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Is prolonged period of prone position effective and safe in mechanically ventilated patients with SARS-CoV-2? A randomized clinical trial

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ABSTRACT

Background: The novel coronavirus has been recently spreading throughout the world, causing severe acute respiratory syndrome (SARS-CoV-2) that necessitates mechanical ventilation. Prone position ventilation is an established method to improve oxygenation in severe acute respiratory distress syndrome (ARDS).
Different protocols were suggested and evaluated for prone position (PP) cycles duration. We performed a randomized controlled study to compare the standard 16 h prone ventilation against extended 24 h prone ventilation in terms of safety and efficacy.
Methods: A total of 52 patients were divided into two groups. **Group (A)** proning cycles that lasted for 16 h every 24 h, **Group (B**): prolonged proning cycles that lasted for continuous 24 h followed by 6 h supine position. Both groups received lung-protective ventilation, arterial blood gases were sampled, static lung compliance was measured before proning and one hour after return to supine position. After three successive cycles, the mean value was measured and recorded.
Results: We found that extending the duration of prone position (PP) sessions from 16 h to 24 h was associated with a significant improvement in PaO_2/FiO_2, significant elevation in static lung compliance and non-significant changes in the rate of extubation. 24 h PP was proven to be safe, with no significant elevation in the rate of complications, and nearly the same impact on survival and length of hospital stay.
Conclusion: Extending PP ventilation to 24 h for COVID-19 ARDS patients is safe and effective.
Trial registration: the trial w registered on November 2021 in ClinicalTrials.gov (CT05109624).

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Prone position; COVID-19; acute respiratory distress syndrome; lung compliance; prolonged proning; lung protective ventilation

1. Background

In December 2021, the number of global confirmed cases of the novel coronavirus disease 2019 (COVID-19) surpassed 279 million, with over 1.6 million deaths [1].

Previous studies have validated a few approaches as therapeutic options for patients with refractory hypoxemia, including higher positive end-expiratory pressure (PEEP) [2], lower tidal volume [3], neuromuscular blocking agents [4], and prone positioning [5].

Oxygenation improvement with PP ventilation in patients with severe acute respiratory distress syndrome (ARDS) was confirmed in many studies, and its application has proven to improve survival rates [5,6], the PROSEVA trial demonstrated that early application and prolonged duration of PP significantly reduced mortality in patients with moderate to severe ARDS [5].

The main mechanisms of PP in the improvement of ARDS patients' condition are reducing regional lung parenchymal heterogeneity [6], enhancing alveolar recruitment in dorsal lung regions, Proning also reduces ventral alveolar expansion and posterior alveolar collapse [7].

It may also contribute to preventing ventilator-induced lung injury (VILI). It would reduce pulmonary stress and strain by reducing the overdistension of aerated non-dependent zones and cyclical small airway/alveolar opening and closing [8,9].

However, the optimal duration of PP sessions remains unclear. It is recommended that patients be kept in PP for at least 12 h [10].

Extending the duration of PP rather than repeating it might be more beneficial since the beneficial effect is linked to the length spent in PP, not to the maneuver perse [11].

Furthermore, PP in COVID-19 patients poses a challenge for healthcare providers due to an elevated risk of exposure, isolation precautions, and sometimes limited personal protective equipment [12].

In the present study, we prospectively compared the usual 16 h PP cycles with extended 24 h PP cycles both offered with the regular lung-protective ventilation in patients with SARS COV 2 regarding the impact on the rate of successful weaning, hospital survival, length of ICU stay, feasibility, and safety.

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2. Trial registration and ethical committee approval

All procedures in studies involving human participants were performed in accordance with the ethical standards of the institutional research committee, as well as with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This work was approved by the Ethics committee of Ain Shams University Hospital (FMASU R 160/2021) on 18/9/2021. The study was prospectively registered with Trial registration and ethical approval: clinical trials (www.clinicaltrials.gov) database ID no (NCT05109624).

3. Methods and measurements

A three-month prospective randomized controlled experiment with double-blinding was conducted at Ain Shams University Hospital from 1 October 2021 to 1 January 2022.

4. Randomization and patient allocation

Eligibility criteria for this study included American Society of Anesthesiologists (ASA) physical status II–III, subjects of sexes, 18–80 years of age, severe ARDS (defined as a PaO_2/FiO_2 ratio of <150 mm Hg, with an FiO2 of ≥0.6, a PEEP of ≥5 CmH_2O, and a tidal volume of 6 ml/Kg of predicted body weight. *Exclusion criteria* included contraindication for PP [5] such as recent face trauma or surgery, Recent Deep venous thrombosis, Unstable spine, femur, or pelvic fractures, hemodynamic instability, pregnancy, Pneumothorax, PP before inclusion.

Before initiating the study, it was essential to get written informed consent from patients or legal guardians.

The study included 52 patients. Then, they were randomized into two equal groups, each consisting of 26 patients, namely group (A) and group (B). **Group (A) control group**: Each proning cycle lasted for 16 h. every 24 h, **Group (B): prolonged prone group**: proning cycles each last for continuous 24 h, followed by 6 h in a supine position.

4.1. Patients' Interventions and Management

Patients in both groups were sedated fully relaxed according to the protocol of our institute with the following:

Propofol: 5 mcg/kg/min (0.3 mg/kg/hr) for at least 5 minutes. Subsequent increments of 5 mcg/kg/min to 10 mcg/kg/min (0.3 mg/kg/hr to 0.6 mg/kg/hr) may be used until the desired clinical effect is achieved. Maintenance rates of 5 mcg/kg/min to 50 mcg/kg/min (0.3 mg/kg/hr to 3 mg/kg/hr) or higher when necessary [13]. Cisatracurium 0.15 mg/kg bolus followed by 3 mcg/kg/min [14].

Participating staff members were provided with guidelines to ensure the best possible standardization of prone positioning. Standard intensive care unit (ICU) beds were used for all patients, and pharmacological therapies were in accordance with the local treatment guidelines of our center.

Patients in our study received isocaloric (25 kcal/kg/day) entral tube feeding with intermittent bolus technique, In patients who didn't tolerate full dose entral nutrition parenteral nutrition was initiated.

All patients were ventilated with a Newport e360 ventilator (Newport Medical, Costa Mesa, CA).

According to our unit standard, PP was done with our trained team; positioning was achieved with foam wedges and pillows, alternating head and neck rotation every 2 h.

Mechanical ventilation was delivered in volume-controlled mode with the constant inspiratory flow, with tidal volume targeted at 6 $ml.kg^{-1}$ predicted body weight (PBW) and PEEP level according to ARDS Network (ARDSnet) "high" PEEP: FiO_2 table (Table 1) [15]. The main aim was to keep plateau pressure of the respiratory system (Pplat), measured by end-inspiratory occlusion maneuver, ≤30 cm H_2O and arterial plasma pH between 7.20 and 7.45. Respiratory frequency (RF) was adjusted to maintain arterial plasma pH within the above range, without exceeding 35 breaths.min-1.

Changes in ventilator settings were permitted throughout the period of proning, and the patient returned to the supine position in the event of

(1) An invasive or imaging procedure.
(2) Cardiopulmonary arrest.
(3) The patient has a stable gas exchange PaO_2/FiO_2 ≥ 150 with FiO_2 less than 60% and PEEP less than 10 cm H2O for greater than or equal to 4 h.

The following variables were measured and recorded:

(1) Demographic characteristics (age, sex, BMI).
(2) Hemodynamics (HR, MAP) every 2 h.
(3) Efficacy of oxygenation and ventilation mean value of 3 successive cycles was measured:
    a. PaO_2/FiO_2 values before pronation and in a supine position 60 minutes after the pronation cycle.
    b. Static lung compliance (Cstat) will be measured before proning and in a supine position 60 minutes after the pronation cycle.
(4) The rate of successful extubation.
(5) Hospital survival.

Table 1. Higher PEEP/ lower FiO_2 ratio [15].

Fio_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16
Fio_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0		
PEEP	18	20	22	22	22	24		

(6) Incidence of complications: facial edema, pressure wounds, lines disconnection, hemodynamic instability, and brachial plexus injury.

4.2. Statistical Methods

Statistical analysis was done using IBM© SPSS© Statistics version 26 (IBM© Corp., Armonk, NY) and MedCalc® Statistical Software version 20 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021).

Categorical variables are presented as numbers and percentages, and intergroup differences are compared using the Pearson chi-squared test or Fisher's exact test.

Normally distributed continuous variables are presented as mean and standard deviation, and differences between groups are compared using the independent-samples t-test.

Using the Kaplan-Meier (KM) method, time to event analysis was done to compare individual KM curves using the log-rank test.

P-values <0.05 are considered statistically significant.

5. Results

Fifty-two patients with ARDS were enrolled in our study, and there was no statistically significant difference between both groups in terms of demographic data and baseline characteristics at inclusion (Table 2).

In the 24 h PP ventilation group, 18 patients survived, two of whom were tracheostomized and were discharged on home ventilation. The rate of survival was (69.2%), whereas the rate of successful extubation was (61.5%). Patients in the control group survived (53.8%), with two being tracheostomized; differences were not clinically significant.

We found that extending the duration of PP induced a statistically significant improvement in PaO2/FiO2 (Table 3) which increased (mmHg) 34.38 ± 23.56 in the control group vs. 46.58 ± 13.89 in the prolonged PP group (P-value = 0.0303) (Figure 1).

Extending the duration of PP resulted also in a statistically significant improvement in (Cstat)) (Table 3); Mean Cstat was 26.8 ± 5.6 and 27.0 ± 6.3 in the control group and prolonged PP group respectively, and after proning it diverged to 32.0 ± 7.2 and 34.9 ± 8.4, the Δ Cstat after three successive cycles was 19.2 ± 5.3 mmHg in the control group and 29.7 ± 12.1 mmHg in the prolonged PP group (p-value of 0.003) (Figure 2).

We found that facial edema was very prevalent (73.1%) in both groups with no significant difference, no limb weakness, nor nerve injuries were encountered, also Twelve patients (46.2%) of the prolonged PP group developed Ventral pressure wounds while ten patients (38.5%) developed ventral pressure wounds in the control group, the difference was not clinically significant, as regard decannulation; it was relatively uncommon only one patient in the control group and two patients in the prolonged PP group (Figure 3), all adverse events are summarized in (Table 4).

There was a trend towards faster extubation in the prolonged proning group as the median time for extubation is 13 (95% CI = 12 to 17) days versus 16 (95% CI = 12 to 21) days in the control group. Incidence rate ratio (IRR) = 1.637, 95% CI = 0.767 to 3.493. The difference is not statistically significant (log-rank chi-squared = 1.625, df = 1, P value = 0.202) (Figure 4).

Table 2. Characteristics of both study groups.

Variable	Control group (n = 26)	Prolonged proning group (n = 26)	Difference	95% CI	P value†
Age (years)	47.8 ± 10.0	51.4 ± 6.8	3.6	−1.2 to 8.3	0.138
Male sex	16 (61.5%)	12 (46.2%)	15.4%	−11.1% to 39.0%	0.266‡
Body weight (kg)	80.5 ± 8.2	77.4 ± 7.7	−3.1	−7.5 to 1.3	0.164
Height (cm)	159.5 ± 8.2	159.8 ± 7.8	0.3	−4.1 to 4.7	0.890
BMI (kg/m^2)	31.3 ± 4.3	30.5 ± 3.8	−0.8	−3.1 to 1.4	0.456
SOFA on admission	6.0 ± 0.9	6.3 ± 1.0	0.3	−0.3 to 0.8	0.329

Data are mean ± SD or count (percentage)
†. Independent-samples t-test unless otherwise indicated
‡. Pearson chi-squared test
95% CI = 95% confidence interval

Table 3. Change in oxygenation index and static compliance in both study groups.

Variable	Control group (n = 26)	Prolonged proning group (n = 26)	Difference	95% CI	P value†
PaO_2/FiO_2 before proning (mmHg)	83.8 ± 30.8	78.9 ± 30.8	4.9	−12.3 to 22.1	0.575
PaO_2/FiO_2 after proning (mmHg)	118.23 ± 42.22	125.38 ± 33.42	7.149	−14.06 to 28.36	0.509
Change in PaO_2/FiO_2 (mmHg)	34.38 ± 23.56	46.58 ± 13.89	12.2	1.42 to 22.978	**0.0303**
Percentage change in PaO_2/FiO_2 (%)	45.46 ± 30.91	71.23 ± 39.97	25.76	5.86 to 45.67	**0.014**
Cstat before proning (l/cmH_2O)	26.8 ± 5.6	27.0 ± 6.3	0.2	−4.0 to 4.4	0.930
Cstat after proning (l/cmH_2O)	32.0 ± 7.2	34.9 ± 8.4	2.9	−2.6 to 8.3	0.295
Change in Cstat (l/cmH_2O)	19.2 ± 5.3	29.7 ± 12.1	10.5	3.9 to 17.2	**0.003**
Percentage change in Cstat (%)	5.2 ± 2.0	7.9 ± 3.6	2.7	0.6 to 4.7	**0.012**

Data are mean ± SD
†. Independent-samples t-test
95% CI = 95% confidence interval

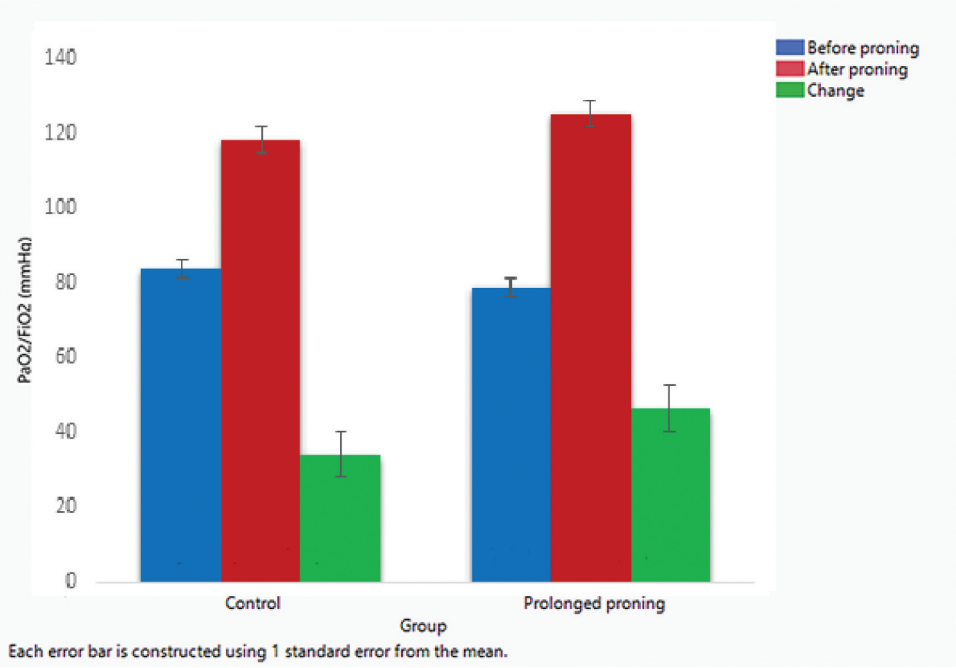

Figure 1. Mean oxygenation index before and after proning in both study groups.

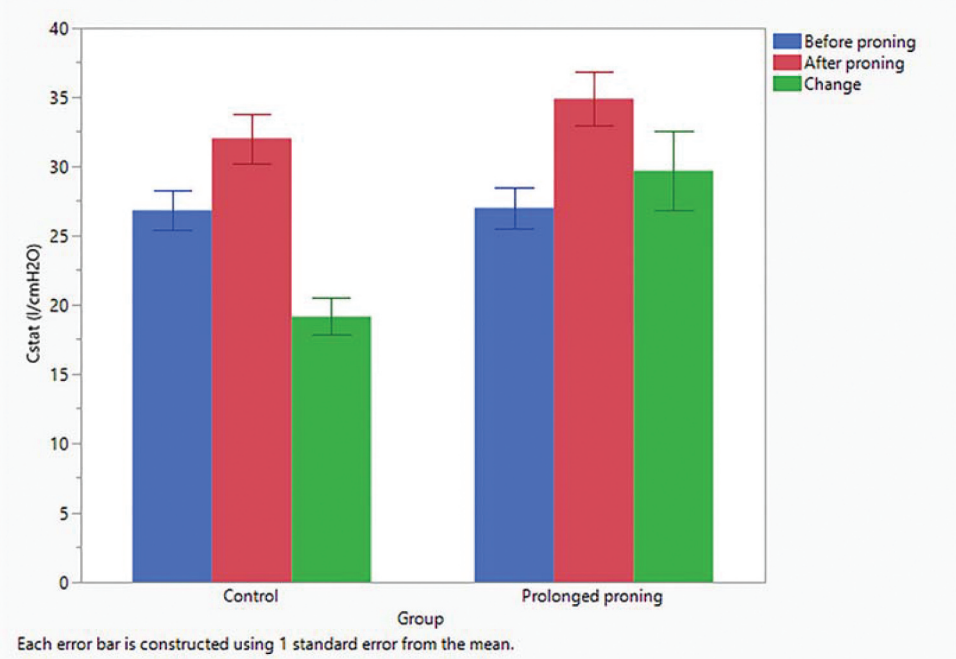

Figure 2. Mean static compliance (Cstat) before and after proning in both study groups.*Error bars represent the standard error (SE).

There was a trend towards better survival rates in the prolonged proning group; median survival in the prolonged proning group is 25 (95% CI = 25 to 25) days versus 23 (95% CI = 19 to 24) days in the control group. The Hazard ratio (HR) = 0.841, with a 95% CI = 0.327 to 2.160. Nonetheless, difference is not statistically significant (log-rank chi-squared = 0.130, df = 1, P value = 0.719) (Figure 5).

6. Discussion

It has recently been shown that the recruitment of posterior lung zones depends on the duration of the positioning [7]. Jochmans et al. [11] suggested extending PP ventilation to at least 24 h in moderate to severe ARDS to get the maximum physiological response. Nonetheless, the safety and feasibility of practicing repeated cycles have not been adequately evaluated.

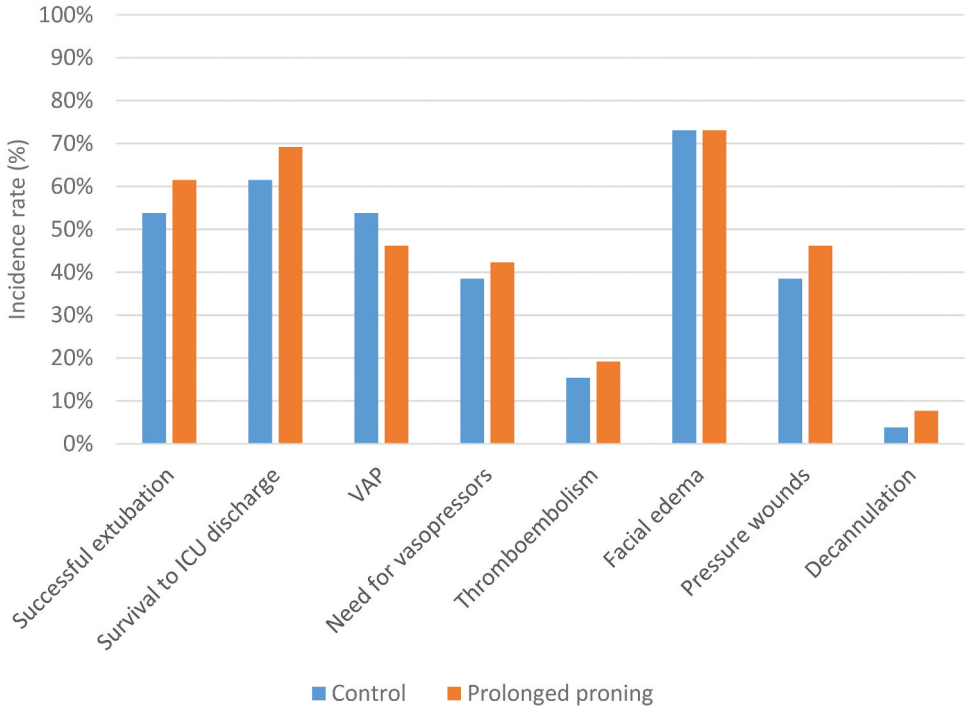

Figure 3. Main outcome measures in both study groups.

Table 4. Main outcome measures in both study groups.

Variable	Control group (n = 26)	Prolonged proning group (n = 26)	Difference	95% CI	P value†
Primary outcomes					
Successful extubation	14 (53.8%)	16 (61.5%)	7.7%	−18.1% to 32.1%	0.575
Survival	16 (61.5%)	18 (69.2%)	7.7%	−17.3% to 31.5%	0.560
Secondary outcomes					
VAP	14 (53.8%)	12 (46.2%)	7.7%	−18.3% to 32.3%	0.579
Need for vasopressors	10 (38.5%)	11 (42.3%)	3.9%	−21.5% to 28.5%	0.777
Thromboembolism	4 (15.4%)	5 (19.2%)	3.9%	−17.2% to 24.7%	>0.999‡
Facial edema	19 (73.1%)	19 (73.1%)	0.0%	−23.3% to 23.3%	>0.999
Pressure wounds	10 (38.5%)	12 (46.2%)	7.7%	−18.1% to 32.1%	0.575
Decannulation	1 (3.8%)	2 (7.7%)	3.9%	−12.2% to 20.6%	>0.999‡
Nerve injury	0 (0.0%)	0 (0.0%)	0.0%	−12.9% to 12.9%	NC

Data are counts and percentages
†. Pearson chi-squared test unless otherwise indicated
‡. Fisher's exact test
95% CI = 95% confidence interval, NC = not calculable

Our study evaluated the safety and patient outcomes of the usual 16 h PPV vs. 24 h in a prospective randomized manner.

Our results revealed that extending the duration of PP ventilation to 24 h is associated with better outcomes regarding oxygenation and Cstat compared to the standard 16 h PP ventilation. It also demonstrated that practicing prolonged PP ventilation is relatively safe.

In a study by Jochmans et al. that was conducted on 103 patients with non-COVID ARDS; PP sessions were extended to evaluate the time required to obtain the maximum physiological effect and to search for parameters related to patient survival in PP. The results showed that proning should be extended at least to 24 h and even more in the event that the PaO2/FiO2 ratio at 24 h remains below 150, particularly since no criteria can predict whether the patient will benefit from it or not [11].

Another 10-patient cohort report by Carsetti et al. [16] compared 16 vs. 36 h PP ventilation in COVID-19 ARDS in which median PaO2/FIO2 before PP was 126 mm Hg, with PP for either 16- or 36- h cycles, PaO2/FIO2 increased significantly to 177 mm Hg and 394 mm Hg, respectively. It is noticeable that patients in this cohort showed better oxygenation outcomes compared to our study, which could be due to higher initial PaO2/FiO2 in Carsetti's cohort. We also believe that this indicates a positive relationship between initial PaO2/FiO2 and the degree of the patient's response to PP, implying that the technique should be implemented earlier.

In contrast to our study, Page et al. [17] found a nonsignificant improvement in PaO2/FiO2 following extending the duration of PP Ventilation to 24 h, which could be attributed to the time of arterial blood gas (ABG) measurement 4–6 h after rotating the patient back to the supine position). On the

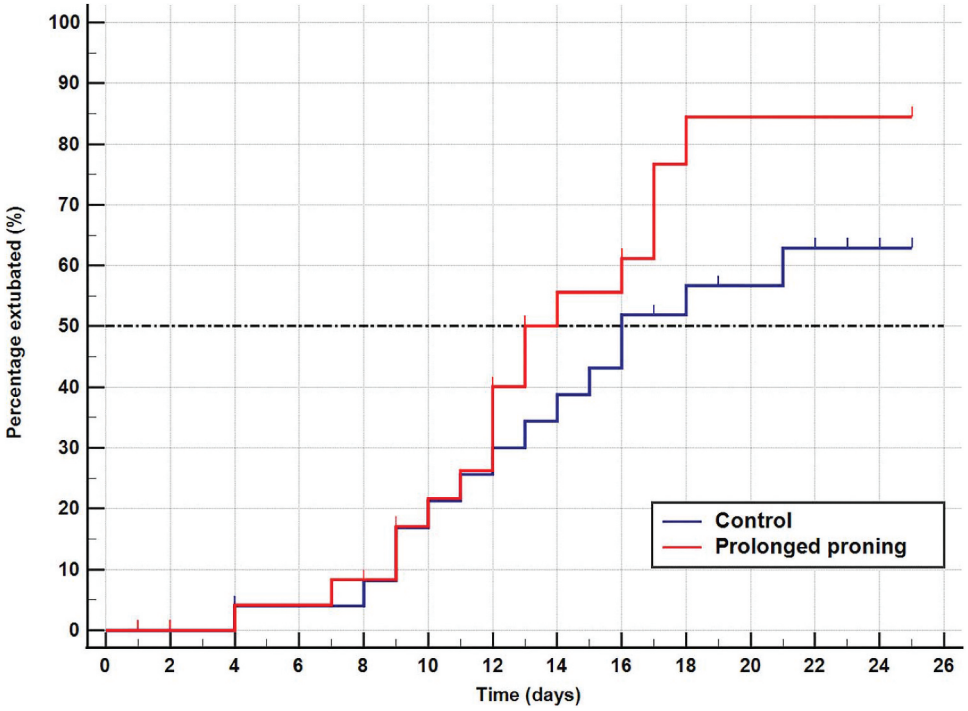

Figure 4. Kaplan-Meier curves for time to extubation in both groups. Median time to extubation in the prolonged proning group is 13 (95% CI = 12 to 17) days versus 16 (95% CI = 12 to 21) days in the control group. Incidence rate ratio (IRR) = 1.637, 95% CI = 0.767 to 3.493. Difference is not statistically significant (log-rank chi-squared = 1.625, df = 1, P value = 0.202).

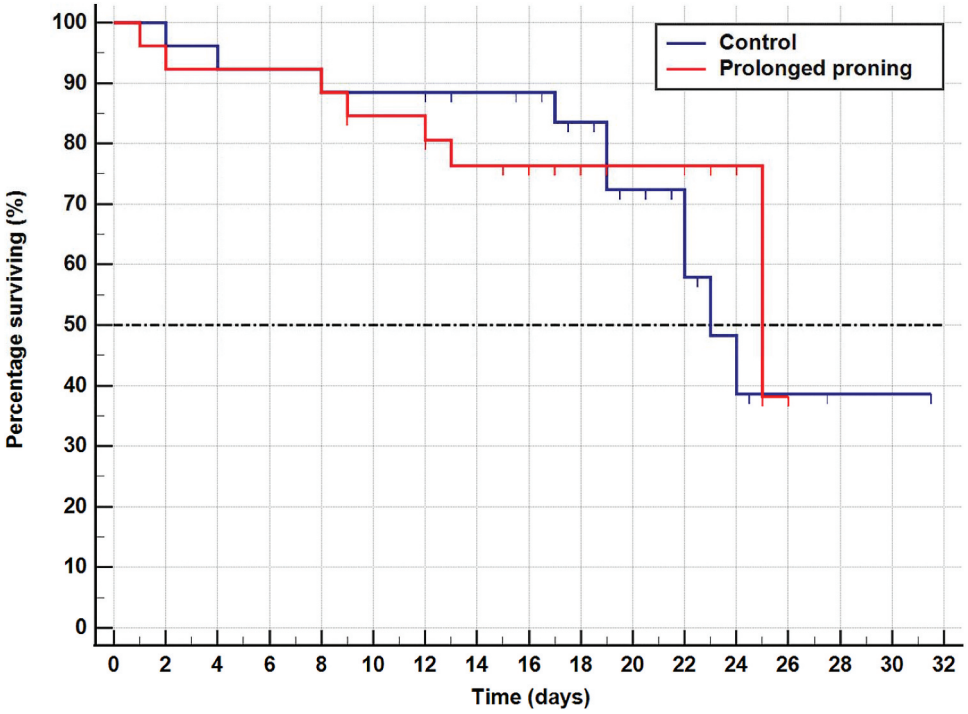

Figure 5. Kaplan-Meier survival curves in both groups. Median survival in the prolonged proning group is 25 (95% CI = 25 to 25) days versus 23 (95% CI = 19 to 24) days in the control group. Hazard ratio (HR) = 0.841, 95% CI = 0.327 to 2.160. Difference is not statistically significant (log-rank chi-squared = 0.130, df = 1, P value = 0.719).

contrary, ABGs in our study were sampled only one hour after supination, which raises questions about the deleterious effect of rotating the patients back to supine position on lung mechanics and oxygenation, as well as the benefitial effect of reducing the intervals between PP cycles.

The effectiveness of PP on long-term outcomes of mortality and intubation rates are conflicting. Our study showed that the survival rate did not improve with extending the duration of PP despite the significant improvement of oxygenation. Sixteen patients (61.5%) and eighteen patients (69.2%) survived In

16 h and 24 h PP ventilation respectively (p-value = 0.56), which is consistent with data provided by Albert et al., who concluded that survival rates remain independent of oxygenation after a retrospective analysis of data collected prospectively by Guérin and colleagues [18].

Surprisingly, we failed to show a significant survival benefit despite the significant improvement in lung dynamics (Cstat). This disagrees with studies that concluded better survival rates with improving lung compliance [19,20] and reducing ventilator-induced lung injury thanks to PP [,18]; However, We found a trend towards better survival in the prolonged PP group, whose Median survival was 25 (95% CI = 25 to 25) days versus 23 (95% CI = 19 to 24) days in the standard 16 h PP group. We think a larger sample size would have shown a significant survival benefit.

Regarding safety, it has been proven that increasing the number of PP hours is safe with no significant increase in the rate of major complications like pressure wounds that were developed in 10 patients (38.5%) in the control group vs. 12 (46.2%) in the prolonged PP group (P-value 0.575). In a cohort study by Douglas et al. [21], who performed prolonged PP ventilation without daily repositioning, wounds were quite frequent. Ventral pressure wounds occurred in (71.7%) vs. (46.2%) in our study, while severe edema occurred in (94%) vs. (73.1%) in ours. This difference is mainly explained by rotating the patients back to the supine position in our study at regular intervals allowing temporary pressure relief.

In terms of hemodynamic instability, hypotensive events requiring vasopressors occurred in 14 patients (53.8%) in the control group vs. 11 (42.3%) in the prolonged PP group showing nonsignificant difference (P-value 0.777), favoring prolonged PP when weighing the benefit/risk balance.

7. Limitations

Our study presents many limitations; first, we assessed average changes in oxygenation and Cstat over three successive proning cycles. We continued the same proning protocol for the study groups until extubation or fulfilling any exclusion criteria. Indeed an extended recording and analysis of data would yield more reliable results.

Another drawback was the small sample size; a larger sample size would indicate more significant results for the PP group's earlier median time of extubation. The study's findings only showed a trend towards earlier extubation in the PP group (13 days) vs. 16 days in the control group.

Changing ventilator settings was allowed during the study period, which may contribute to the improvement of measured parameters.

Due to the lack of special rotational beds, a trained clinical team experienced in safe repositioning techniques was required, which was time-consuming.

The hemodynamic effect of extending the duration of PP was evaluated in our study by the number of patients who needed vasopressors. This finding might be misleading since many other factors might necessitate starting vasopressor, with septic shock being a significant cause in our study groups.

Arterial carbon dioxide tension was measured yet not recorded nor analyzed, because changes in ventilator settings were freely allowed during the study so changes in PaCO2 wouldn't reflect accurately changes in pulmonary dead space fraction and lung efficiency to remove CO2, we focused on a PaO2/FiO2 as a standard for improvement of pulmonary gas exchange.

8. Conclusion

PP ventilation is both effective and safe, it should be considered as a fundamental part of lung-protective ventilation of COVID-19 ARDS.

It can be an option for future pandemics to reduce the work burden of healthcare workers.

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Disclosure statement

The authors declare no conflict of interest, financial or otherwise.

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References

[1] J.h U. Coronavirus resource center. 2021 [cited 2021 Dec 15]. Available at: https://coronavirus.jhu.edu/. Published 2020.
[2] Meade MO, Cook DJ, Guyatt GH, et al. Lung open ventilation study investigators. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial JAMA. JAMA. 2008 Feb 13; 299(6):637–645.
[3] Brower RG, Matthay MA, Morris A, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. Acute Respiratory Distress Syndrome Network. Engl J Med. 2000 May 4t;342(18):1301–1308.

[4] Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med. ACURASYS Study Investigators. 2010 Sept 16th;363(12):1107–1116.
[5] Guérin C, Reignier J, Richard J-C, et al. PPing in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159–2684.
[6] Guérin C. Prone position. Curr Opin Crit Care. 2014;20 (1):92–97.
[7] Mezidi M, Parrilla FJ, Yonis H, et al. Effects of positive end-expiratory pressure strategy in supine and PP on lung and chest wall mechanics in acute respiratory distress syndrome. Ann Intensive Care. 2018;8(1):86.
[8] Cornejo RA, Díaz JC, Tobar EA, et al. Effects of prone positioning on lung protection in patients with acute respiratory distress syndrome. Am J Respir Crit Care Med. 2013;188(4):440–448.
[9] Richter T, Bellani G, Scott Harris R, et al. Effect of prone position on regional shunt, aeration, and perfusion in experimental acute lung injury. Am J Respir Crit Care Med. 2005;172(4):480–487.
[10] Fan E, Del Sorbo L, Goligher EC, et al.; Mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med. 2017 May 1;195(9):1253–1263. Erratum in: Am J Respir Crit Care Med. 2017 Jun 1;195(11):1540. PMID: 28459336.
[11] Jochmans S, Mazerand S, Chelly J, et al. Duration of prone position sessions: a prospective cohort study. Ann Intensive Care. 2020;10(1):1–9.
[12] Lucchini A, Giani M, Elli S, et al. Nursing activities score is increased in COVID-19 patients. Intensive Crit Care Nurs. 2020;59:102876.
[13] Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med. 2013;41(1):263–306.
[14] Barash PG, Cahalan MD MK, Cullen, BF, et al. Clinical anesthesia 8th 2017; 1370. Wolters Kluwer Health.
[15] Brower RG, Lanken PN, MacIntyre N, et al. National heart, lung, and blood institute ARDS clinical trials network: higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med. 2004;351:327–336.
[16] Carsetti A, Damia Paciarini A, Marini B, et al. Prolonged PP ventilation for SARS-CoV-2 patients is feasible and effective. Crit Care. 2020;24(1):225.
[17] Page DB, Vijaykumar K, Russell DW, et al. Prolonged prone positioning for COVID-19-induced acute respiratory distress syndrome: a randomized pilot study. Ann Am Thorac Soc. 2021 Sept 7th;18(7):1260–1261. Epub ahead of print. PMID: 34491885.
[18] Guérin C, Albert RK, Keniston A, et al. Proseva Investigators. PP-induced improvement in gas exchange does not predict improved survival in the acute respiratory distress syndrome. Am J Respir Crit Care Med. 2014;189(4):494–496.
[19] Modrykamien AM, Daoud Y. Factors among patients receiving prone positioning for the acute respiratory distress syndrome found useful for predicting mortality in the intensive care unit. Bayl. Univ. Med. Cent. Proc. 2018;31:1–5. [CrossRef].
[20] Guérin C. Prone ventilation in acute respiratory distress syndrome. Eur Respir Rev. 2014Jun;23(132):249–257. PMID: 24881080.
[21] Douglas IS, Rosenthal CA, Swanson DD, et al. Safety and outcomes of prolonged usual care prone position mechanical ventilation to treat acute Coronavirus Disease 2019 hypoxemic respiratory failure. Crit Care Med. 2021;49(3):490–502.