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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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How Long Should the Prone Position be Applied in the Treatment of SARS-CoV-2 ARDS?

SARS-CoV-2 ARDS Tedavisinde Yüzüstü Pozisyon Ne Kadar Süre Uygulanmalıdır?

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ABSTRACT *Objective:* The importance of prone positioning has increased with the density of coronavirus disease-2019-related acute respiratory distress syndrome (C-ARDS) during the pandemic process. It is aimed to investigate the effect of prolonged duration of prone positioning in C-ARDS patients on the blood gas parameters at the time after supine positioning (post-prone effect), the feasibility, the safety, and the mortality for 28 days.
Materials and Methods: This study was a single-center prospective observational study with 1000 beds, 432 of which were intensive care units. Severe and moderate ARDS; the blood gas parameters (PaO_2/FiO_2, PaO_2, SpO_2 etc.) of the patients who were applied the standard prone (16 hours) and the extended prone (36 hours) position were compared.
Results: It was observed that PaO_2/FiO_2 PaO_2 and SpO_2 values measured at the 8th hour (t4) (post-prone) after the prone was placed in the supine position in the prolonged prone group were higher than before the prone (t1) ($p<0.001$). In the standard prone group, PaO_2/FiO_2, PaO_2, and SpO_2 values were not maintained in the post-prone period and were even lower than before the prone. The mortality of patients in the standard prone group was 51.7% (n=31); in the prolonged prone group, the mortality was 45% (n=27).
Conclusion: With the application of the prolonged prone position, it has been observed that C-ARDS patients have better blood gas exchange with less manpower without harming the patients (pressure ulcer, retinal damage, joint damage, etc.).
Keywords: Prone position, COVID-19, respiratory distress syndrome, PaO_2/FiO_2, pandemic

ÖZ *Amaç:* Pandemi sürecinde koronavirus hastalığı-2019'a bağlı akut respiratuvar distres sendromu (C-ARDS) yoğunluğunun artması ile yüzüstü pozisyonun önemi artmıştır. C-ARDS hastalarında uzamış yüzüstü pozisyon sürelerinin hasta sırtüstü pozisyona çevrildikten sonra (post-yüzüstü etki) kan gazı parametreleri üzerine etkisinin, uzamış yüzüstü uygulamasının uygulanabilirliğinin, güvenliğinin ve 28 günlük mortalite üzerine etkisinin araştırılması amaçlanmıştır.
Gereç ve Yöntem: Bu çalışma, 432'si yoğun bakım ünitesi olmak üzere toplam 1000 yataklı, tek merkezli, prospektif, gözlemsel bir çalışmadır. Şiddetli ve orta ARDS; standart yüzüstü (16 saat) ve uzatılmış yüzüstü (36 saat) pozisyonu uygulanan hastaların kan gazı parametreleri (PaO_2/FiO_2, PaO_2, SpO_2 vb.) karşılaştırıldı.
Bulgular: Uzamış yüzüstü grubunda yüzüstü sonrası sırtüstü pozisyona alınarak 8. saatte (t4) (post-yüzüstü) bakılan PaO_2/FiO_2, PaO_2 ve SpO_2 değerlerinin yüzüstü öncesine (t1) göre yüksek olduğu gözlenmiştir ($p<0,001$). Standart yüzüstü grubunda ise PaO_2/FiO_2 PaO_2 ve SpO_2 değerlerinin post-yüzüstü dönemde korunmadığı hatta yüzüstü öncesine göre daha düşük olduğu görülmüştür. Standart yüzüstü grubundaki hastaların mortalitesi %51,7 (n=31); uzamış yüzüstü grubunda ise mortalite %45'dir (n=27).
Sonuç: Uzamış yüzüstü pozisyonu uygulaması ile C-ARDS hastalarında daha az iş gücüyle hastalara zarar vermeden (bası yarası, retina hasarı, eklem hasarı vb.) daha iyi kan gazı değişimi olduğu görülmüştür.
Anahtar Kelimeler: Yüzüstü pozisyon, COVİD-19, solunum güçlüğü sendromu, PaO_2/FiO_2, pandemi

Introduction

Due to the severe acute respiratory syndrome coronavirus 2 pandemic in the world, the intensity of coronavirus disease-2019 (COVID-19)-related acute respiratory distress syndrome (C-ARDS) has increased in intensive care units (ICUs) (1). It is observed that ARDS developed in 42% of the patients admitted to the hospital with COVID-19 pneumonia; the mortality rate in patients treated in the ICU and treated with invasive mechanical ventilation (IMV) due to COVID-19 associated ARDS (C-ARDS) ranges from 65.7% to 94% (2,3). The importance of prone positioning has increased during the pandemic process, and it has been applied in 70% of patients followed in the ICU due to C-ARDS, a prone position for 12-16 hours is recommended under IMV (4). In a meta-analysis, neuromuscular blockade and prone positioning and lung protective mechanical ventilation (low tidal volume ventilation) were found to reduce mortality by 23% (5). In another meta-analysis, prone positioning for more than 12 hours was associated with lower mortality in patients (6). Studies have shown that early and extended prone positioning is more effective in ARDS patients (6-8).

In studies with computed tomography (CT) and electrical impedance tomography in patients with C-ARDS, prone position was found to be associated with lung recut, reduced atelectotrauma, and improved ventilation-perfusion compatibility (9). COVID-19 patients; improvement in continuous oxygenation (post-prone effect) can only be achieved after a longer duration and several pronation cycles (9-11). Those that caused excessive workload, fatigue and viral load for healthcare personnel due to the insufficent number of healthcare personnel in the face of the serious increase in the number of critically ill patients in need of ICU during the pandemic process (3,12).

The primary aim of this study is to investigate the effect of the first 16-hour prone position and 36-hour prone position applications on blood gas exchange (oxygenation) and continuity of this effect at the post-prone period in C-ARDS patients in the ICU. Secondary targets are to determine whether the total number of prone positions, the feasibility and safety of prolonged prone application, and its effect on 28-day mortality.

Materials and Methods

This is a single-center, prospective, observational study. It was approved by the University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee with the decision number 2021-07-10 (date: 05.04.2021). Informed consent was obtained from the relatives of all patients included in the study.

Patients who were treated in COVID-19 ICU between April 1, 2021 and February 1, 2022, and diagnosed with COVID-19 according to the COVID-19 guideline of the World Health Organization (13) [polymerase chain reaction (PCR) (Bio-Speedy COVID-19 RT-Qper detection Kit-Bioksen, Turkey) (+) and thorax CT is compatible with covid pneumonia], were included in this study. The diagnosis of ARDS was made according to the Berlin criteria (14). Of the 1550 patients admitted to the ICU for C-ARDS, 1240 had Horowitz ratio partial arterial oxygen pressure/fraction of inspired oxygen (PaO_2/FiO_2) <150 mmHg (Figure 1). Since 454 of these patients died within 24 hours after being admitted to the ICU, 412 of these patients PCR test is negative, only there is lung involvement in thorax CT and 254 were excluded from the study due to problems in data collection (Figure 1).

Randomization was done with the closed envelope method, the patients were classified into two groups as standard and extended prone position according to the

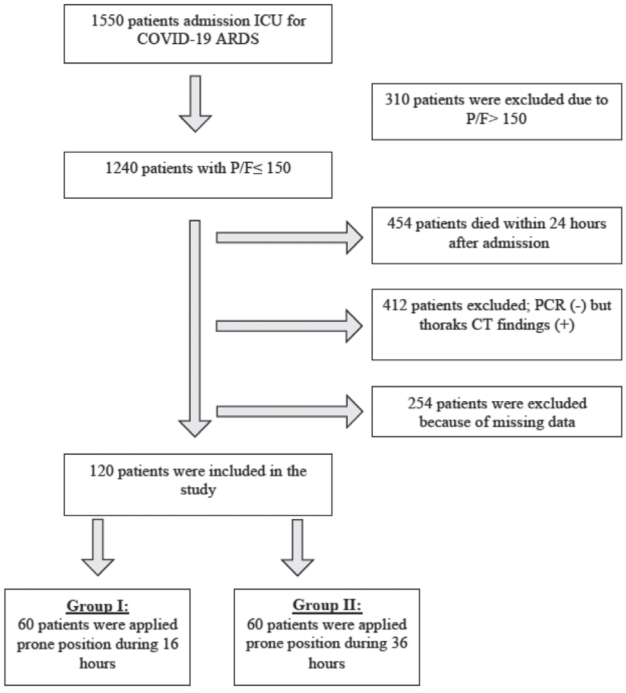

Figure 1. Flow chart showing the patient groups included in the study
ICU: Intensive care unit, COVID-19: coronavirus disease-2019, ARDS: acute respiratory distress syndrome, PaO_2/FiO_2: partial arterial oxygen pressure/fraction of inspired oxygen,, PCR: polymerase chain reaction, CT: computed tomography

duration of prone position: 16 hours of prone positioning was determined as standard prone, and 36 hours of prone positioning was determined as extended prone (Figure 1). Patients with PaO_2/FiO_2 <150 mmHg, PEEP ≥5 cmH_2O, FiO_2 ≥0.60 were placed in the prone position and followed up with control blood gases in every 4 hours. Patients who remained in the standard prone position for 16 hours were evaluated as a group (group 1). If hemodynamic stability continues in the prone position after 16 hours, the duration of the prone position is extended to 36 hours. Patients who remained in the prone position for 36 hours (extended prone) were also considered as a second group (group 2). Patients in both groups were kept in the supine position for 8 hours in order to complete post-prone nursing care and to prevent compression complications.

Prone positioning was performed regardless of the time of day to the orotracheal intubated patients with PaO_2/FiO_2 <150 mmHg, PEEP ≥5 cmH_2O, FiO_2 ≥0.60, who were deeply sedated, and invasive artery monitoring, central venous pressure catheter (CVP) and for the enteral feeding nasogastric tube was applied. The prone team consisted of three nurses, two health personnel, an assistant doctor and a general practitioner. The patients were positioned by placing a thoracic pillow under the shoulder and a pelvic pillow at the level of the iliac bones, leaving the neck free. The head pillow was placed to avoid pressure points on the eyes, nose or chin. The arms were placed on the sides of the body with the palms facing up. In every 4 hours, head was repositioned and eye care was performed. Protective mechanical ventilation was applied by allowing a tidal volume of 6-8 mL/kg based on estimated body weight, a positive end expiratory pressure (PEEP) of 8-14 cmH_2O, a plateau pressure equal to or lower than 30 cmH_2O with pressure regulated volume control mod.

All patients who were over the age of 18, whose PCR (+) and thorax CT was compatible with COVID pneumonia, were treated as intubated due to severe and moderate ARDS according to Berlin criteria, with PaO_2/FiO_2 <150 mmHg, PEEP ≥5 cmH_2O and FiO_2 ≥0.60 were included in this study. Patients under 18 years of age, with mild C-ARDS according to the Berlin criteria, whose prone position were terminated due to hemodynamic instability (systolic blood pressure <90 mmHg or mean arterial pressure <60 mmHg), who could not be prone positioned due to the unstable vertebral and pelvic fractures or long bone fractures, who could not be prone positioned due to open abdominal wound and due to the late period of pregnancy, with increased intracranial pressure (>30 mmHg) or with decreased cerebral perfusion pressure (<60 mmHg), who were diagnosed with pulmonary embolism by thoracic CT angiography were excluded from the study.

All patients were ventilated under deep sedation and neuromuscular blockade and in volume control mode with a GE Carescape R860™ (USA) mechanical ventilator. After stabilization of the patients at the admission to ICU, the first pre-prone (t1) Horowitz (PaO_2/FiO_2) ratios, SpO_2, blood gas parameters [PaO_2, partial arterial carbon dioxide pressure ($PaCO_2$)], inotropic and/or vasopressor doses has been recorded. The same values were recorded at the 16th hour (t2) of the prone position of both groups, at the 36th hour (t3) in the prolonged prone group (group 2) and after the patients were placed in the supine position of both groups at the 8th hour (t4). The values recorded at t1, t2, t4 periods were compared between the two groups. The t3 parameter was not able to taken from the standard prone group (group 1). For this reason, t3 was not evaluated between groups, the elongated prone group (group 2) was evaluated within itself. In both groups; age, gender, body mass index (BMI), comorbidity; acute physiology and chronic health evaluation-II (APACHE-II) and sequential organ failure assessment (SOFA) scores at the admission to the ICU, length of stay (LOS) in ICU, duration of mechanical ventilation, number of ventilator-free days (VFday) and twenty-eight-day mortality of the patients were recorded. Whether they were tracheostomized, the number of prone positioning, complications (pressure sores, venous stasis-edema, nerve and joint injuries, accidental removal of endotracheal tube and CVP, retinal damage, vomiting, transient arrhythmias) were also recorded.

For edema that may occur in the physical examination after the prone position; it was classified after the compression as 1 mm depression (+), 2 mm depression (++), 3 mm depression (+++) (15). Evaluation of pressure ulcers was made according to the Revised Pressure Sore Staging System (16). Stage 1 pressure injury was defined as intact skin with localized areas of unbleached erythema, Stage 2 as partial-thickness skin loss with exposed dermis, Stage 3 as full-thickness skin loss, and Stage 4 as full-thickness skin and tissue loss.

Statistical Analysis

Sample e-power calculation was calculated using PASS 2008 program. For our two-group and 3-period (common period number in both groups) study, articles on similar

topics were scanned and by reference to these studies; for a 15% difference in the predicted oxygenation changes between the groups, our sample number calculated against α=0.05 and 80% Power is 60 for the 1st group and 60 for the 2nd group, and a total of 120 people will be taken.

SPSS 25.0 (IBM Corporation, Armonk, New York, United States) and PAST 3 (Hammer, Ø., Harper, D.A.T., Ryan, P.D. 2001. Paleontological statistics) programs were used in the analysis of the variables. The conformity of univariate data to normal distribution was evaluated with the Shapiro-Wilk francia test, while homogeneity of variance was evaluated with the Levene test. While the Mardia (Dornik and Hansen omnibus) test was used for the conformity of multivariate data to normal distribution; the Box-M test was used for variance homogeneity. While the Independent-Samples t-test was used together with the Bootstrap results in the comparison of two independent groups according to quantitative data, the Mann-Whitney U test was used together with the Monte Carlo results. Friedman's Two-Way test was used to compare measurements of dependent quantitative variables with more than two repetitions, and Stepwise step-down comparisons were used for post-hoc test. In comparison of categorical variables, Pearson chi-square, Fisher Exact and Fisher-Freeman-Holton tests were tested with Monte Carlo Simulation technique and column ratios were compared with each other and expressed according to Benjamini-Hochberg corrected p value results. The odds ratio was used with 95% confidence intervals to show how many times more people with a risk factor were than those without. While quantitative variables were expressed as mean [standard deviation (SD)] (minimum/maximum) and median (25%/75%) in the tables, categorical variables were shown as n (%). The variables were analyzed at 95% confidence level, and a p-value less than 0.05 was considered significant.

Results

This study was conducted on a total of 120 patients diagnosed with C-ARDS. Forty-three (35.8%) of the patients were female and 77 (64.2%) were male. Between the two groups; no statistically significant difference was found in patients' age (p=0.781), BMI (p=0.236), APACHE-II score (p=0.222), SOFA score (p=0.609), number of days without ventilator (VFday) (p=0.378), LOS in ICU (p=0.967), IMV durations (p=0.333), tracheostomy rates (p=0.855) and comorbidities (p=0.163). Considering the 28-day mortality, although 28-day mortality was lower in the prolonged prone group, no statistically significant difference was found (Table 1). The number of patients receiving noradrenaline (p=0.602) and dopamine (p=0.444) and their total daily intake were similar, but no statistically significant difference was found. Adrenaline was found to be statistically significantly higher in the prone position in the standard prone group (p=0.017) (Table 1). The median values for the number of prone positions in the standard prone and extended prone groups were calculated as 6 and 4, respectively, and were considered statistically significant (p=0.001) (Table 1). The mean/median, SD/interquartile range, number, percentage and p-values of the parameters mentioned above are presented in Table 1.

In the prone position (t2) compared to the pre-prone (t1) values, a statistically significant increase was observed in PaO_2/FiO_2 (p=0.543), PaO_2 (p=0.733) and SpO_2 (p=0.398) values, that were similar in both groups in the pre-prone period (t1) (p<0.001). In the standard prone group, the post-prone supine PaO_2/FiO_2 and PaO_2 values were not preserved at the 8th hour (t4) and were even lower than the pre-prone (t1) values. In the prolonged prone group, it was observed that PaO_2/FiO_2, PaO_2 and SpO_2 values measured at the 8th hour (t4) by being placed in the supine position after the prone were higher than before the prone (t1) (p<0.001). It was observed that the PCO_2 values before the prone (t1) (p=0.306) and prone position (t2) were similar in both groups; and the PCO_2 value measured at the 8th hour (t4) in the supine position after the prone group was statistically significantly lower in the extended prone group (p=0.001) (Table 2).

A statistically significant difference was found in the edema rates of the groups (p<0.001). The rate of edema (++) in the standard prone (group 1) group was statistically significantly higher than in the prolonged prone (group 2) group (p=0.001). No statistically significant differences was found between the two groups in pressure ulcers (p=0.198), joint damage (p=1.000), nerve damage (p=1.000), orotracheal tube (OTT) complications (p=0.496) and central venous catheter complications (p=0.496). Retinal damage and need for total parenteral nutrition (TPN) were not observed in any of the patients (Table 3).

Table 1. Demographic data and using of vasoactive drugs				
	Total (n=120)	**Prone 16th hour (n=60)**	**Prone 36th hour (n=60)**	**p-value**
Sex (female), n (%)	43 (35.8)	27 (45)	16 (26.7)	0.056[c]
Age, mean ± SD (min-max)	61.9±11.9 (35-89)	61.6±10.5 (38-84)	62.2±13.1 (35-89)	0.781[t]
BMI, median (q1/q3)	27 (24.9/29)	26.6 (24.2/29.1)	27.3 (25.5/29)	0.236[u]
APACHE, median (q1/q3)	21 (15/25)	20 (14/25)	22.5 (15/25.5)	0.222[u]
SOFA scores, mean ± SD min-max (median)	10.02±3.90 0-21 (10)	10.20±4.48 1-21 (11)	9.83±3.24 0-15 (10)	0.609
VFdays, mean ± SD min-max (median)	5.73±6.08 0-32 (4)	5.05±4.94 0-24 (4)	6.42±7.02 0-32 (5.5)	0.378
Days of intubation, median (q1/q3)	16 (12/20)	17.5 (12.5/20)	16 (12/19)	0.333[u]
Lenght of ICU stay, median (q1/q3)	20 (16/28)	22 (16/25.5)	19.5 (16/28)	0.967[u]
Total prone number, median (q1/q3)	6 (4/6)	6 (6/8)	4 (4/5)	**<0.001[u]**
Mortality for 28 days, n (%)				0.831[c]
Alive	43 (35.8)	20 (33.3)	23 (38.3)	0.234[u]
Exitus	58 (48.3)	31 (51.7)	27 (45)	0.341[u]
ICU	19 (15.8)	9 (15)	10 (16.7)	0.224[u]
Tracheostomy, n (%)	58 (48.3)	30 (50)	28 (46.7)	0.855[c]
Comorbidity, n (%)	97 (80.8)	45 (75)	52 (86.7)	0.163[c]
Pre-prone				
Noradrenaline dosage (mcg/kg/min), median (q1/q3)	0.3 (0.2/0.5)	0.4 (0.2/0.6)	0.3 (0.2/0.5)	0.305[u]
Noradrenaline dosage, (mcg/kg/min), n (%)	87 (72.5)	44 (73.3)	43 (71.7)	0.999[c]
Adrenaline dosage, (mcg/kg/min), n (%)	8 (6.7)	7 (11.7)	1 (1.7)	0.061[f]
Dopamine dosage, (mcg/kg/min), n (%)	17 (14.2)	11 (18.3)	6 (10)	0.295[c]
Prone				
Noradrenaline dosage, (mcg/kg/min), median (q1/q3)	0.3 (0.2/0.6)	0.3 (0.2/0.8)	0.3 (0.2/0.5)	0.551[u]
Noradrenaline dosage, (mcg/kg/min), n (%)	103 (85.8)	53 (88.3)	50 (83.3)	0.602[c]
Adrenaline dosage, (mcg/kg/min), n (%)	10 (8.3)	9 (15)	1 (1.7)	**0.017[c] 10.4 (1.3-85)[or]**
Dopamine dosage, (mcg/kg/min), n (%)	18 (15)	11 (18.3)	7 (11.7)	0.444[c]

[t]Independent t-test (Bootstrap); [u]Mann-Whitney U test (Monte Carlo); [f]Fisher's Exact test (Monte Carlo), [c]Pearson chi-square test (Monte Carlo); post-hoc test: Benjamini-Hochberg correction; [or]odds ratio (95% confidence interval); 1: percentile 25, q3: percentile 75; [A]Significant for prone 16th h (t1) group, [B]Significant for prone 36th h (t3) group, SD: standard deviation, min-max: minimum-maximum, SOFA: sequential organ failure assessment, SD: standard deviation, VFdays: ventilator-free days, ICU: intensive care unit

Table 2. Parameters of artery blood gas samples during prone positions and after prone				
		Group 1 (n=60)	**Group 2 (n=60)**	**p-value**
		Median (q1/q3)	**Median (q1/q3)**	
PaO_2/FiO_2				
t1	A	95 (79/110)	92 (79/102)[All]	0.534[u]
t2	B	103 (87/122.5)[A,D]	139 (116.3/170)[All]	**<0.001[u]**
t3	C	-	167 (137/201)[All]	-
t4	D	81.5 (69.5/100)	114 (100/138)[All]	**<0.001[u]**

Table 2. Continued				
		Group 1 (n=60)	**Group 2 (n=60)**	**p-value**
		Median (q1/q3)	**Median (q1/q3)**	
p-value for intra prone groups		**<0.001[f]**	**<0.001[f]**	
Changes				
(t1-t2)		10 (5/15)	40 (28.5/80)	**<0.001[u]**
(t1-t3)		-	86 (45/122)	**-**
(t1-t4)		-7 (-21/2)	20.5 (0.5/60)	**<0.001[u]**
(t2-t4)		21.5 (6.5/28)	23.5 (-6.5/55.5)	0.368[u]
(t3-t4)		-	54 (15.5/102)	-
SpO_2				
t1	A	92 (87/95)	91 (89.5/93)[All]	0.398[u]
t2	B	94 (93/96)[A]	96 (94/97)[All]	0.884[u]
t3	C	-	97 (96/98)[A,B]	-
t4	D	92 (86/95.5)	96 (95/97)[A,B]	**<0.001[u]**
p-value for intra prone groups		**0.019[f]**	**<0.001[f]**	
Changes				
(t1-t2)		1 (-1/5)	4 (1/8)	0.074[u]
(t1-t3)		-	5.5 (3.5/8)	**-**
(t1-t4)		0.5 (-4/4)	5 (3/8)	**<0.001[u]**
(t2-t4)		2 (-1/6)	-1.5 (-4.5/1)	**<0.001[u]**
(t3-t4)		-	0 (-1/1.5)	**-**
PO_2				
t1	A	71 (59.5/80.5)	69 (64/75)[B,C,D]	0.733[u]
t2	B	74 (64.5/87)[A,D]	89.5 (76/109)	**<0.001[u]**
t3	C	-	100.5 (80/120)	**-**
t4	D	65.5 (59.5/78.5)	83 (77/99)	**<0.001[u]**
p-value for intra prone groups		**<0.001[f]**	**<0.001[f]**	
Changes				
(t1-t2)		6 (-0.5/15.3)	20 (8/34)	**<0.001[u]**
(t1-t3)		-	30 (12.5/57)	**-**
(t1-t4)		1 (-17/9)	16 (3.5/29.5)	**<0.001[u]**
(t2-t4)		9 (-0.5/20)	1 (-12/24.5)	0.349[u]
(t3-t4)		-	20.5 (-9/39)	-
PCO_2				
t1	A	50 (42/58)	47.5 (41/56.5)	0.306[u]
t2	B	49.5 (43/58)	48 (41/54)[D]	0.397[u]
t3	C	-	44 (41/51.5)	-
t4	D	48.5 (43/56)	41 (37.5/48)	**0.001[u]**
p-value for intra prone groups		0.641[f]	**0.008[f]**	
C				
(t1-t2)		1.5 (-5.5/6.5)	1 (-5.5/8)	0.918[u]
(t1-t3)		-	-0.5 (-13.5/6.5)	-
(t1-t4)		-1 (-12/10)	-6 (-13.5/2)	0.229[u]
(t2-t4)		1 (-7.5/11)	6.5 (-5/15)	0.076[u]
(t3-t4)		-	3 (-6/13)	-

[u]Mann-Whitney U test (Monte Carlo); [f]Friedman test (Monte Carlo); post-hoc test: Stepwise step-down comparisons; q1: percentile 25, q3: percentile 75; [All]Expresses significance for all periods, [A]Expresses significance compared to before prone (t1), [B]Expresses significance according to the 16th hour (t2), [C]Express the significance according to the 36th hour (t3), [D]Expresses significance according to the 8th hour supine (t4) position, PaO_2/FiO_2: partial arterial oxygen pressure/fraction of inspired oxygen

Table 3. Complications of prone position					
		Total	Group 1 (n=60)	Group 2 (n=60)	p-value
Edema, n (%)		104 (86.7%)	60 (100%)	44 (73.3%)	<0.001
	(+)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-
	(++)	13 (10.8%)	12 (20.0%)	1 (1.7%)	0.001
	(+++)	91 (75.8%)	48 (80.0%)	43 (71.7%)	0.286
Pressure ulcers, n (%)		67 (55.8%)	30 (50.0%)	37 (61.7%)	0.198
	Grade I	21 (17.5%)	8 (13.3%)	13 (21.7%)	0.230
	Grade II	23 (19.2%)	12 (20.0%)	11 (18.3%)	0.817
	Grade III	18 (15.0%)	8 (13.3%)	10 (16.7%)	0.799
	Grade IV	5 (4.2%)	2 (3.3%)	3 (5.0%)	1.000
In need of TPN, n (%)		0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Retinal damage, n (%)		0 (0.0%)	0 (0.0%)	0 (0.0%)	-
Joint damage, n (%)		1 (0.8%)	1 (1.7%)	0 (0.0%)	1.000
Nerve damage n (%)		1 (0.8%)	0 (0.0%)	1 (1.7%)	1.000
Complications due to OTT, n (%)		2 (1.7%)	2 (3.3%)	0 (0.0%)	0.496
Complications due to CVP, n (%)		2 (1.7%)	0 (0.0%)	2 (3.3%)	0.496

TPN: Total parenteral nutrition, OTT: orotracheal tube, CVP: central venous pressure catheter

Discussion

In this study; pre-prone, prone and post-prone (post-prone effect) values of blood gas parameters of C-ARDS patients who were applied standard prone position (16 hours) and prolonged prone position (36 hours) were compared (Figure 2). Significant improvement was observed in PaO_2/FiO_2, PaO_2 and SpO_2 values with prone positioning in both groups compared to pre-prone values, which was found to be compatible with the literature (4,7,17-21). It was calculated that the post-prone PaO_2/FiO_2 ratios of the patients who were applied the prolonged prone position were significantly higher when compared to the patients who were applied the standard prone position (19). This improvement in the PaO_2/FiO_2 ratio after the prone position has been shown in many studies and is defined as the post prone effect (19). It has been shown that the prolonged prone position during the epidemic is more beneficial than the standard prone position, in the early period in C-ARDS patients (7-11). In another study, standard prone (16 hours) and prolonged prone (36 hours) applied in C-ARDS patients were compared and it was observed that oxygenation improved significantly during the prone position (7).

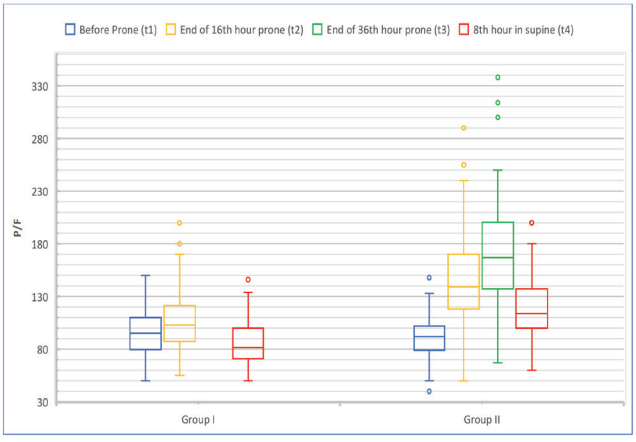

Figure 2. Change of PaO_2/FiO_2 values according to time zones
PaO_2/FiO_2: partial arterial oxygen pressure/fraction of inspired oxygen

Although there was no difference between the pre-prone and prone $PaCO_2$ values of the patients in the prolonged prone position and the patients in which the standard prone position was applied; the post-prone $PaCO_2$ values of the prolonged prone group were calculated as significantly lower. It is known that the prone position significantly reduces $PaCO_2$ in C-ARDS patients (22). However, this effect has been shown to be better with lengthening the prone position (17).

Although the patients in the prolonged prone group had better blood gas values, there was no significant difference between the two groups in terms of 28-day mortality when compared with the patients in the standard prone position (p=0.831). In similar studies, mortality was found to be lower in patients treated with prolonged prone compared to other patients (21,23,24). In some studies, as in this study, no difference in mortality was found between the patients who were applied the prolonged prone and the patients who were treated with the standard prone (25,26).

A significant difference was found between the median value of the prone positioning numbers of the standard prone position group and the prolonged prone position groups (6 vs. 4, respectively). It is thought that the application of prolonged prone position in this way can reduce the number of prone positioning, the workload of the hospital staff and the complications that may occur during the procedure (3,7).

There was no statistically significant difference in the incidence of pressure ulcers between the two groups (p=0.198), and 55.8% of the patients had pressure ulcers. It has been reported that pressure ulcers, the most common complication of prone positioning, are 56.9% in the standard prone position application and this rate is much higher than in the supine position (27,28). In patients with C-ARDS, the risk of pressure injury increases due to the application of prone positioning for long periods (>16 hours) (24,28). In a study, it was observed that there was no increase in the incidence of pressure ulcers in patients who applied the prolonged prone position (36 hours), and other complications of the prone position were not reported (7).

Edema (++) was observed in 12 (20%) patients in the standard prone group and in 1 (1.7%) patient in the prolonged prone group, which was statistically significant (p=0.001). Similarly, 9 patients (15%) who needed adrenaline in the standard prone group and 1 patient (1.7%) in the prolonged prone group were found to be statistically significant (p=0.017).

In this study, the need for TPN and retinal damage were not observed in the patients. Joint damage developed in one patient in the standard prone group and nerve damage in one patient in the prolonged prone group (p=1.000). It was observed that the OTT of 2 patients in the standard prone group was displaced, and the central catheter of 2 patients in the prolonged prone group was displaced (p=0.496). Complications such as temporary desaturations, dislocation of catheters and endotracheal tubes, accidental disconnection of the oxygen support system, retinal damage, transient arrhythmias, ischemic neuropathy, gastric bloating, gastroesophageal reflux and vomiting with the application of the prone position have been reported in the literature (24).

There was no difference between the two groups in terms of patient demographic data. The patient characteristics of this study are similar to other studies (29,30).

With prolonged prone positioning, better blood gas exchange was observed in C-ARDS patients without harming the patients (pressure sore, retinal damage, joint damage, etc.).

Since there was no electronic recording system in the pandemic hospital where the study was conducted and the researchers were at high risk of contagiousness, mechanical ventilation parameters (PEEP, peak, plateau, respiratory frequency, delta pressure etc.) could not be recorded at the bedside. Therefore, mechanical ventilation support could not be evaluated.

Conclusion

It was observed that the improvement in blood gas parameters was better with the prolonged prone position in C-ARDS, and this effect lasted longer in the post-prone period. It has also been shown to be feasible and reasonably safe. It can be applied as a good option to reduce the risks that arises in every position change and to reduce the workload of healthcare workers, especially during the peak periods of the pandemic.

Ethics

Ethics Committee Approval: It was approved by the University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital Ethics Committee with the decision number 2021-07-10 (date: 05.04.2021).

Informed Consent: Informed consent was obtained from the relatives of all patients included in the study.

Authorship Contributions

Surgical and Medical Practices: T.Y., C.Ç., A.P., Concept: S.A., Z.Ç., Design: S.A., Y.T.Ş., Z.Ç., Data Collection and Process: T.Y., C.Ç., A.P., Analysis or Interpretation: S.A., Y.T.Ş., Z.Ç., Literature Search: T.Y., Y.T.Ş., Z.Ç., Writing: T.Y.

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