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Compliance to not only prone but also lateral and supine positioning improves outcome in hospitalised COVID-19 patients

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Abstract

Background: Positioning of the patient is a common strategy to increase oxygenation in the management of acute respiratory distress syndrome. The aim of this study is to demonstrate the effects of our positioning approach on disease outcomes in COVID-19 patients with respiratory failure, by comparing patients compliant to positioning and not.

Methods: COVID-19 patients who were admitted to our internal medicine inpatient clinic and developed hypoxaemia and underwent positioning during hospital stay were retrospectively investigated for compliance to positioning. Rates of mortality, intensive care unit admission, intubation, initiation of anti-inflammatory treatment and length of hospital stay were compared between patients with and without compliance to positioning.

Results: A total of 144 patients were enrolled in this study (97 compliant with positioning, 47 incompliant with positioning). Rates of ICU admission (7.2% vs 25.5%, $p < .001$), anti-inflammatory treatment initiation (68% vs 97.9%, $p < .001$) and length of hospital stay (5 (2-16) days vs 12 (3-20) days, $p < .001$) were significantly reduced in patients compliant with positioning.

Conclusion: Prone or other positioning should be considered in patients with noninvasive oxygen support for the potential to reduce rates of intensive care unit admissions, airway interventions, anti-inflammatory treatment initiation and mortality.

1 | INTRODUCTION

Supine and prone positions have different effects regarding lung mechanics. Providing more homogenous ventilation of the lungs is recommended in the management of acute respiratory distress syndrome (ARDS) and prone positioning of the patient is a common strategy to increase oxygenation.[1] Prone positioning lowers the pleural pressure gradient in favour of independent lung zones and shifts lungs in coherence with the chest cavity, therefore provides a more homogenous strain and ventilation of the alveoli, contributing to better oxygenation.[2,3] Furthermore, prone positioning increases functional residual capacity and chest wall elasticity, resolves atelectasis in posterior lung zones, facilitates an even distribution of elasticity among all lung zones, improves ventilation/perfusion ratio, reduces alveolar shunt and helps mobilisation of secretions.[4] Prolonged prone positioning (at least 12 hours a day) in early stages of ARDS have been demonstrated to improve oxygenation and reduce mortality in intubated patients.[5]

Coronavirus disease 19 (COVID-19)-related ARDS has been argued to differ from classic ARDS since worse lung compliance was

observed in COVID-19 cases.[6,7] In COVID-19 cases, dysregulation of pulmonary perfusion, parenchymal microthrombi and non-cardiogenic pulmonary oedema (ARDS-like) were reported as three different mechanisms held responsible for hypoxaemia.[6,7] Affected lung zones often vary in COVID-19. Instead of diffuse involvement such as classic ARDS, patchy and asymmetrical involvement has been observed in notable amount of cases. Therefore, in patients without response to prone positioning, alternative positions (right/left lateral decubitus, right/left swimmer's) with respect to affected lung zones may be beneficial. Hence, positioning approach of our inpatient clinic comprises different positions in addition to prone, applied according to blood oxygen saturation response and imaging findings of the patients.

Herein, we aimed to demonstrate the effects of our positioning approach on disease outcomes in COVID-19 patients with respiratory failure, by comparing patients compliant to positioning and not.

What's known

- Prone positioning is a well-known approach and associated with a significant benefit on oxygenation in ARDS

What's new

- Lateral and supine positions also seem beneficial in hypoxaemia because of COVID-19
- Individualising the positioning protocol may be considered since the distribution of involved lung zones vary in the course of COVID-19

2 | MATERIALS AND METHODS

This retrospective single-centre study was conducted in Ankara City Hospital from August 15 to 1 December 2020. Ethical approval of the study was obtained from the Ethics Committee of Ankara City Hospital.

Patients who were admitted to internal medicine inpatient clinic with a positive COVID-19 PCR test result from sputum or throat swab, with varying clinical status from mild to severe respiratory failure were investigated for eligibility. Patients who developed hypoxaemia with a blood oxygen saturation of ≤94% or a loss of 3% of oxygen saturation in ambient air for at least 24 hours and underwent positioning during hospital stay were enrolled. Age <18 years, intubation prior to admission, pregnancy, immediate need of invasive mechanical ventilation (altered mental status, fatigue) in first 24 hours of admission, vasopressor requirement to maintain median arterial pressure >65 mm Hg, contraindications for prone positioning therapy (recent abdominal or thoracic surgery or trauma, facial, pelvic or spine fracture, untreated pneumothorax), presence of do-not-resuscitate or do-not-intubate order were set as exclusion criteria.

Standard positioning approach, which has routinely been applied in our clinic, comprises six positions (prone, left/right lateral decubitus, left/right swimmer's, supine) (Figure 1). We individualise positioning by measuring blood oxygen saturation in each position for five minutes and determining the two positions with best blood oxygen saturation. Patients then are requested to maintain the two positions throughout the day, switching in 6- to 8-hour intervals, with breaks according to tolerance. Maintenance of blood oxygen saturation from 92% to 95% and patients' compliance to positioning is followed during staff inter visits on a 24/7 basis. Blood oxygen saturation is reevaluated in each position after three days for reorganising the positioning regimen. Reevaluation is brought forward in case of new-onset hypoxaemia.

Hospitalisation, management and discharge of the patients were decided according to the guidelines of the Turkish Ministry of Health.[8] All patients received standard of care medical approach comprising hydroxychloroquine, low molecular weight heparin, acetylsalicylic acid, favipiravir and additional anti-inflammatory treatment when indicated.

Information regarding demographics, comorbidities, clinical, laboratory and imaging features, administered medications, duration and characteristics of positioning approach, patients' compliance to positioning, presence of intubation, ICU admission and mortality were collected from hospital database and records using a standardised case report form. All data were checked by two physicians (OG and EKG), and then a third researcher (EC) determined any differences in interpretation between the two primary reviewers. Patient thereafter divided into two groups by compliance to positioning according to daily follow-up records and rates of mortality, intensive care unit admission, intubation, initiation of anti-inflammatory treatment and length of hospital stay were compared.

Statistical analyses were made by Statistical Package for the Social Studies version 22 software. Normality of variables were investigated by Shapiro-Wilks test. Continuous variables were given as mean ± standard deviation and median (minimum-maximum) according to normality. Continuous variables were compared between groups with either Student's *t* test or Mann-Whitney-*U* test according to normality. Nominal and categorical variables were presented in percentages and compared by χ^2. $p \leq .05$ were accepted as statistically significant.

3 | RESULTS

A total of 144 patients were enrolled in this study (97 compliant with positioning, 47 incompliant with positioning). No significant differences were observed in demographics, comorbidities, symptoms and baseline laboratory evaluations between groups except for age (Age, median (IQR) 60.0 (53.0-70.0) vs 55.0 (47.0-62.0), $p = .018$), c-reactive protein (CRP) (CRP, median (IQR): 27.5 (61.5) mg/l vs 46.0 (81.75) mg/l, $p = .02$) and d-dimer (D-dimer, median (IQR) 0.68 (0.75) vs 0.43 (0.41), $p = .004$) levels (Table 1). Course of CRP, d-dimer levels and changes in oxygen need during 15 day follow up were presented in Figures 2 and 3.

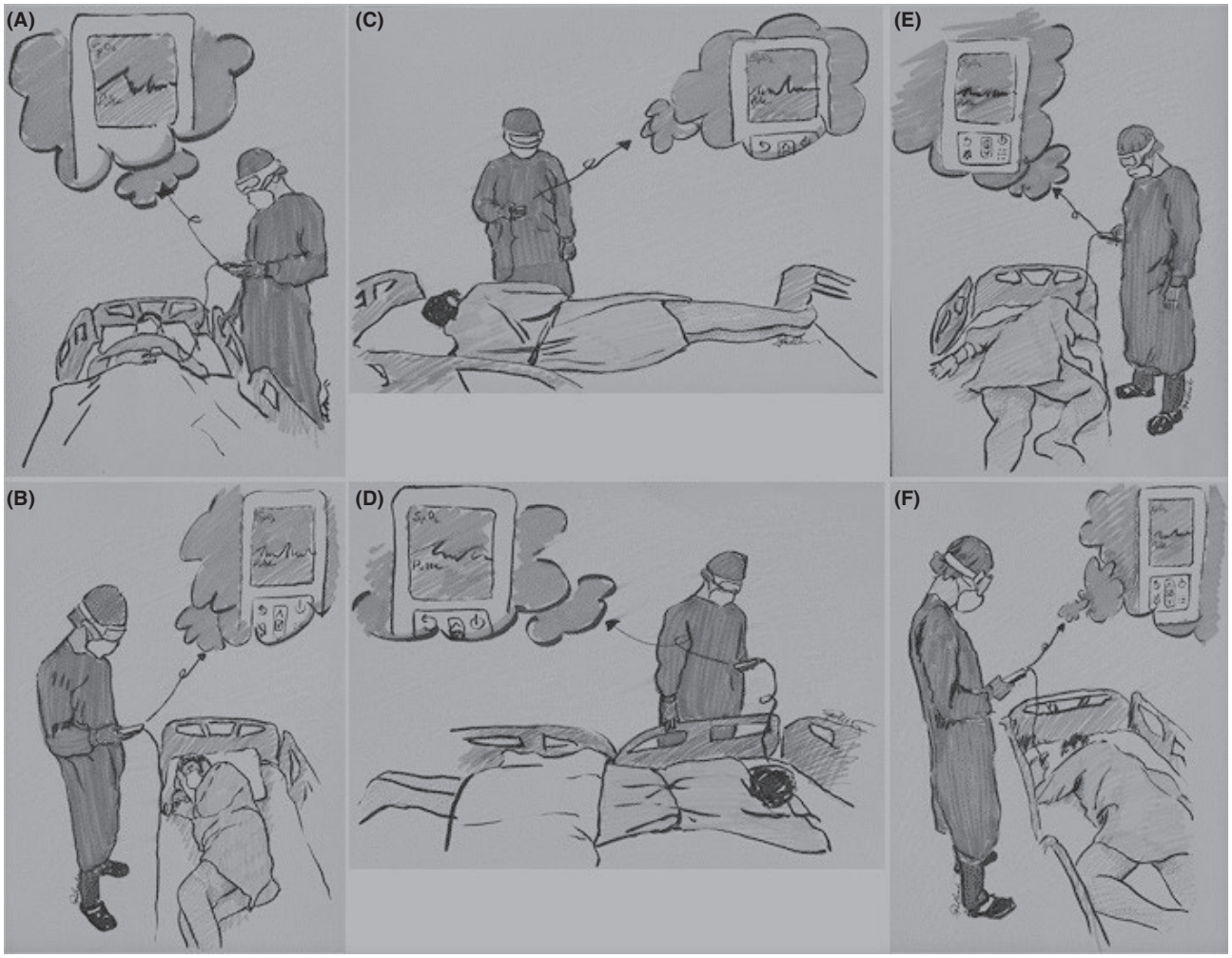

FIGURE 1 Patient positioning (A) supine, (B, C) left/right lateral decubitus, (D) prone, (E, F) left/right swimmer's

Patient outcomes were given in Table 2. Duration of positioning was median 12 (3-20) vs 5 (2-16) days in compliant and incompliant patients. Rates of ICU admission (7.2% vs 25.5%, $p < .001$), anti-inflammatory treatment initiation (68% vs 97.9%, $p < .001$) and length of hospital stay (5 (2-16) days vs 12 (3-20) days, $p < .001$) were significantly reduced in patients compliant with positioning.

4 | DISCUSSION

Ongoing pandemic of COVID-19 is still a major global health problem, with increasing demand for ICU admission all around the world. To date, there are no specific pharmacological therapies for COVID-19-induced respiratory failure, although several are undergoing clinical trials. Increasing demand for ICUs makes it inevitable to manage patients in general inpatient wards with ICU approach. Prone positioning is a feasible, safe, well-known approach and associated with a significant benefit on oxygenation, which can be applied to patients with hypoxaemia and involvement in gravity-dependent zones of the lungs.[9,10] Early initiation of prone positioning was reported to reduce the requirement for respiratory support, intubation rate and progression to critical condition.[11] Since various zones of the lungs can be involved in an asymmetric and patchy manner in COVID-19 pneumonia, lateral and supine positions may be options in patients who cannot tolerate prone positioning. Lateral position may be associated with beneficial effects on gas exchange, especially in unilateral widespread infiltrates as ventilation and perfusion increases in down sided zones.[12] Likewise, supine position may also be beneficial according to placement of lung infiltrates. Our results demonstrated individualising positioning with respect to blood oxygen saturation is related to the shorter hospital stay. This is the first experience of prone/lateral/supine positioning in spontaneously breathing patients with COVID-19 who were treated with various types of noninvasive oxygen support. Optimal positioning may allow patients time to recover lung function and may be used as a rescue strategy for severe hypoxaemia in the general wards.

Positioning has been a routine approach in the management of COVID-19 pneumonia in our clinic in an individualised manner as mentioned previously, however, notable amount of patients do not comply with positioning for various reasons. Our results revealed that compliance with positioning decreased the rate of ICU

TABLE 1 Demographics, symptoms, comorbidities and laboratory parameters in groups

	Patients incompliant to positioning (n = 47)	Patients compliant to positioning (n = 97)	*P*
Male sex, number (%)	37 (78.7)	67 (69.1)	.23
Median age, y, median (IQR)	60.0 (53.0-70.0)	55.0 (47.0-62.0)	.018
Symptoms, number (%)			
Cough	21 (44.7)	39 (40.2)	.61
Fever	29 (61.7)	54 (55.7)	.49
Dyspnoea	16 (34.0)	35 (36.1)	.81
Headache	6 (12.8)	16 (16.5)	.56
Arthralgia	13 (27.7)	29 (29.9)	.78
Myalgia	32 (68.1)	61 (62.9)	.54
Diarrhoea	2 (4.3)	1 (1.0)	.20
Nausea and vomiting	4 (8.5)	4 (4.1)	.28
Anosmia	1 (2.1)	4 (4.1)	.54
Ageusia	1 (2.1)	4 (4.1)	.54
Comorbidities, number (%)			
Hypertension	20 (42.6)	29 (29.9)	.13
Diabetes	14 (29.8)	20 (20.6)	.2
Asthma or COPD	4 (8.5)	2 (2.1)	.069
CHD	10 (21.3)	19 (19.6)	.81
Renal disease	2 (4.3)	0 (0.0)	.1
Laboratory parameters, median (IQR)			
Creatinine, mg/dL	1.0 (0.4)	0.9 (0.2)	.011
AST, U/L	43.1 (20.0)	37.2 (20.1)	.098
ALT, U/L	41.9 (25.8)	41.6 (30.0)	.96
LDH, U/L	291 (181)	278 (122)	.212
CRP, mg/L	46 (81.75)	27.5 (61.5)	.02
ESR, mm/h	27 (29)	24 (29.5)	.240
Ferritin, µg/L	324 (343.5)	310.0 (477)	.258
WBC, 10^9/L	7.1 (3.7)	6.1 (3.0)	.070
Lymphocyte, 10^9/L	1.2 (0.9)	1.0 (0.4)	.15
Platelet, 10^9/L	206.7 (84.9)	223.9 (92.9)	.29
Haemoglobin, G/D	14.0 (1.5)	13.8 (1.8)	.65
D-dimer, mcg/mL	0.68 (0.75)	0.43 (0.41)	.004
Fibrinogen, g/L	4.59 (1.45)	4.4 (2.05)	.26

Abbreviations: ALT; alanine aminotransferase; AST; aspartate aminotransferase; CHD; coronary heart disease; CRP: C-reactive protein; ESR; erythrocyte sedimentation rate; IQR: interquartile range; LDH; lactate dehydrogenase; WBC; white blood cell count.

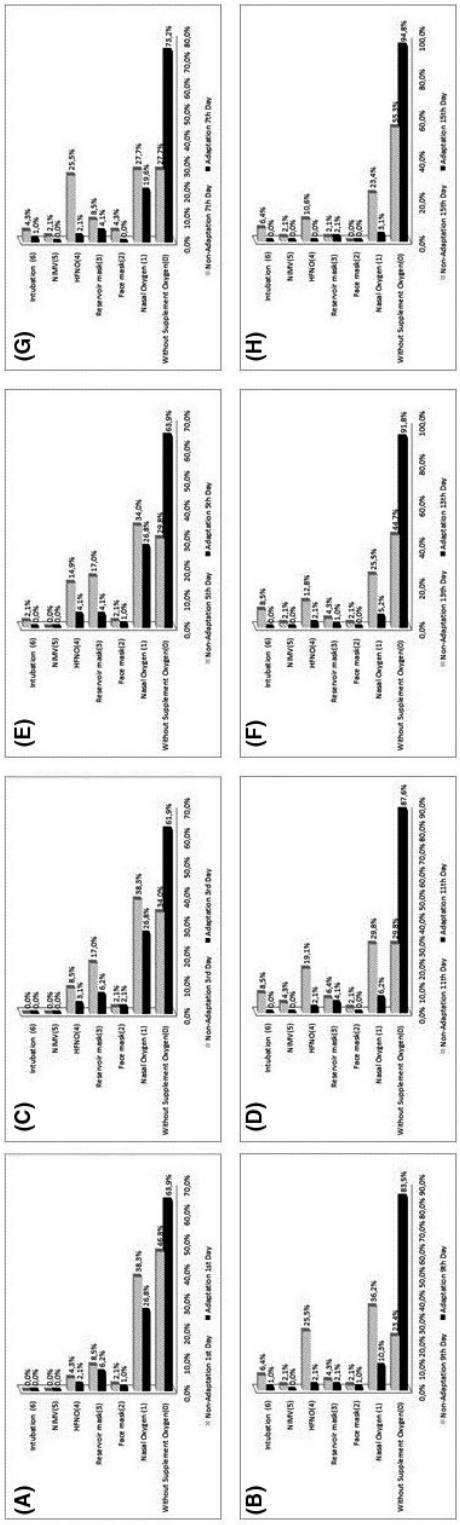

FIGURE 2 Changes in number of patients with oxygen support during 15th day follow-up in patients with and without adaptation to positioning

admission. Since ICUs are overloaded with COVID-19 patients, optimal positioning during noninvasive oxygen support may be useful to improve oxygenation and prevent ICU transfers.

The optimal duration of positioning is still unknown. Most studies have used either repeated sessions of prone ventilation

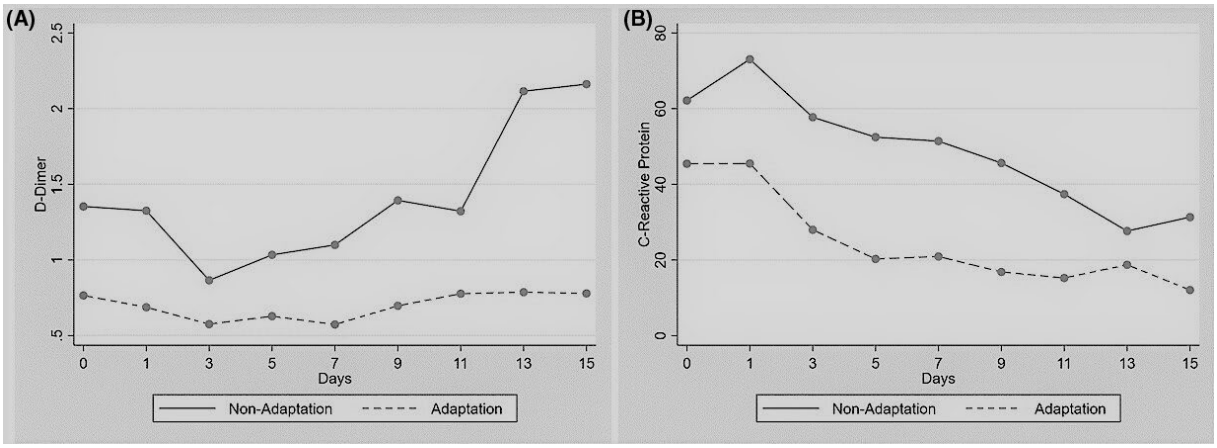

FIGURE 3 Course of C-reactive protein and D-dimer levels in patients with and without adaptation to positioning

TABLE 2 Outcomes in patient groups

	Patients incompliant to positioning (n = 47)	Patients compliant to positioning (n = 97)	*P*
Duration of symptoms on admission, days, median (IQR)	5.0 (3.0-9.0)	6.0 (3.0-10.0)	.59
Positioning duration, days, median (IQR)	12 (3-20)	5 (2-16)	<.001
Inpatient duration, days, median (IQR)	16.0 (13.0-22.0)	8.0 (6.0-10.0)	<.001
Anti-inflammatory treatment administration, number (%)	46 (97.9)	66 (68.0)	<.001
Admission to ICU, number (%)	12 (25.5)	7 (7.2)	.002
Mortality, number (%)	4 (8.5)	0 (0.0)	.004

Abbreviations: ICU; intensive care unit; IQR; interquartile range.

lasting 6-8 eight hours per day or prolonged prone ventilation lasting 17-20 hours per day.[1,4,13-15] Munshi et al[5] demonstrated at least 12 hours/day and Lee et al[16] reported at least 10 hours/day of prone positioned ventilation reduced mortality in patients with severe ARDS, in meta-analyses. In a randomised controlled trial, Mancebo et al[14] revealed early continuous prone positioning reduced mortality by 25% in severe ARDS patients. Similarly, Xu et al[11] set target prone positioning in COVID-19 pneumonia as longer than 16 hours/day for utmost beneficial effects. Accordingly, in adult patients with severe ARDS, prone ventilation for 12-16 hours per day is recommended in WHO Interim guidance.[17] Our positioning protocol comprises switching between two of the pre-described six positions with highest blood oxygen saturation obtained in 6 to 8 hour intervals and maintaining the positioning protocol as long as possible during the day. In patients compliant with the positioning, rates of ICU admission and anti-inflammatory treatment initiation were significantly reduced.

The retrospective nature of this study, small sample size, lack of randomisation and propensity score matching indicates cautious interpretation of our results since selection bias cannot be ruled out.

5 | CONCLUSIONS

Prone or other positioning should be considered in patients with noninvasive oxygen support for the potential to delay or prevent transfer to ICU, individualising the positioning protocol may be considered since distribution of involved lung zones vary in the course of severe hypoxaemia or ARDS because of COVID-19. With this simple manoeuvre, we assume it may be possible to reduce airway interventions, anti-inflammatory treatment rate and mortality.

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DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available on reasonable request from the corresponding author.

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