154, p=0.118).**

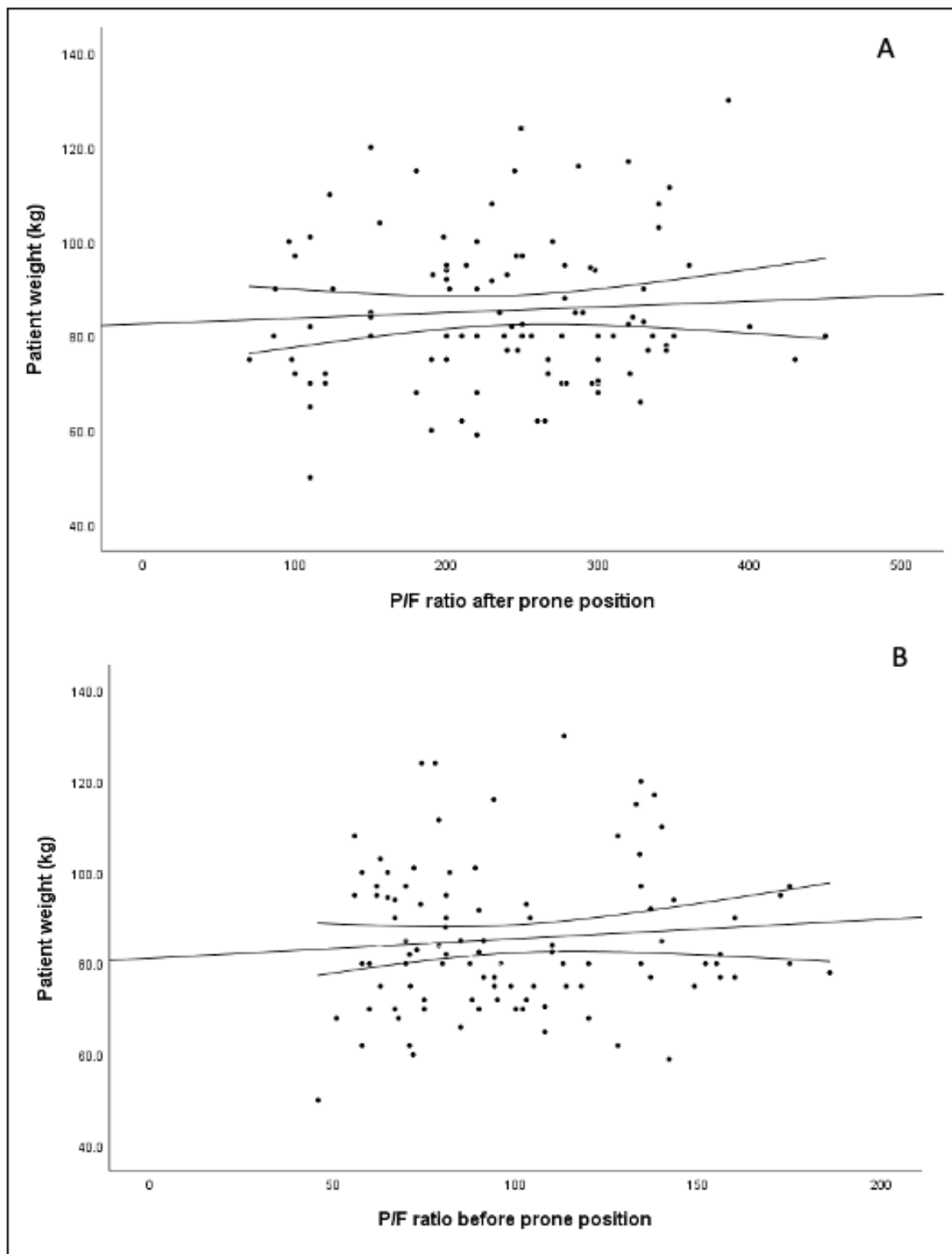
Oxygenation index with weight were also related without statistical significance PaO<sub>2</sub>/FiO<sub>2</sub> before prone position / patient weight (kg) (r= 0.042, p=0.670), PaO<sub>2</sub>/FiO<sub>2</sub> after

prone position/ patient weight (kg) (r=0.060, p=0.546) (Figure 5).



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**Fig**



**Fig5. Correlation between oxygenation index with patient weight: 5A. PaO<sub>2</sub>/FiO<sub>2</sub> before prone position /patient weight (r= 0.042, p=0.670); 5B. PaO<sub>2</sub>/FiO<sub>2</sub> after prone position /patient weight (r=0.060, p=0.546).**

The sample was categorized according to the groups of the study ( $\leq 48$  hours compared with  $>48$  hours prone position),

however no significant p-values were found in any of the groups.

**DISCUSSION**

The pandemic generated in the month of December 2019 changed paradigms in terms of ventilatory support measures

worldwide, initially in mid-February; the World Health Organization (WHO) operationally defined "coronavirus disease 2019 (COVID-19)". (8)

## Difference in Days of Mechanical Ventilation in Prone Position Less than 48 Hours Compared to More than 48 Hours in Critical Patients with Sdra and Covid-19

The Coronaviridae (CoV) family is distinguished by being viruses with an RNA genome which can measure from 26 to 32 kb in length, and are classified into 4 types this family of viruses infects humans, as well as several species of animals which may or may not develop specific symptomatology, there are 6 phenotypes that infect humans, but 4 were identified that can develop respiratory distress syndrome with its own complications (9). On January 3, 2020, in bronchoalveolar lavage fluid samples, the new coronavirus 2019 (2019-nCoV) was identified as the cause of the new symptomatology (10) (9).

There is a wide variety of clinical manifestations in patients with SARS-CoV-2 in endemic areas, ranging from an asymptomatic phenotype, acute respiratory distress syndrome (ARDS) or even multiple organ failure (MOF) and subsequent death. Since its inception in various study protocols, fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased white blood cell counts and radiographic evidence of pneumonia have been clinically reported. Organ dysfunction, shock, ARDS, acute cardiac injury and acute kidney injury, and death can occur in severe cases. (11)

SARS-CoV-2 disease led to a great deal of research aimed at determining the best tool for mechanical ventilation in patients who develop ARDS. However, despite multiple data regarding ventilatory management secondary to complications such as ARDS due to SARS-CoV-2, all results remain unclear or contradictory as the disease came to change many paradigms in ventilatory therapeutics.

Patients with severe and later critical illness develop ARDS, hence its importance in proper ventilatory protocols. Acute respiratory distress syndrome is an entity defined by the American European Consensus Conference as the most severe form of acute lung injury, and in this understanding it is a critical pathology; it is an inflammatory process that leads to pulmonary edema and has as immediate consequences deep hypoxemia, decreased pulmonary distensibility and increased pulmonary short circuits and increased dead space. At the histopathological level, severe inflammatory damage to the alveolar-capillary barrier, depletion of surfactant factor and loss of effective lung tissue were observed (12).

The latest definition for ARDS was made in Europe as Berlin criteria in which it defines ARDS by the presence of a known clinical lesion or new respiratory symptoms in less than 7 days, with acute hypoxemia ( $\text{PaO}_2 / \text{FiO}_2 \leq 300$  mmHg), in a ventilated patient with a positive end-expiratory pressure (PEEP) of at least 5 cm  $\text{H}_2\text{O}$ , and bilateral opacities not fully explained by heart failure or volume overload, in this same consensus use the  $\text{PaO}_2 / \text{FiO}_2$  ratio to distinguish severity: mild ( $200 < \text{PaO}_2 / \text{FiO}_2 \leq 300$  mmHg), moderate ARDS ( $100 < \text{PaO}_2 / \text{FiO}_2 \leq 200$  mmHg) and severe ARDS ( $\text{PaO}_2 / \text{FiO}_2 \leq 100$  mmHg). A number of pathologies condition critical state and develop ARDS with the same pathophysiology, patients with COVID 19 have demonstrated a different

pattern of behavior that in some cases of pulmonary involvement does not comply as a phenotype of pure ARDS (13).

Prone ventilation has been shown to substantially decrease mortality in patients with ARDS, in the context of this epidemic has also shown improvement and decreased mortality in patients who develop severe ARDS by COVID-19, in multiple trials these benefits demonstrated significant improvement in survival of patients with prone positioning. However, several meta-analyses have suggested that survival is significantly improved with prone positioning compared to supine positioning among patients with severely hypoxemic ARDS, the advantages to changing this position were first described by Douglas et al. (1977). Piehl et al. (1976) reported that oxygenation improved when the position was changed from supine to prone position (14).

Taking into account these pathophysiological aspects of the progression of COVID-19 pneumonia to non-classical ARDS, protocols have been developed that correlate the use of this maneuver to improve  $\text{PaO}_2/\text{FiO}_2$  indices in patients with COVID-19.

Shang et al. (2020) in the expert statement entitled "Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China" a recommendation is made for the use of prone positioning in patients with severe COVID-19 with a Grade 1+ (strong recommendation), where it was found that prone positioning has beneficial effects on oxygenation, lung recruitment support maneuver, perfusion ratio, improved oxygenation and  $\text{CO}_2$  elimination, homogeneous distribution of ventilation and reduced risk of VILI (Ventilator Induced Injury). In addition to making this recommendation they emphasize initiating early pronation in moderate to severe ARDS ( $\text{PaO}_2/\text{FiO}_2 < 150$  mmHg), and/or hypercapnia (15,16,17).

One of the large studies that began to standardize prone positioning in patients with ARDS secondary to SARS-CoV-2 was in Jiangsu province. They identified patients with ARDS or extensive pleural effusion and initiating the use of high-flow nasal prongs or noninvasive mechanical ventilation (NIV), and prone position with which they presumably avoided fluid overload. In those who presented deterioration of  $\text{PaO}_2/\text{FiO}_2$  and required advanced airway management, the prone position was used for more than 16 h. The second study reports the experience in a Wuhan Hospital, where patients with a  $\text{PaO}_2/\text{FiO}_2$  less than 150 mmHg were placed in prone position for 24 h. In total, seven of 12 patients included in the study spent at least one day in prone position (18).

Currently the duration of prone sessions is still not standardized, defined or clear, the latest international recommendations is to leave the patient at least 12 h (22), however in the PROSEVA study an average of 17 h is recommended for pronation, other meta-analyses included

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recommendations from 7 to 18 h however with many biases, since the prone position depended on the shifts of health workers, parameters outside lung protection and risks in contagiousness of changes in position. (19)

Further research on prone positioning should address treatment sessions and timing of intervention; prone positioning in combination with optimal tidal volume and PEEP; and different target populations, assessing outcomes such as major morbidities, patient safety, and mortality. (20) The efficacy of prone decubitus in terms of mortality was demonstrated when sessions were 8 hours per day and subsequently extended to 16 hours. It has not been reported whether more time could benefit us in increasing oxygenation indices, except for the study reported by Sebastien Jochmans et. al. (2020) where he concluded that prone position sessions should be prolonged for at least 24 h and extended if the PaO<sub>2</sub>/FiO<sub>2</sub> ratio at 24 h remains below 150 (21), therefore, thinking that the more hours in prone decubitus, the less lung injury induced by ventilation, improvement of oxygenation indices and fewer days of mechanical ventilation was the justification for the study.

Within all the demographic characteristics of the study with a total of 104 patients, a mean age of 52 years was observed with a predominance of men as a result of ARDS secondary to SARS-CoV-2 infection, in the 2016 study by P. Concha et. al. where prolonged prone decubitus was evaluated, they included 17 patients with similar demographic characteristics to this study where the predominant sex was male (60%) with a mean age of 60 years (22).

In the study, statistical significance was reported in the days of mechanical ventilation with a  $p = <0.001$ , for the group of patients with a time of  $> 48$  hours in prone position a mean number of days of mechanical ventilation of 12.4 days was reported (4.2) and for those with 48 hours a mean of 5.96 days of mechanical ventilation was reported (4.28), resulting in fewer days of mechanical ventilation in those who underwent fewer hours of prone position, in the study of P. Concha et. Al. (2016) reported a mean of 25 days of mechanical ventilation with 85 % of sessions prolonged more than 24 hours however the population was not categorized, and the sample is smaller than the one included in this study. Statistical significance was reported in the days of mechanical ventilation with a  $p = <0.001$ , for the group of patients with a time of  $> 48$  hours in prone position a mean number of days of mechanical ventilation of 12.4 days was reported (4.2) and for those with 48 hours a mean of 5.96 days of mechanical ventilation (4.28), resulting in fewer days of mechanical ventilation in those who underwent fewer hours of prone position; P. Concha et. Al. (2016) reported a mean of 25 days of mechanical ventilation with 85 % of sessions prolonged more than 24 hours however the population was not categorized, and the sample is smaller than the one included in this study.

Regarding the days of stay in ICU Jordi Mancebo et. Al. (2005) Multicenter trial of mechanical ventilation in prone position ( $>16$ h) included 136 patients and reported that the length of stay in the intensive care unit was shorter in non-survivors compared to survivors, but did not differ between the supine and prone groups unlike what was reported in this study where fewer days of stay in the ICU were recorded, for the 48-hour group with a mean of 8.2 days (SD) compared to the  $> 48$  hours group with a mean of 11.6 days (SD),  $p = 0.004$ . (23)

For the 48-hour group, a mean of 30.39 h (14.3) was reported vs. the  $>48$  h group, with a mean of 94.68 h (24.95), with significant difference  $p = 0.001$  in comparison with the study by Sebastien Jochmans et. al. (2020), descriptive, single-center study where the duration of prone decubitus sessions was evaluated and it was found that the duration (h) in prone position where the maximum effect is obtained is between 16 h and 18 h, with no significant difference.

The same study reported a delta of the PaO<sub>2</sub>/FiO<sub>2</sub> index of 175 ( $p = < 0.001$ ) (with patients in prone position), categorizing the population only by the position (prone), guaranteeing at least 24 h. However, in this research work we obtained a significant difference ( $p = <0.001$ ) for the PaO<sub>2</sub>/FiO<sub>2</sub> ratio after the prone session with a mean of 240.35 (82.09), likewise in the 48-hour group we obtained a mean of 201.43 (74.35) vs. the  $> 48$ -hour group 277.79 (71.54). 79 (71.54) and we concluded that the patients who underwent prone ventilation for more than 48 hours obtained an improvement in their PaO<sub>2</sub>/FiO<sub>2</sub> indices, which supports us that sessions of more than 48 hours of prone ventilation provide greater improvement in PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

In the study by David B. Page et al. (2021) specify, in addition to improvement in oxygenation indices, some interesting data. In their study evaluating 57 patients, at 96 h, patients randomized to a prolonged prone position had a higher total duration in the prone position (56.6 vs. 45.7 h;  $p = 0.02$ ). Those in the prolonged prone positioning arm had longer duration in h with a mean (23.1 vs. 14.9 h;  $p < 0.01$ ) and similar duration of supine sessions (9.0 vs. 11.5 h;  $p = 0.46$ ). They also reported that patients in the traditional prone group (16 h) had a mean of 5.81 ICU days, 4.15 without ventilator and 2.58 days without hospitalization; patients in the prolonged pronation group had 6.27 without ventilator, 4.35 without ICU and 2.25 days without hospitalization (24).

In the comparative study of P. Concha et al. (2016), complications due to prone position were reported without statistical significance, in the first study it was reported that the most frequent adverse effect in 100% of patients was facial edema, the rate of pressure ulcers of grade  $\geq 2$  at day 7 of the beginning of prone decubitus was 47% in face and 29% in thorax however with remission at discharge of patients. In this study, a significant relationship was obtained between prone time in hours / adverse effects on pronation with an  $r =$

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0.312,  $p=0.087$ , which shows that adverse effects should not be a limiting factor for hours in prone.

In the study by Filippo Binda et al. (2021) supported the results regarding complications secondary to prone positioning they concluded that the use of prone positioning in patients with COVID-19 was a safe and feasible treatment, also in obese patients, who might deserve more vigilance and active prevention by intensive care unit staff.(25)

### CONCLUSION

In patients with ARDS due to SARS-CoV-2 the improvement in oxygenation index with prone position  $>48$  h is greater compared to those who remained  $\leq 48$  h, however, the time (days) under mechanical ventilation was shorter in the  $<48$  h group; complications had no impact on the time spent in prone.

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### CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest

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