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Impact of the prone positioning in patients with severe COVID-19 in an acute care hospital in the Autonomous City of Buenos Aires

Impacto del decúbito prono en pacientes con COVID-19 grave en un hospital de agudos de la Ciudad Autónoma de Buenos Aires

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ABSTRACT

Introduction: Prone positioning (PP) was the most used strategy in patients with COVID-19 and refractory hypoxemia. Our objective was to describe the clinical characteristics and evolution of patients with severe Covid-19 who required this procedure. Also, to evaluate the relationship between risk factors and mortality.

Materials and methods: Observational retrospective descriptive study. Patients older than 18 years with COVID-19 under mechanical respiratory assistance (MRA) who required PP were included. Follow-up was carried out for 28 days. Complications associated with PP were recorded. Factors associated with mortality were analyzed using Cox regression.

Results: PP was applied in 28 patients. The mean age was 52.43 years, and the median Charlson Score was 1 [0.00, 2.00]. The median number of MRA days was 17.00 [IQR, (interquartile range) 13.00, 23.00], and 28.6% of patients managed to be extubated. The median number of days at the ICU (Intensive Care Unit) was 19.50 [IQR 14.00, 23.50], with 53.6% mortality. 35.7% of patients needed 2 PP cycles with a predominant duration of 24-36 hours. 89.4% had pressure ulcers (PUs). Patients who died had spent fewer days at the ICU (16 vs 28; p = 0.006), and only one of them had managed to be extubated (1 vs 7, p = 0.011). No factors associated with mortality were found in the Cox regression.

Conclusion: the study population consisted predominantly of males, average age close to the fifth decade, with a mortality of approximately 50%. No statistically significant relationship was found between risk factors and mortality.

Key words: COVID-19, Care units intensive, Prone position, Coronavirus SARS, Decubitus ulcers

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RESUMEN

Introducción: El decúbito prono (DP) fue la estrategia más utilizada en paciente con COVID-19 e hipoxemia refractaria. Nuestro objetivo fue describir las características clínicas y evolución de los pacientes con Covid-19 grave que requirieron este procedimiento. Evaluar la relación entre factores de riesgo y mortalidad.

Materiales y métodos: Estudio descriptivo retrospectivo observacional. Se incluyeron los pacientes mayores de 18 años con COVID-19 bajo asistencia respiratoria mecánica (ARM) que requirieron DP. Se efectuó seguimiento durante 28 días. Se registraron las complicaciones asociadas al DP. Se analizaron factores asociados a la mortalidad utilizando regresión de Cox.

Resultados: Se realizó DP en 28 pacientes. La edad promedio fue de 52.43 años y una mediana de Score de Charlson de 1 [0.00, 2.00]. La mediana de días de ARM fue de 17.00 [RIQ 13.00, 23.00] y un 28,6% logró ser extubado. La mediana de días en UTI fue de 19.50 [RIQ 14.00, 23.50] con una mortalidad del 53,6%. El 35,7% necesito 2 ciclos de DP con una duración predominante de 24-36 hs. El 89,4% tuvo lesiones de UPP. Los que fallecieron tuvieron menos días de UTI (16 vs 28; p=0,006) y solo uno de ellos había logrado ser extubado (1 vs 7, p = 0.011). No se encontraron factores asociados a la mortalidad en la regresión de Cox.

Conclusión: La población estudiada resultó predominantemente masculina y de edad promedio cercana a la quinta década de vida, con una mortalidad aproximada al 50%. No se encontró relación estadísticamente significativa entre factores de riesgo y mortalidad.

Palabras claves: COVID-19, terapia intensiva, decúbito prono, úlceras por presión

INTRODUCTION

Since the beginning of 2020, the new disease COVID-19, caused by the SARSCoV-2 virus, has overwhelmed the Intensive Care Units (ICUs) around the world with large volumes of critically ill patients. As of October 2021, approximately 238,390,000 cases and 4,859,000 deaths have been reported worldwide.[1] COVID-19 infection affects the respiratory system and causes acute respiratory distress syndrome (ARDS) in 61-81% of patients, with severe bilateral interstitial pneumonia, which require intensive care.[2, 3]

Epidemiological information about patients with severe COVID-19 in low- and middle-income populations has been scarce, but some Latin American countries with national-level databases have reported valuable information.[4, 5] In Argentina, the Argentine Society of Intensive Care launched a prospective multicenter cohort study with the objective of describing epidemiological and clinical characteristics, treatments received, and outcomes in COVID-19 patients who required invasive mechanical ventilation[6] during the first outbreak of the pandemic. This study has been very helpful to face the second wave in our country.

The marked decrease in mortality observed in several studies that were carried out in the last 15 years[7] supports the use of prone positioning (PP) along with the strategy of protective lung ventilation as part of the treatment of refractory hypoxemia in ARDS.[8] The response may differ from one patient to another, but PP results in improvements in respiratory mechanics, gas exchange, and a reduction in pulmonary heterogeneity, potentially decreasing the risk of developing mechanical ventilation-induced lung injury.[9]

However, prone positioning also has complications, such as: unplanned extubation, accidental removal of arterial or venous catheters, hemodynamic instability, brachial plexus injury, corneal injuries, and pressure ulcers (PUs).[10, 11]

The ICU is a risk area in terms of the development of pressure injuries. Patients in the ICU mostly have altered consciousness due to the effects of analgesic-sedative drugs; they may have numerous catheters, access routes, and monitoring sensors that can be poorly positioned; excess moisture in the area that may increase the risk of developing pressure ulcers by five times.[12]Also, tissue oxygenation may be altered due to failure of the pulmonary ventilation/perfusion ratio, and the use

of vasoactive drugs that can lead to vasoconstriction, reducing peripheral capillary flow. Moreover, critically ill patients undergo metabolic changes that can lead to negative nutritional balance and hypoalbuminemia, resulting in an increase in edema[13]. The analysis of Ponsetti et al about PP complications concludes that there are fewer PUs in patients who have received adequate nutrition, with a very high percentage of patients in prone position experiencing malnutrition (82.9%) during their hospitalization at the ICU.[10] All of these factors contribute to the formation of PUs and difficulty in healing.

The primary objective of our study was to describe the clinical and demographic characteristics as well as the evolution of a cohort of patients with severe Covid-19 who required PP; also, to identify the prevalence of complications associated with this procedure and to evaluate the relationship between risk factors and mortality.

MATERIALS AND METHODS

A descriptive retrospective observational study was carried out during the period from May 15, 2021, to July 27, 2021, at the Hospital General de Agudos José María Penna.

The sample was collected in the Emergency Department, and Intensive Care Units were organized to meet the demand during this period.

Patients were followed up for 28 days since their admission to the ICU.

The sample included patients older than 18 years with COVID-19 who needed mechanical respiratory assistance (MRA) upon admission to the ICU and required prone positioning as a rescue maneuver for refractory hypoxemia. Patients who had missing data in the outcome variables for analysis and homeless patients were excluded; therefore, it was not possible to collect the necessary information.

Data collection was carried out through secondary sources such as patients' medical records and a form created specifically for this study by the hospital's Kinesiology Department specifically for this study. Patients' personal data were not included, instead they were coded using sequential numbers based on their admission date.

Recorded variables

Demographic data and clinical characteristics of patients were recorded, including the date of intubation, age, sex, obesity (body mass index > 30), and Charlson Comorbidity Index (CCI).

The following variables related to PP complications were gathered:

- Those associated with the rotation maneuver (caused during the procedure): accidental extubation, loss of lines.
- Those associated with the period of time spent in such position: PUs, location, corneal injuries, facial edema, shoulder injury (injuries developed by prolonged PP care), and difficult venous access (a complication that requires patients to be returned to the dorsal decubitus position in order to gain better access for line placement).
- Those associated with hemodynamia: hemodynamic instability (developed in response to the maneuver).

Recording of PUs was divided into chest, knee, frontoorbicular, foot, chin, tibia, humerus, and nose.

The other variables related to the prone positioning were: number of PP cycles (recorded up to a maximum of six cycles) and duration of each cycle (divided into four groups according to the time spent in PP: 6 hr-8 hr, 12 hr-16 hr, 24 hr-36 hr, 48 hr-72 hr).

In addition, data related to hospital stay were collected: days of MRA, days of ICU stay, weaning from MRA, extubation, tracheostomy, decannulation, and ICU discharge status (alive/dead).

Then, the sample was divided into surviving and deceased patients, and the same variables mentioned above were compared between these two groups.

We evaluated potential risk factors explaining mortality in our patient cohort. Some of them were: age, sex, CCI, obesity, number of prone cycles, extubation, and tracheostomy.

Procedure

In order to standardize care, a PP protocol was applied to COVID-19 patients that covered clinical criteria for installing the decubitus, performing the procedure, and ending it.

Before considering PP, each patient was ventilated with a protective ventilation strategy (tidal volume 6-8 ml/kg of predicted body weight, titrated PEEP [positive end-expiratory pressure], plateau pressure <30 cmH_2O, working pressure <16 cmH_2O, and FiO2 with a target SpO_2 of 88-92%).[9] If despite this ventilatory strategy, the PaO_2/FiO_2 was <150 with FiO2> 0.6, the patient was subjected to the prone positioning.

Considering the critical conditions of patients with COVID-19, at least four healthcare professionals and an experienced team leader (physicians, kinesiologists, and nurses) were required during the maneuver to coordinate each step, so as to minimize all possible risks.

Statistical analysis

Continuous variables were described as mean and standard deviation or median (Mn) and interquartile range (IQR 25:75), as appropriate, based on the Lilliefors normality test. Categorical variables were reported as frequency and percentage. The comparison between the different groups was carried out using the Student's t-test, Wilcoxon test, or Fisher's exact test. A Cox regression was conducted to search for risk factors associated with mortality.

RESULTS

Between May 15, 2021, and July 27, 2021, 50 patients diagnosed with COVID-19 were admitted to the ICU, of whom 45 (90%) required MRA, and 28 patients required prone positioning for the treatment of refractory hypoxemia, forming the final sample (Figure 1).

The cohort of patients who required prone positioning had a mean age of 52.43 (± 9.54) years, with a majority of male patients (75%), a mean

Charlson Score of 1 [0.00, 2.00]; and 50% (14) had obesity. The median number of MRA days was 17.00 [IQR 13.00, 23.00] and 28.6% (8) managed to be weaned and extubated at the ICU. 14.8% (4) had to be tracheostomized due to prolonged mechanical ventilation. The median number of days at the ICU was 19.50 [IQR 14.00, 23.50], with 53.6% mortality (15). 35.7% (10) of the patients required 2 cycles of PP due to a poor response to the maneuver, with a predominant time interval of 24-36 hours in all cycles (table 1.1). The more common complications were PUs, with 89.4% (25). The most frequent PUs were: facial edema in 67.9% (19) of patients, knee lesions in 57.1% (16), and fronto-orbicular lesions in 60.7% (17). Regarding the complications produced during the procedure, none of the patients presented accidental extubation and/or accidental removal of lines. (Table 1.2).

The same variables described were compared between alive and deceased groups of patients at 28 days of follow-up. It was found that those who died had spent fewer days at the ICU (16 vs 28; p = 0.006) and only one of them had managed to be extubated (1 vs 7, p = 0.011). (Table 2)

No risk factors associated with mortality were found in the Cox regression of patients who required prone positioning. (Table 3)

DISCUSSION

The new outbreak of COVID-19 in the year 2021 in Argentina brought about some differences in the clinical and demographic characteristics presented by patients, compared to the first period of the pandemic in our country.

The percentage of patients who required MRA and subsequently PP as a maneuver against refractory hypoxemia is consistent with what has been published so far.[6, 14-17]

Males were predominant in our cohort, just like in the literature[18], but age and the presence of CCI differ from other studies. Our median age (52, 43 years) is moderately lower than what has been

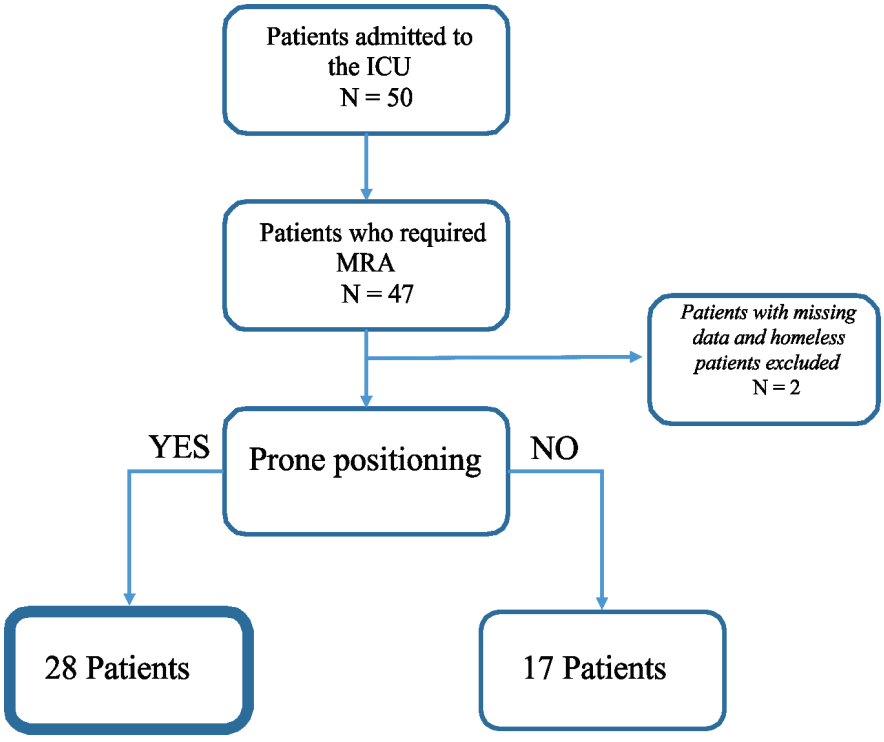

Figure 1. Flow diagram.

TABLE 1.1. Clinical and demographic characteristics of patients who required prone positioning

N	28
Area (%)	
Age (mean (SD))	52.43 (9.54)
Sex = M (%)	21 (75.0)
Charlson Index (Median [IQR])	1.00 [0.00. 2.00]
Obesity = Yes (%)	14 (50.0)
Prone positioning cycles (%)	
1	5 (17.9)
2	10 (35.7)
3	5 (17.9)
4	3 (10.7)
5	2 (7.1)
6	3 (10.7)
Time_1st_cycle (%)	
12-16 hr	1 (3.6)
24-36 hr	22 (78.6)
48-72 hr	5 (17.9)
Time_2nd_cycle (%)	
12-16 hr	1 (4.3)
24-36 hr	14 (60.9)
48-72 hr	8 (34.8)
Time_3rd_cycle = 48-72 hr (%)	5 (33.3)
Time_4th_cycle (%)	
12-16 hr	1 (11.1)
24-36 hr	6 (66.7)
48-72 hr	2 (22.2)
Time_5th_cycle (%)	
24-36 hr	3 (60.0)
48-72 hr	1 (20.0)
6-8 hr	1 (20.0)
Time_6th_cycle = 6-8 hr (%)	1 (33.3)
Extubation = Yes (%)	8 (28.6)
TQT = Yes (%)	4 (14.3)
Weaning = Yes (%)	8 (28.6)
Days of MRA (median [IQR])	17.00 [13.00. 23.00]
Decannulation = No (%)	28 (100.0)
Days at the ICU (median [IQR])	19.50 [14.00. 23.50]
Patient's condition upon discharge = alive (%)	13 (46.4)

ICU: Intensive Care Unit; TQT: tracheostomy; MRA: mechanical respiratory assistance

TABLE 1.2. Complications associated with prone positioning

PUs = Yes (%)	25 (89.3)
Chest = Yes (%)	5 (17.9)
Knee = Yes (%)	16 (57.1)
Fronto-orbicular = Yes (%)	17 (60.7)
Foot = Yes (%)	8 (28.6)
Chin = Yes (%)	8 (28.6)
Tibia = Yes (%)	6 (21.4)
Humerus = Yes (%)	2 (7.1)
Nose = Yes (%)	7 (25.0)
Accidental extubation = Yes (%)	0 (0.0)
Corneal injuries = Yes (%)	2 (7.1)
Facial edema = Yes (%)	19 (67.9)
Shoulder injury = No (%)	28 (100.0)
Hemodynamic instability = Yes (%)	9 (32.1)
Difficult venous access = Yes (%)	2 (7.1)
Accidental removal of lines = No (%)	28 (100.0)

PUs: pressure ulcers

shown in both our country and Europe.[6, 15, 19] This is possibly due to the delay in the vaccination program, which may have primarily exposed younger people during this 'second wave' while protecting the elderly. This could also explain why our CCI value is low compared to what has been described so far. In the sole multicenter study developed in Argentina on COVID-19 patients, Estensoro et al found that CCI is an independent predictor of mortality. It should be noted that although only 25% of their sample had the same age range as ours, and a large percentage of analyzed patients adopted the prone positioning, the analysis was performed on the entire patient population[6].

A meta-analysis conducted in the United States by Popkin et al found that obesity was a predictor of mortality in COVID-19 patients.[20] Although half of our patients had a BMI (body mass index) > 30, that characteristic wasn't related to this outcome, with no differences between the group of those who survived and those who died after 28 days.

Over the years, very diverse data have been reported regarding complications related to prone positioning in patients with ARDS. The study of Curley et al[21] didn't report any critical incidents in more than 200 PP procedures, while in the study by Mancebo et al, a high incidence of complications was described, and 7.9% of unplanned extubations were reported. No deaths were reported in any of them.[22] However, in their scoping review, Araújo et al found that 67% of the studies revealed complications in the use of prone positioning. The most common complications included accidental extubation (78%), pressure injury (50%), and facial edema (50%)[23]. Patients in prone position may have

TABLE 2. Comparison between groups of alive/dead patients

	Dead	Alive	p value
n	15	13	
Area (%)			0.188
Age (mean (SD))	53.20 (8.84)	51.54 (10.58)	0.654
Sex = M (%)	10 (66.7)	11 (84.6)	0.396
Charlson Index (Median [IQR])	1.00 [0.00. 2.00]	1.00 [1.00. 1.00]	0.883
Obesity = Yes (%)	7 (46.7)	7 (53.8)	1.000
Prone positioning cycles (%)			0.881
1	2 (13.3)	3 (23.1)	
2	5 (33.3)	5 (38.5)	
3	3 (20.0)	2 (15.4)	
4	1 (6.7)	2 (15.4)	
5	2 (13.3)	0 (0.0)	
6	2 (13.3)	1 (7.7)	
Time 1st cycle (%)			0.812
12-16 hr	0 (0.0)	1 (7.7)	
24-36 hr	12 (80.0)	10 (76.9)	
48-72 hr	3 (20.0)	2 (15.4)	
Time_2nd_cycle (%)			1.000
12-16 hr	1 (7.7)	0 (0.0)	
24-36 hr	8 (61.5)	6 (60.0)	
48-72 hr	4 (30.8)	4 (40.0)	
Time 3rd cycle = 48-72 hr (%)	4 (44.4)	1 (16.7)	0.580
Time 4rd cycle (%)			0.444
12-16 hr	0 (0.0)	1 (25.0)	
24-36 hr	3 (60.0)	3 (75.0)	
48-72 hr	2 (40.0)	0 (0.0)	
Time_5th_cycle (%)			0.400
24-36 hr	3 (75.0)	0 (0.0)	
48-72 hr	1 (25.0)	0 (0.0)	
6-8 hr	0 (0.0)	1 (100.0)	
Time 6th cycle = 6-8 hr (%)	1 (50.0)	0 (0.0)	1.000
PUs = Yes (%)	13 (86.7)	12 (92.3)	1.000
Chest = Yes (%)	2 (13.3)	3 (23.1)	0.639
Knee = Yes (%)	10 (66.7)	6 (46.2)	0.445
Fronto-orbicular = Yes (%)	10 (66.7)	7 (53.8)	0.700
Foot = Yes (%)	4 (26.7)	4 (30.8)	1.000
Chin = Yes (%)	6 (40.0)	2 (15.4)	0.221
Tibia = Yes (%)	5 (33.3)	1 (7.7)	0.173
Humerus = Yes (%)	2 (13.3)	0 (0.0)	0.484
Nose = Yes (%)	4 (26.7)	3 (23.1)	1.000
Accidental extubation = Yes (%)	0 (0.0)	0 (0.0)	1.000
Corneal injuries = Yes (%)	1 (6.7)	1 (7.7)	1.000
Facial edema = Yes (%)	11 (73.3)	8 (61.5)	0.794
Shoulder injury = No (%)	15 (100.0)	13 (100.0)	NA
Hemodynamic instability = Yes (%)	6 (40.0)	3 (23.1)	0.435
Difficult venous access = Yes (%)	2 (13.3)	0 (0.0)	0.484
Accidental removal of lines = No (%)	15 (100.0)	13 (100.0)	NA
Extubation = Yes (%)	1 (6.7)	7 (53.8)	0.011
TQT = Yes (%)	1 (6.7)	3 (23.1)	0.311
Weaning = Yes (%)	1 (6.7)	7 (53.8)	0.011
Days of MRA (median [IQR])	16.00 [12.50. 20.50]	26.00 [14.00. 28.00]	0.067
Decannulation = No (%)	15 (100.0)	13 (100.0)	NA
Days at the ICU (median [IQR])	16.00 [13.00. 20.50]	28.00 [17.00. 28.00]	0.006
Patient's condition upon discharge = ALIVE (%)	0 (0.0)	13 (100.0)	<0.001

ICU: Intensive Care Unit; PUs: pressure ulcers; TQT: tracheostomy; MRA: mechanical respiratory assistance

TABLE 3. Cox regression TQT: tracheostomy

Variable	Crude Odds Ratio			Adjusted Odds Ratio		
	Hazard ratio	95% CI	p value	Hazard ratio	95% CI	p value
Age	0.99	0.95-1.05	0.997	–	–	–
Sex	0.58	0.20-1.70	0.32	–	–	–
Charlson Index	1.08	0.87-1.34	0.48	–	–	–
Obesity	1.20	0.43-3.33	0.73	–	–	–
Prone positioning cycles	0.99	0.73-1.35	0.95	–	–	–
Extubation	0.20	0.03-1.55	0.13	0.15	0.02-1.1	0.07
TQT	0.21	0.03-1.64	0.14	0.15	0.02-1.2	0.07

TQT: traqueostomía

a higher risk of displacement and twisting of the orotracheal tube due to the spatial configuration of the position with respect to the airways, which causes a dilation of the airways due to gravitational action on local anatomical structures, thus leading to extubation.[24] Compared to the relatively high incidence (13.3%) observed in the study by Guérin et al[7], no accidental extubations were reported in our cohort. The detailed knowledge of the procedure and its execution by a multidisciplinary team may have contributed to this result.

The substantially higher prevalence of PUs in our sample compared to other studies could be explained by a multicausal situation.[25, 26, 27, 28] The severity of the condition, the presence of several factors (inadequate nutrition, tissue hypoxia, skin moisture, use of inotropic agents, hours of proning, etc.) that these patients suffer during their stay in the ICU, the high workload/physical and psychological exhaustion of healthcare personnel ratio may have negatively affected the quality of care, to some extent, thus explaining the high percentage of PUs. This shows that better prevention and care measures can have an impact on or reduce complication rates.[29] The presence of PUs was identified as an independent predictor of mortality in patients with MRA.[30] They increase the length of hospital stay, burden the healthcare system budget, and constitute an indicator of quality of care.[31] This highlights the importance of standardizing records, care, and prevention strategies.

The frequency of pressure ulcers found in our study is higher than that reported by two systematic reviews where pressure ulcers occurred in 34% and 43% of cases, respectively.[32, 33, 34] From a clinical standpoint, we believe it would have been important to differentiate pressure ulcers basing on severity and extension, taking into account the different impacts they have in terms of treatment and patient morbidity. In addition, in our study, pressure ulcers caused by proning developed in patients who underwent multiple PP maneuvers and remained in that position for more than 24 consecutive hours. It is important to highlight that all pressure ulcers were grade I and II, and no high-grade ulcers (III and IV) were detected. Low-grade pressure ulcers have less serious consequences, and none of our patients required special care or treatment. Once their condition improved and PP was no longer performed, the skin fully recovered in all patients. It should be noted that although there was no statistical significance between the occurrence of PUs and hours of proning, a trend was observed. Facial edema was present in a high percentage of patients, but it quickly improved upon returning to the supine position.

With regard to risk factors, preexisting conditions, age, and the CCI, along with physiological alterations (changes in oxygenation, presence of hypotension, acidosis, acute kidney injury, and activation of coagulation) and mechanical ventilation variables were independent predictors of hospital mortality in the Argentine SATICOVID study.[6] Vences et al found that also in Peru mortality was associated with age (patients aged 60 or older), inflammatory markers, and lung involvement.[35]However, in our analysis we didn't find any risk factors associated with mortality. We believe that this may be due to the age range of admitted patients that was discussed earlier, as well as the small size of the analyzed cohort.

While this is the first record and analysis carried out in our Hospital on critically ill COVID-19 patients, this study presents among its main limitations the sample size and the single-center nature of it, as well as the bias that is typical of a retrospective analysis, depending on the quality of the information collected.

During the pandemic, the extensive use of the prone position in a large number of critically ill patients represented the greatest challenge for the health team of the Intensive Care Unit[11] and offered a unique opportunity to refine clinical protocols, establish more precisely the prevalence of adverse effects and complications, and identify possible areas for improvement in the implementation of this important intervention.[14]

CONCLUSION

The study population consisted predominantly of males with an average age close to the fifth decade, and an mortality of approximately 50%. In order to improve the management of critically ill COVID-19 patients in the ICU in this pandemic context, the presence of an experienced and dedicated multidisciplinary team would imply an improvement in the procedure, resulting in a possible decrease in serious complications induced by proning. On the other hand, the prevalence of minor complications (pressure injuries) could be related to the severity of COVID-19, without a clear association with proning, thus suggesting a combination of multiple pathogenic mechanisms.

Conflict of interest

Authors have no conflict of interest to declare.

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