RESEARCH LETTER

Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure

Patients with coronavirus disease 2019 (COVID-19) are at risk for acute respiratory distress syndrome.[1] In intubated patients with severe acute respiratory distress syndrome, early and prolonged (at least 12 hours daily) prone positioning (PP) improves oxygenation and decreases mortality.[2,3] Because intensive care units (ICUs) are overloaded with patients with COVID-19, awake PP may be useful to improve oxygenation and prevent ICU transfers.[4] The objective of the study was to evaluate the feasibility, efficacy, and tolerance of PP in awake patients with COVID-19 hospitalized outside the ICU.

Editorial

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Methods | This prospective, single-center, before-after study was conducted among awake, nonintubated, spontaneously breathing patients with COVID-19 and hypoxemic acute respiratory failure requiring oxygen supplementation. The patients were admitted to Aix-en-Provence Hospital (France) from March 27 to April 8, 2020.

All consecutive patients with confirmed COVID-19 were screened and considered eligible if they (1) required oxygen supplementation and (2) had chest computed tomography findings suggestive of COVID-19 with posterior lesions. The main exclusion criteria were acute respiratory failure requiring intubation and impaired consciousness. The same oxygen

Table. Characteristics of Patients and Main Results

Characteristic	Total (N = 24)[a]	PP subgroups <1 h (n = 4)	1-<3 h (n = 5)	≥3 h (n = 15)
Baseline characteristics				
Age, mean (SD), y	66.1 (10.2)	63.8 (7.8)	61 (7.9)	68.4 (11.1)
Sex, No. (%)				
Women	8 (33)	2 (50)	1 (20)	5 (33)
Men	16 (67)	2 (50)	4 (80)	10 (67)
BMI >30, No. (%)	5 (23)	1 (50)	1 (20)	3 (20)
High blood pressure, No. (%)	6 (26)	1 (25)	2 (50)	3 (20)
SOFA score, mean (SD)	2.8 (0.9)	3.5 (0.7)	2.8 (0.8)	2.7 (1)
Oxygen supplementation, No. (%)				
<4 L/min	16 (67)	2 (50)	3 (60)	11 (73)
≥4 L/min or HFNC	8 (33)	2 (50)	2 (40)	4 (27)
Respiratory rate, mean (SD), breaths/min	18 (2.7)	18.3 (4)	20 (3.6)	17.3 (1.8)
Gas exchange and VAS scores before PP				
Pao_2, mean (SD), mm Hg	72.8 (14.2)	79.7 (11.7)	66.4 (8.9)	73.6 (15.9)
$Paco_2$, mean (SD), mm Hg	34.1 (5.3)	39.7 (4.6)	32.4 (3.9)	33.5 (5.4)
VAS, median (IQR)[b]				
Dyspnea	3 (2-5)	3 (1-3)	5 (3-7)	2 (1-5)
Discomfort	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1)
Gas exchange and VAS scores during PP[c]				
Pao_2, mean (SD), mm Hg	91 (27.3)		73 (12.1)	94.9 (28.3)
$Paco_2$, mean (SD), mm Hg	32.8 (4.5)		32 (3)	33 (4.8)
VAS, median (IQR)[b]				
Dyspnea	2 (1-4.5)		7 (2-8)	2 (1-4)
Discomfort	4 (1-5.5)		2 (2-4)	4 (1-6)
Gas exchange and VAS scores after resupination[c]				
Pao_2, mean (SD), mm Hg	77.6 (11.5)		77 (2)	77.8 (13)
$Paco_2$, mean (SD), mm Hg	32.3 (5.1)		28.7 (5.9)	33.3 (4.7)
VAS, median (IQR)[b]				
Dyspnea	2.5 (1-5)		5 (4-7)	2 (1-4)
Discomfort	0 (0-1)		0 (0-1)	0 (0-1)

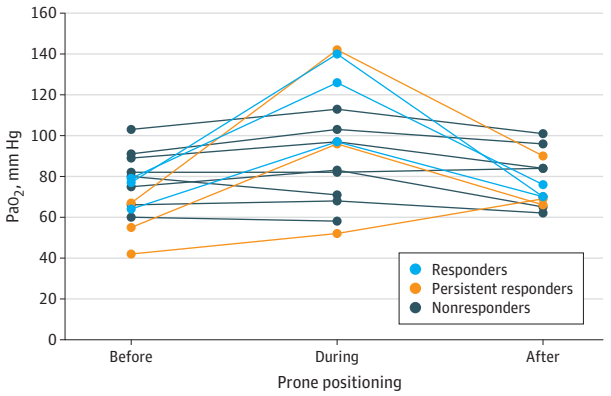
Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HFNC, high-flow nasal cannula; IQR, interquartile range; $Paco_2$, partial pressure of arterial carbon dioxide; Pao_2, partial pressure of arterial oxygen; PP, prone positioning; SOFA, Sequential Organ Failure Assessment (score range, 0-24); VAS, visual analog scale.

[a] Missing data: SOFA score for 2 patients, high blood pressure profile for 1, BMI for 2, respiratory rate for 8, before-PP VAS scores for 1, arterial blood gases before PP for 2, and $Paco_2$ for 1. VAS scores were missing during PP for 5 and after resupination for 7. During PP, arterial blood gases were missing for 7 patients and after resupination for 9. The 4 patients unable to sustain PP ≥1 were excluded from evaluations after baseline.

[b] The VAS was a 10-cm line anchored with no breathlessness or discomfort at 0 cm and maximum possible breathlessness or discomfort at 10 cm; 1 cm represents minimum clinically significant difference.

[c] During PP: 1 to 2 hours after patients were placed in PP. After resupination: 6 to 12 hours after resupination.

Figure. Individual Partial Pressure of Arterial Oxygen (Pao_2) Variation for Patients Who Sustained Prone Positioning (PP) for at Least 3 Hours



During PP indicates the 1 to 2 hours after proning and after PP indicates the 6 to 12 hours after resupination. Responders to PP = Pao_2 increase ≥20% between before and during PP. Persistent responders to PP = Pao_2 increase ≥20% between before PP and after resupination. All the persistent responders are also responders. One patient among the 15 refused arterial blood gases during PP and after resupination. For 2 patients, arterial blood gases after resupination were missing.

supply (device and fraction of inspired oxygen) was maintained during the study. Arterial blood gases were performed just before PP, during PP, and 6 to 12 hours after resupination.

The main outcome was the proportion of responders (partial pressure of arterial oxygen [Pao_2] increase ≥20% between before and during PP). Secondary outcomes included Pao_2 and partial pressure of arterial carbon dioxide ($Paco_2$) variation (difference in Pao_2 or $Paco_2$ between before and during PP or after resupination), feasibility (proportion of patients sustaining PP ≥1 hour and ≥3 hours), and proportion of persistent responders (Pao_2 increase ≥20% between before PP and after resupination). Tolerance was monitored with 10-cm visual analog scales for dyspnea and discomfort, anchored with no breathlessness or discomfort at 0 cm and maximum possible breathlessness or discomfort at 10 cm. Adverse events were monitored.

Patients were followed up for 10 days until April 18, 2020. Institutional review board approval was obtained. Written informed consent from patients was required.

Variations of Pao_2 were compared using a Wilcoxon signed-rank test for patients tolerating PP for 3 hours or more with a $P < .01$ (2-sided) to adjust for test multiplicity. Analyses were conducted using Stata version 14.0 (StataCorp).

Results | A total of 88 patients with COVID-19 were admitted during the period. Sixty-three patients did not meet inclusion criteria. Among the 25 eligible, 24 agreed to participate; of those, 4 (17%) did not tolerate PP for more than 1 hour, 5 (21%) tolerated it for 1 to 3 hours, and 15 (63%) tolerated it for more than 3 hours. Characteristics of the patients and main results are displayed in the **Table**. The median time from admission to first PP was 1 day (interquartile range, 0-1.5). Neither sedation nor anxiolytics were used.

Six patients were responders to PP, representing 25% (95% CI, 12%-45%) of the 24 patients included and representing 40% (6/15) (95% CI, 20%-64%) of the patients who sustained PP for 3 hours or more. Three patients were persistent responders. Among patients who sustained PP for 3 hours or more, Pao_2 increased from a mean (SD) of 73.6 (15.9) mm Hg before PP to 94.9 (28.3) mm Hg during PP (difference, 21.3 mm Hg [95% CI, 6.3-36.3]; $P = .006$) (**Figure**). No significant difference was found between Pao_2 before PP and Pao_2 after resupination ($P = .53$). None of the included patients experienced major complications. Back pain was reported by 10 patients (42%) during PP. At the end of a 10-day follow-up period, 5 patients required invasive mechanical ventilation. Four of them did not sustain PP for 1 hour or more and required intubation within 72 hours.

Discussion | In this study of patients with COVID-19 and hypoxemic respiratory failure managed outside the ICU, 63% were able to tolerate PP for more than 3 hours. However, oxygenation increased during PP in only 25% and was not sustained in half of those after resupination. These results are consistent with findings from previous small studies of PP in nonintubated patients.[5,6] A trial of PP may be a mechanism to select patients who will do well or it may be useful in a subset.

The study had several limitations. The sample was small, a single episode of PP was evaluated, the follow-up was short, clinical outcomes were not assessed, and causality of the observed changes cannot be inferred.

Further studies to identify optimal PP regimens and patients with COVID-19 in whom it may be beneficial are warranted.

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