



# Evaluation of the efficiency and complications of the consecutive proning in COVID-19 ICU: a retrospective study

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## Abstract

**Purpose** We aimed to evaluate and compare the efficacy and complications of three consecutive prone positions (PP) in COVID-19 ICU.

**Materials and method** Patients with ARDS and placed in PP for 3 times (PP1, PP2, PP3) consecutively were included. Arterial blood gases (ABG), partial pressure of arterial oxygen/fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ ) ratios, partial pressure of carbondioxide ( $\text{PaCO}_2$ ), PEEP, and  $\text{FiO}_2$  were recorded before (bPP), during (dPP), and after (aPP) every prone positioning. Eye, skin, nerve, and tube complications related to PP were collected.

**Results** In all positions,  $\text{PaO}_2$  value during PP was significantly higher than  $\text{PaO}_2$  before and after prone position ( $p=0.001$ ).  $\text{PaO}_2$  values were similar in all (PP1, PP2, PP3) bPP arterial blood gases. We found difference in  $\text{PaO}_2$  values during prone position between the first (PP1) and second proning (PP2). When each prone was evaluated within itself,  $\text{PaO}_2/\text{FiO}_2$  increases after proning compared to before proning.  $\text{PaO}_2/\text{FiO}_2$  during PP were higher compared to before proning ones.  $\text{PaO}_2/\text{FiO}_2$  during PP1 was significantly higher compared to during PP3 ( $p=0.005$ ). In PP3, PEEP values bPP, dPP, and aPP were significantly higher than PEEP values after the second prone ( $p=0.02$ ,  $p=0.001$ ,  $p=0.01$ ). In the third prone,  $\text{PaCO}_2$  levels were higher than in PP1 and PP2. There were eye complications in 13, tube-related complications in 10, skin complications in 30, and nerve damage in 1 patient.

**Conclusion** We believe that a more careful decision should be made after the second prone position in patients who have to be placed in sequential prone position.

**Keywords** Covid -19 · Intensive Care Unit · Prone position

## Introduction

In the literature, many trials report the benefits of prone positioning in terms of oxygenation and survival in the management of acute respiratory distress syndrome (ARDS) [1–5]. Prone position which has shown to be beneficial in ARDS improves the ventilation-perfusion matching and the oxygenation by recruiting the dorsal atelectatic lung areas [6, 7]. During the COVID-19

pandemic, as recommended by the World Health Organization, many intensivists considered prone positioning as a part of invasive ventilation strategy in ARDS patients [8–10]. When looking at COVID-19-related prone position studies, the duration and the number of prone sessions vary. Although there are some studies searching about the optimum duration of the prone position, there is a paucity of publications regarding the number and effectiveness of prone sessions. The answers to the questions “Does every prone session has similar effect?” and “How many prone sessions are recommended to consider the benefit/risk ratio?” are unclear.

We conducted a retrospective study to reveal the complications and compare the outcomes of each prone session in terms of oxygenation, PEEP levels, and  $\text{PaO}_2/\text{FiO}_2$  ratios in patients who underwent three subsequent prone positions.

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## Materials and method

We designed a retrospective single center study. After Ministry of Health COVID 19 Scientific Research Evaluation Commission and Local Ethic Committee approval, thirty-one patients who had a positive test result for SARS-CoV-2 RNA through nasopharyngeal swab and underwent three subsequent prone positions for 16 h were enrolled in the study. Medical data of the patients were obtained from patients' files which are strictly filled during the pandemic. PP indication of our intensive care unit (ICU) was in case of severe ARDS with  $\text{PaO}_2/\text{FiO}_2 < 150$  despite a  $\text{PEEP} > 10 \text{ cmH}_2\text{O}$ . Hemodynamically unstable patients were not a candidate for PP. Prone positions were performed with the use of neuromuscular blocking agents and sedatives in a controlled ventilation mode. Prone positioning was performed manually by using pillows, foam face cushions, and longitudinal foams. Due to our ICU protocol and mechanical ventilator settings, the target was 6 ml/kg (ideal body weight) tidal volume and  $< 30 \text{ cmH}_2\text{O}$  end inspiratory plateau pressure, and respiratory rate was arranged in order to keep  $\text{PaO}_2$  35–45 mmH<sub>2</sub>O. All the patients were left in PP for 16 h.

Arterial cannulation was present in all patients and arterial blood gas (ABG) results (before, during, and after proning) were recorded from the patient files. The ABG before proning, after proning, and during proning were withdrawn within 10 min before, within 10 min after, and at the 8th hour of proning respectively. The ventilator settings simultaneous to ABG and calculated  $\text{PaO}_2/\text{FiO}_2$  ratios were obtained from strictly filled ICU forms. Eye, nerve, and tube-related complications were harvested from nursing care part of patients' ICU records.

In the study, version 21 of SPSS (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, USA) was used. The distribution characteristics of the variables were examined with the Kolmogorov-Smirnow and Shapiro-Wilk tests. Descriptive statistics for continuous variables were shown as mean  $\pm$  standard deviation for those with normal distribution characteristics, and as median and interquartile range for those who did not. The change clinical parameters were analyzed with the  $3 \times 3$  design and Generalized Estimating Equation Model method, taking into account the position (before, during, and after the prone) and session (first, second, and third session) variables. Bonferroni correction was used for pairwise comparisons. The threshold value for statistical significance in all analyses was accepted as  $p < 0.05$ .

## Results

Ninety-three prone sessions and 279 ABG were evaluated.

## Evaluation of $\text{PaO}_2$ results

In all positions,  $\text{PaO}_2$  value during prone position was significantly higher than  $\text{PaO}_2$  before and after prone position ( $p = 0.001$ ). In PP1,  $\text{PaO}_2$  during prone position was higher than  $\text{PaO}_2$  before and after the session ( $p < 0.001$ ).  $\text{PaO}_2$  after the session was significantly higher than before the session ( $p = 0.02$ ). In PP2,  $\text{PaO}_2$  during session was significantly higher than before and after session ( $p < 0.001$ ).  $\text{PaO}_2$  after positioning was significantly higher than before positioning ( $p = 0.03$ ). In PP3,  $\text{PaO}_2$  during the session was higher than before and after the session ( $p < 0.001$ ). There was no significant difference between  $\text{PaO}_2$  after and before positioning ( $p = 0.3$ ).

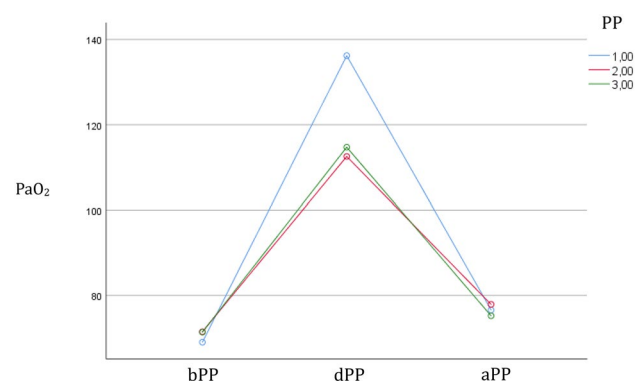
$\text{PaO}_2$  values were similar in all (PP1, PP2, PP3) bPP arterial blood gases. While  $\text{PaO}_2$  during PP2 was significantly higher than  $\text{PaO}_2$  during PP1, there was no statistical difference between PP2 and PP3 (Fig. 1).

## Evaluation of $\text{FiO}_2$ results

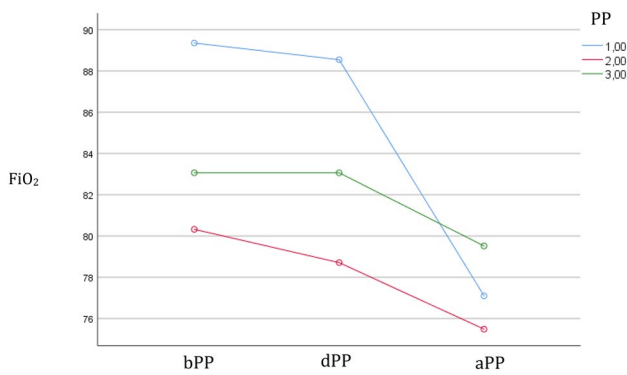
In PP1 and PP2,  $\text{FiO}_2$  levels were similar between bPP and dPP while  $\text{FiO}_2$  after proning was significantly lower than bPP and dPP ( $p = 0.001$ ,  $p = 0.004$  respectively). In PP3,  $\text{FiO}_2$  levels were similar between bPP, dPP, and aPP. In PP3,  $\text{FiO}_2$  level after proning was significantly higher than  $\text{FiO}_2$  level after PP2 (Fig. 2).

## Evaluation of $\text{PaO}_2/\text{FiO}_2$ results

When each prone was evaluated within itself,  $\text{PaO}_2/\text{FiO}_2$  ratio significantly increases after proning compared to before proning (Fig. 3).  $\text{PaO}_2/\text{FiO}_2$  ratios during prone position were significantly higher compared to before proning ones.



**Fig. 1** Partial oxygen pressure levels before prone position (bPP), during prone position (dPP), and after prone position (aPP) in the first prone position (PP1), second prone position (PP2), and third prone position (PP3)



**Fig. 2** Fraction of inspired oxygen (FiO<sub>2</sub>) levels before prone position (bPP), during prone position (dPP), and after prone position (aPP) in the first prone position (PP1), second prone position (PP2), and third prone position (PP3)

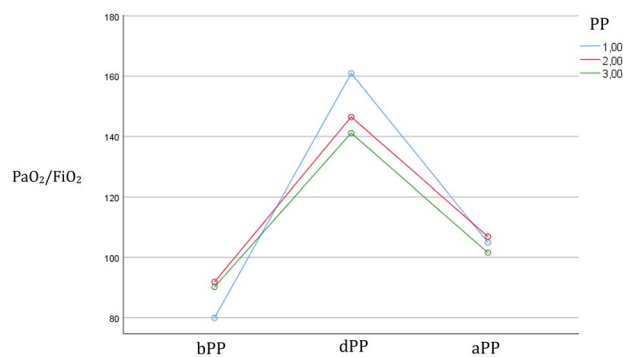
PaO<sub>2</sub>/FiO<sub>2</sub> during PP1 was significantly higher compared to PP3 ( $p=0.005$ ).

**Evaluation of PEEP results**

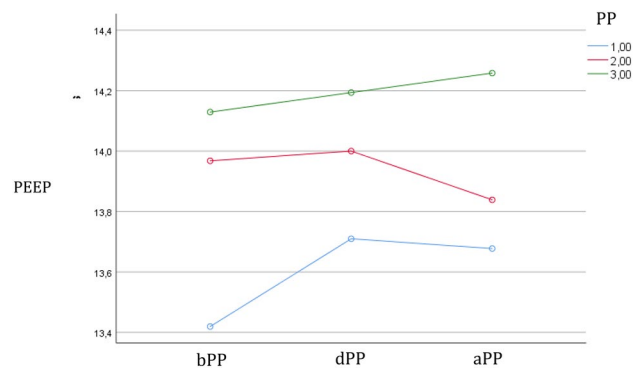
The PEEP values during PP1 and PP2, PP2, and PP3 were similar ( $p=0.1, p=0.3$ ). In PP3, PEEP values bPP, dPP, and aPP were significantly higher than PEEP values after PP2 ( $p=0.02, p=0.001, p=0.01$  respectively). In the third proning, the PEEP value after proning was significantly higher than the PEEP value before PP1 ( $p<0.05$ ) (Fig. 4).

**Evaluation of PaCO<sub>2</sub> according to prone sessions**

In PP3, PaCO<sub>2</sub> level during positioning was significantly higher than PaCO<sub>2</sub> before the session ( $p=0.05$ ). In the third prone, PaCO<sub>2</sub> level during proning was significantly higher than the PaCO<sub>2</sub> level during PP1 and PP2 ( $p=0.01, p=0.01$ ) (Fig. 5).



**Fig. 3** Partial oxygen pressure/fraction of inspired oxygen ratio, before prone position (bPP), during prone position (dPP), and after prone position (aPP) in the first prone position (PP1), second prone position (PP2), and third prone position (PP3)

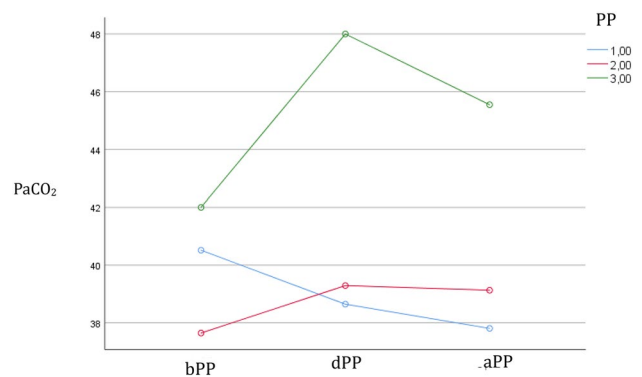


**Fig. 4** Positive end-expiratory pressure (PEEP), before prone position (bPP), during prone position (dPP), and after prone position (aPP) in the first prone position (PP1), second prone position (PP2), and third prone position (PP3)

There were eye complications in 13, tube-related complications in 10, skin complications in 30, and nerve damage in 1 patient.

**Discussion**

In the COVID-19 ICU settings, PP takes an important role as a part of the mechanical ventilation strategy against ARDS. In this study, we report the results of our study assessing and comparing the ventilator settings and arterial blood gases of each prone session of three subsequent PP. The main findings of our study are as follows: (1) in all prone sessions, PaO<sub>2</sub> and PaO<sub>2</sub>/FiO<sub>2</sub> ratios during PP were significantly higher than PaO<sub>2</sub> before and after PP; (2) in the second PP session, FiO<sub>2</sub> level during prone was significantly lower than the first and third PP; (3) PaCO<sub>2</sub> level was significantly higher in the third proning. According to these results, we can say that the least beneficial



**Fig. 5** Partial carbon dioxide pressure (PaCO<sub>2</sub>), before prone position (bPP), during prone position (dPP), and after prone position (aPP) in the first prone position (PP1), second prone position (PP2), and third prone position (PP3)

prone session was the third one. The reason for this result may be the progression of the underlying lung pathology until the third session. The PROSEVA trial revealed the beneficial effects of prone positioning during mechanical ventilator management on outcomes in terms of 28-day and 90-day mortality [1]. In the PROSEVA trial, the PP was performed everyday up to day 28, the average number sessions were  $4 \pm 4$  per patient, and the mean duration was  $17 \pm 3$  h per session. A systematic review and meta-analysis found that prone positioning at least 12 h daily reduces mortality in patients with moderate to severe ARDS ( $\text{PaO}_2/\text{FiO}_2 < 200$ ) [6]. In our retrospective study, the patients were severe ARDS with  $\text{PaO}_2/\text{FiO}_2$  ratio  $< 150$  and the duration of prone positions was 16 h with 24–48-h intervals. In their study, Jochmans et al. searched the optimal duration of PP to obtain the maximum beneficial effect and they concluded that it should be at least 24 h or longer depending on the  $\text{PaO}_2/\text{FiO}_2$  ratio [11]. The number of prone sessions per patient was  $2.2 \pm 1.8$  and the duration of proning was  $21.5 \pm 5$  h. They also reported the lung mechanic data in addition to ABG and ventilator settings. In the study, the increment of  $\text{PaO}_2$  and decrement of  $\text{PaCO}_2$  and  $\text{FiO}_2$  were significant before and after the first PP. In our study,  $\text{PaO}_2$  in bPP was significantly higher than aPP in the first ( $p = 0.02$ ) and second session ( $p = 0.03$ ), but in the third session there was no statistically significant difference ( $p = 0.3$ ). Our study does not include lung mechanics data, as in our ICU these data are not routinely recorded to patient files.

In the third prone session, PEEP values bPP, dPP, and aPP were significantly higher than PEEP values after the second prone ( $p = 0.02$ ,  $p = 0.001$ ,  $p = 0.01$ ). When we looked at the PEEP levels during prone positions, we found that there was no statistical significance between them.

Corneal abrasions, pressure ulcers, tube-related complications such as unplanned extubation, and nerve injuries are important complications of PP which are not rare [12–16]. A study reported that 77% of the patients presented pressure sore after PP therapy in the COVID-19 pandemic. An interesting result came from a meta-analysis, which showed no significant difference in ocular injury between a prone and supine group in ICU [17]. Although many studies report the PP complications in terms of ocular, skin, and tube, the number of PP sessions is unclear; we recorded our PP complications after three subsequent sessions. We had 30 skin, 13 ocular, 1 nerve, and 10 tube-related complications totally at the end of all sessions.

This study has some limitations. First the severity of COVID-19 infection may differ between patients and there is not any standard method to homogenize the patient group in terms of infectious parameters, radiological findings, and respiratory parameters. The number of our patients was

limited as our inclusion criteria required 3 consecutive prone positions of 16 h.

In conclusion, although the positive effects of the prone position have been proven in ARDS, we may not get the same response every time in consecutive positions. In our study, we observed that the positive effects decreased and the  $\text{PaCO}_2$  levels increased in third proning. Considering the difficulties of prone positioning and nerve, skin, ocular, and other complications, we believe that a more careful decision should be made after the second prone position in patients who need to be placed in sequential prone position.

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