RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

Response to Awake Prone Position in Nonintubated Individuals With COVID-19

Vanessa M Oliveira, Ruy A Barcellos, Daniele M Piekala, Miriane MS Moretti, Dulce I Welter, Angela E Candaten, Stefania G Cioato, Karina C Machado, and Gracieli N Deponti

BACKGROUND: Prone positioning is used for patients with ARDS undergoing invasive mechanical ventilation; its effectiveness in nonventilated awake patients is unclear. We aimed to evaluate the effectiveness of the prone maneuver in decreasing the risk of intubation and increasing the odds of favorable events. METHODS: We prospectively evaluated 66 subjects with COVID-19-related moderate ARDS who were admitted to the ICU; treated with high-flow nasal cannula, noninvasive ventilation, a reservoir mask, or a nasal cannula; and subjected to awake prone maneuvers from March 1, 2020–August 30, 2020. The following factors were recorded at ICU admission: age, sex, prior illness, simplified acute physiology score 3, body mass index, and changes in gas exchange after and before prone positioning. Subjects were divided into a group of responders and nonresponders according to a 20% increase in the P_{aO_2}/F_{IO_2} ratio before and after the maneuver. The need for intubation within 48 h of the start of the maneuver was also evaluated. We also analyzed the differences in mortality, ICU length of stay, hospital length of stay, and duration of mechanical ventilation. A generalized estimating equation model was applied to preprone and postprone means. To control for confounding factors, multivariate Poisson regression was applied. RESULTS: Forty-one subjects age 54.1 y ± 12.9 were enrolled. Responders showed increased S_{pO_2} ($P < .001$), P_{aO_2} ($P < .001$), and P_{aO_2}/F_{IO_2} ratios ($P < .001$) with the maneuver and reduced breathing frequency. Responders had shorter lengths of stay in the ICU ($P < .001$) and hospital ($P < .003$), lower intubation rates at 48 h ($P < .012$), fewer days of ventilation ($P < .02$), and lower mortality ($P < .001$). Subjects who responded to the maneuver had a 54% reduction in the risk of ventilation and prolonged stay in the ICU. CONCLUSIONS: Among the responders to prone positioning, there were fewer deaths, shorter duration of mechanical ventilation, shorter ICU length of stay, and shorter hospital length of stay. *Key words: COVID-19; hypoxemic respiratory failure; intubation; prone positioning; awake prone; ARDS.* [Respir Care 0;0(0):1–●. © 0 Daedalus Enterprises]

Introduction

Prone positioning improves oxygenation and mortality among patients with moderate ARDS who receive mechanical ventilation.[1] The mortality benefit cannot be explained solely by improved oxygenation and has been linked to decreased overdistention and cyclic alveolar recruitment/derecruitment within tidal breaths, with a decreased risk of ventilator-induced lung injury.[2] Multiple studies support the safety, feasibility, and efficacy of prone positioning in awake, nonintubated subjects with COVID-19-related pneumonia.[3-12] Spontaneous breathing by patients with acute hypoxemic respiratory failure can generate high respiratory drives and forceful inspiratory efforts, leading to lung injury

The authors are affiliated with Prone Teaching and Research Group, ICU Department, Hospital de Clinicas de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil.

The authors have disclosed no conflicts of interest.

The study was performed at Hospital de Clinicas de Porto Alegre, ICU Department, Porto Alegre, Rio Grande do Sul, Brazil.

Correspondence: Vanessa M Oliveira PhD, Ramiro Barcellos 2350, Av. Protásio Alves, 211 - Santa Cecilia, Porto Alegre, Brazil 90035–903. E-mail: vmoliveira@hcpa.edu.br.

DOI: 10.4187/respcare.08982

RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

similar to ventilator-induced lung injury. Prone positioning combined with noninvasive ventilation (NIV)/CPAP may help patients mitigate this detrimental effect, in part by reducing regional hyperinflation.[13] The impact of improved oxygenation on clinical outcomes such as survival remains unclear.

Many questions remain unanswered when considering the use of awake prone positioning. For example, what are the effects of awake prone positioning on patient outcomes? Which patients are most likely to benefit, and which ones should be excluded? The objective of the study was to compare the characteristics and variables between the responding and nonresponding groups and check whether a delay exists in intubation in 48 h. We also examined whether failure (intubation in 48 h) was associated with unfavorable outcomes.

QUICK LOOK

Current knowledge

Prone positioning is an established evidence-based practice for patients with ARDS undergoing invasive mechanical ventilation, although the evidence of its efficacy in nonventilated awake patients is limited. Awake prone positioning in nonintubated patients with COVID-19 could avoid endotracheal intubation, reduce the use of critical care resources, and improve survival.

What this paper contributes to our knowledge

We found that prone positioning in awake, spontaneously breathing subjects with COVID-19 was tolerable and safe. Subjects who responded to the maneuver had lower mortality and shorter ICU and hospital lengths of stay.

Methods

Study Design and Participants

In this single-center prospective study, we enrolled a convenience sample of 83 subjects admitted to the ICU from March 1, 2020–August 30, 2020, who had moderate ARDS. Subjects were eligible for inclusion if they were 18–80-y old and had been admitted to the hospital with a confirmed diagnosis of COVID-19-related pneumonia requiring supplemental oxygen. Patients were excluded if they were pregnant, uncooperative, had an altered mental status, or had a COPD requiring home NIV or oxygen therapy. The institutional review board approved the study and waived the need for informed consent from the participants because we analyzed the identified data collected from electronic medical records. This research was approved by the Ethics Committee on Human Research of the Hospital de Clinicas de Porto Alegre research board (CAAE 61274316.1.5327) and was reported according to the STROBE guidelines.[14]

Procedures

For all the subjects, a diagnosis of COVID-19 was made by reverse transcription-polymerase chain reaction using a nasal swab. After enrollment, baseline data were collected from each subject and included sex, age, body mass index (BMI), comorbidities, baseline arterial blood gas measurement (an arterial line was placed), type of oxygen support (reservoir mask, high-flow nasal cannula [HFNC], NIV, or nasal cannula), and ventilation parameters, including F_{IO_2}, ROX index, and subjective comfort. Some subjects alternated periods of NIV and HFNC during the day. Each subject was helped into the prone position. More than one prone session was performed for most subjects. The subject was then encouraged to maintain the prone position for at least 120 min before being helped back into the supine position. The subject was considered intolerant to the maneuver if the maneuver was interrupted within 10–60 min due to worsening of dyspnea, worsening of saturation, low back pain, or general discomfort in the prone position. Prone positioning sessions were allowed in the days after the first session according to the clinician's judgment. We collected data only from the first prone session for each subject. Comfort was assessed by asking the subject how they would evaluate the presence of anxiety in terms of "yes" or "no." The subjects were followed up until hospital discharge to assess intubation or death.

Outcomes

The objectives of the study were to identify predictors of the response to prone positioning. Subjects were classified according to their response to prone positioning as responders and nonresponders, with a 20% increase in the P_{aO_2}/F_{IO_2} ratio from the supine to the prone position being considered a response.

We recorded whether intubation was delayed or there was no intubation in the responder group. We also examined whether failure was associated with unfavorable outcomes, including hospital and ICU length of stay, and duration of mechanical ventilation. The successful group was defined as no intubation within 48 h after prone positioning. The secondary outcomes were tolerance to the maneuver, P_{aCO_2}, and improvement in the P_{aO_2}/F_{IO_2} ratio and S_{pO_2}/F_{IO_2} ratio.

Statistical Analysis

We presented continuous data as summary indicators to account for different distribution shapes. We calculated the

RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

Table 1. Characterization of the Sample Population

Variables	Responders ($n = 19$, 46.3%)	Nonresponders ($n = 22$, 53.7%)	P
Age, y	54.9 ± 12.7	52.4 ± 15.3	.58
Sex			> .99
Male	13 (68.4)	15 (68.2)	
Female	6 (31.6)	7 (31.8)	
Comorbidities			
Diabetes	2 (10.5)	7 (31.8)	.14
Hypertension	10 (52.6)	9 (40.9)	.66
Obesity	10 (52.6)	12 (54.5)	> .99
Neoplasm	0	2 (9.1)	.49
Heart disease	1 (5.3)	2 (9.1)	> .99
Pulmonary disease	0	1 (4.5)	> .99
Asthma	1 (5.3)	2 (9.1)	> .99
SAPS 3	48.5 ± 9.5	52.7 ± 10.1	.18
BMI, kg/m^2	31.6 ± 5.5	30.2 ± 7.6	.49
Time from symptoms to prone, d	9.2 ± 2.9	8.4 ± 3.8	.46
Median prone sessions per d, no.	1 (1–3)	1 (1–4)	.71
Median time proned, d	1.5 (1–2)	1 (1–3)	.99
Median duration of prone positioning, h	120 (105–120)	120 (60–120)	.27
Median ROX preprone	3.8 (3.3–5.4)	3.4 (2.8–4.4)	.17
Right ventricular dysfunction	1 (5.3)	1 (4.5)	> .99
Nitric oxide	0	2 (9.1)	.49
ECMO	0	1 (4.5)	> .99
Ventilatory support during the maneuver			.41
Mask with reservoir	11 (57.9)	12 (54.5)	
HFNC	8 (42.1)	7 (31.8)	
NIV	0	2 (9.1)	
Nasal cannula	0	1 (4.5)	
NIV acute phase	8 (42.1)	12 (54.5)	.63
NIV failure			.05
Yes	1 (5.3)	8 (36.4)	
No	7 (36.8)	5 (22.7)	
Did not use	11 (57.9)	9 (40.9)	
HFNC	9 (47.4)	9 (40.9)	.92
Alternating use, NIV+HFNC			.40
Yes	0	2 (9.1)	
Not	14 (73.7)	15 (68.2)	
Not applicable	5 (26.3)	5 (22.7)	
Tolerated the maneuver	17 (89.5)	12 (54.5)	.03
Reported anxiety during the maneuver	2 (10.5)	2 (10.0)	> .99
Needed medication to tolerate the maneuver	4 (21.1)	2 (9.5)	.39

Data are presented as n (%), mean ± SD, or median (25–75%).
SAPS 3 = simplified acute physiology score 3
BMI=body mass index
ROX index =oxygen saturation/F_{IO_2}/breathing frequency
ECMO = Extracorporeal membrane oxygenation
HFNC = high-flow cannula nasal
NIV = noninvasive ventilation

mean (SD) and median (interquartile range) for continuous variables based on their distributions. The normality of the data was assessed using the Shapiro-Wilk test. Categorical variables are presented as absolute and relative frequencies. We compared the distributions of continuous variables between subgroups defined by the response using unpaired Student t test. In case of asymmetry, the Mann-Whitney test was used. To compare proportions, Pearson chi-square or Fisher exact tests was used. To compare the preprone and postprone means, Student t test for paired samples was applied. In cases of asymmetry, the Wilcoxon test was used. To control for confounding factors, a multivariate

RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

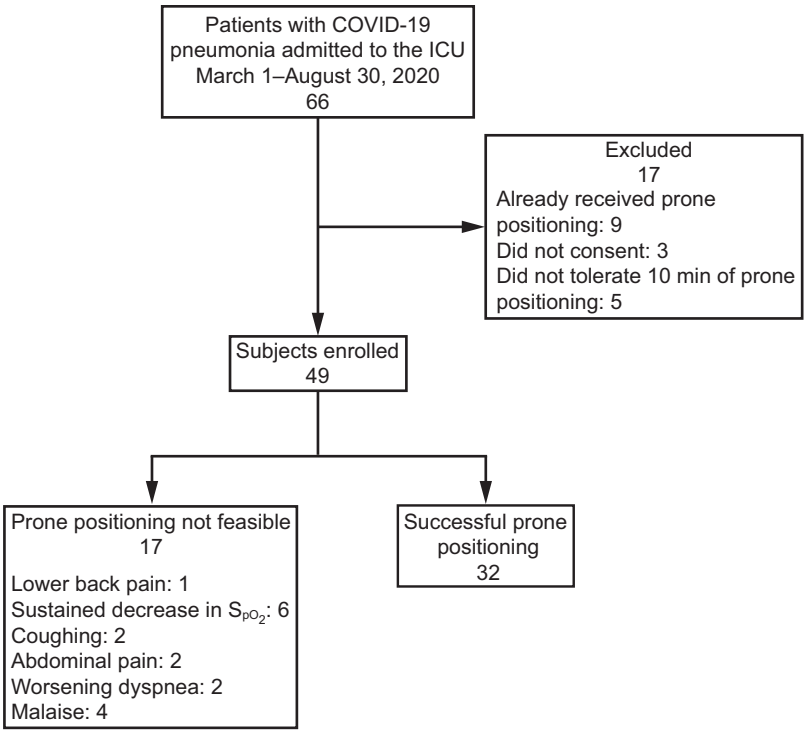

Fig. 1. Flow chart.

Poisson regression model was applied. For the comparison of preprone and postprone means according to the response to the maneuver, the generalized estimating equation model was applied. The linear model was used for variables with symmetric distribution, and the gamma model was used for those with asymmetric distribution. To control for confounding factors, the multivariate hierarchical Poisson regression model was applied. The construction of the blocks was based on the literature. The level of significance adopted was 5% ($P < .05$), and the analyses were performed using the SPSS version 21.0 program (IBM, Armonk, New York).

Results

Between March 1, 2020–August 30, 2020, 66 patients with COVID-19–related pneumonia were admitted to the hospital's ICU. Nine patients were excluded from the study because they had undergone the maneuver in the emergency department or general care; 5 were excluded because they could not tolerate 10 min of the maneuver (4 patients were intubated; 2 died on admission to the ICU), and 3 did not consent to undergo the maneuver. Therefore, 49 subjects underwent the prone maneuver while awake. Due to loss of data from 8 subjects, we analyzed the maneuver of 41 subjects. Although 29 (70.7%) of the subjects tolerated the awake prone maneuver, 4 subjects reported anxiety, and medication was administered to 4 subjects (Table 1). Moreover, 12 subjects did not complete the maneuver (60–120 min); and the reported causes were lower back pain (1 subject), a sustained fall in oxygen saturation (2 subjects), coughing crisis (2 subjects), abdominal pain (1 subject), worsening dyspnea (2 subjects), and malaise (4 subjects) (Fig. 1).

The subjects were divided into 2 groups according to whether the prone maneuver was successful. The response to the prone position was considered an increase in the P_{aO_2}/F_{IO_2} ratio > 20% from the supine to the prone position. The need for intubation within 48 h of the maneuver was evaluated. Table 1 shows the characteristics of the study population. The mean ages of the subjects in the responder group and nonresponder group were 54.9 y ± 12.7 and 52.4 y ± 15.3, respectively; and the mean BMIs were 31.6 kg/m^2 ± 5.5 and 30.2 kg/m^2 ± 7.6, respectively. The number of male subjects was 13 (68.4%) in the responder group and 15 (68.2%) in the nonresponder group. Common comorbidities included hypertension in 10 (52.6%) responders and 9 (40.9%) nonresponders and diabetes in 2 (10.5%) subjects in the responder group and 7 (31.8%) subjects in the nonresponder group. The simplified acute physiology score (SAPS) 3 was 48.5 ± 9.5 in the responder group and 52.7 ± 10.1 in the nonresponder group. The subjects were admitted to the hospital for a mean of 9.2 d ± 2.9 after symptom onset and 8.4 d ± 3.8 after symptom onset, respectively. The median number of daily prone positioning sessions was 1 (1–3), with a duration of 120

RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

Table 2. Before and After Prone Respiratory Parameters

Variables	Responders ($n = 19$, 46.3%)	Nonresponders ($n = 22$, 53.7%)	P
Frequency, breaths/min			
Preprone	28.5 ± 5.3	30.3 ± 7.7	.36
Postprone	23.3 ± 5.5	27.5 ± 5.4	.02
Δ (95% CI)	−5.1 (−8.2 to −2.0)	−2.8 (−5.5 to −0.1)	.27
P	.001	.045	
Arterial pH			
Preprone	7.44 ± 0.03	7.42 ± 0.04	.02
Postprone	7.43 ± 0.03	7.41 ± 0.05	.11
Δ (difference)	−0.01 (−0.03 to 0)	−0.01 (−0.03 to 0.01)	.88
P	.02	.25	
P_{aCO_2}			
Preprone	37.2 ± 3.9	35.3 ± 3.9	.11
Postprone	37.9 ± 3.7	38.6 ± 9.7	.76
Δ (difference)	0.7 (−0.9 to 2.4)	3.3 (−0.4 to 6.9)	.21
P	.39	.08	
S_{pO_2}, %			
Preprone	93.7 ± 3.1	90.9 ± 4.8	.02
Postprone	97.5 ± 2.1	95.5 ± 2.8	.01
Δ (difference)	3.8 (2.6–5.1)	4.6 (2.7–6.5)	.53
P	< .001	< .001	
F_{IO_2}			
Preprone	0.83 ± 0.16	0.83 ± 0.20	.97
Postprone	0.79 ± 0.17	0.85 ± 0.17	.22
Δ (difference)	−0.04 (−0.11 to 0.03)	0.02 (−0.03 to 0.08)	.16
P	.29	.37	
P_{aO_2}			
Preprone	72.4 ± 26.3	96.7 ± 59.0	.07
Postprone	109.3 ± 29.1	83.4 ± 43.5	.02
Δ (difference)	37.1 (23.2–50.8)	−13.4 (−25.1 to −1.6)	< .001
P	< .001	.03	
S_{pO_2}/F_{IO_2}			
Preprone	119.1 ± 33.4	119.2 ± 41.1	.99
Postprone	131.5 ± 42.5	119.0 ± 34.8	.30
Δ (difference)	12.4 (−7.0 to 31.8)	−0.2 (−11.2 to 10.8)	.27
P	.21	.97	
P_{aO_2}/F_{IO_2}			
Preprone	90.7 ± 39.2	118.3 ± 57.7	.06
Postprone	148.1 ± 61.1	100.7 ± 47.6	.001
Δ (difference)	57.5 (37.5–77.4)	−17.6 (−28.5 to −6.7)	< .001
P	< .001	.002	

Data are presented as n (%) unless otherwise noted.

min (80–120) for the first session; and the number of prone positioning sessions in groups was 1.5 (1–2) for responders and 1.0 (1–3) for nonresponders, with a duration of 120 min (80–120). The ROX index before the maneuver in responders and nonresponders was 3.8 (3.3–5.4) and 3.4 (2.8–4.4), respectively. During the maneuver, 33 (80.4%) subjects were treated with reservoir masks, 15 (10.5%) with an HFNC, 2 (4.5%) with NIV, and 1 (4.5%) with a nasal cannula. Alternating use of NIV and an HFNC was applied to 2 (9.1%) subjects in the nonresponder group (Table 1). Table 2 shows the arterial blood gas values and ventilation parameters between the responder and nonresponder groups. The responder group showed a reduction in breathing frequency with the maneuver ($P < .001$); S_{pO_2} increased in both groups after the maneuver ($P < .001$), and P_{aO_2} and P_{aO_2}/F_{IO_2} ratio increased in postmaneuver responders ($P < .001$).

The intubation rate was higher in the nonresponder group, although the difference was not significant ($P =$

RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

Table 3. Outcomes According to Responder and Nonresponder Group

Variables	Responders ($n = 19$, 46.3%)	Nonresponders ($n = 22$, 53.7%)	*P*
Intubation in 24–48 h	4 (21.1)	11 (50.0)	.11
No intubation	14 (73.7)	9 (40.9)	
Outcomes			< .001
Survived	18 (94.7)*	10 (45.5)	
Died	0	10 (45.5)*	
Remained hospitalized	1 (5.3)	2 (9.1)	
ICU discharge			.001
Yes	18 (94.7)*	9 (40.9)	
No	0	9 (40.9)*	
Remained hospitalized	1 (5.3)	4 (18.2)	
Discharged within 28 d			.02
Yes	14 (73.7)*	9 (40.9)	
No	1 (5.3)	8 (36.4)*	
Hospital transfer	3 (15.8)	1 (4.5)	
Remained hospitalized	1 (5.3)	4 (18.2)	
Median duration of ventilation, d	0 (0–3.0)	14 (0–24.5)	.02
Median ICU length of stay, d	6 (4.0–0)	17 (7.0–27.5)	.04
Median hospital length of stay, d	11.0 (7.0–15.0)	19.5 (11.5–30.0)	.04

Data are presented as *n* (%), mean ± SD, or median (25–75%). * Statistically significant association according to the residual test adjusted to 5% significance.

Table 4. Poisson Regression Models to Assess Factors Independently Associated With Response

Variables	Relative Risk (95% CI)	*P*
Block 1 - Sociodemographic		
Age	1.01 (0.98–1.03)	.56
Male	1.00 (0.49–2.04)	.99
Block 2 - Comorbidities		
Diabetes	0.37 (0.11–1.28)	.11
Hypertension	1.49 (0.80–2.80)	.21
BMI	1.02 (0.97–1.07)	.47
Block 3 - SAPS 3	0.97 (0.93–1.02)	.28
Block 4 - Types of ventilation		
Failure NIV		
Yes	1.00	
No	4.99 (0.69–35.90)	.11
Not used	4.93 (0.74–33.00)	.10
HFNC	1.36 (0.55–3.38)	.51
Reservoir mask during the maneuver	1.23 (0.48–3.15)	.66

Δ = difference between pre-post moments
BMI = body mass index
SAPS 3 = simplified acute physiology score 3
NIV = noninvasive ventilation
HFNC = high-flow nasal cannula

.11). Responders had lower mortality ($P < .001$), a higher rate of discharge from the ICU ($P < .001$) and hospital discharge at 28 d ($P < .02$), fewer days of mechanical ventilation ($P = .02$), and shorter ICU and hospitals lengths of stay ($P = .04$) (Table 3). Independent factors related to response to prone maneuver, such as sociodemographic factors, comorbidity, SAPS 3, and type of ventilation, showed no statistically significant association (Table 4). The evaluation of the effect of the response to the maneuver in relation to the outcomes intubation, mortality, and length of stay in the ICU and hospital demonstrated that subjects who responded to the maneuver had a 54% reduction in the risk of ventilation and prolonged length of stay in the ICU (Table 5).

RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

Table 5. – Evaluation of the Effect of the Response to the Maneuver on the Outcomes of Intubation, Mortality, ICU Length of Stay, and Hospital Length of Stay

Variables	Relative Risk (95% CI)	*P*
Categorical outcomes		
Intubation in 24–48 h	0.42 (0.16–1.11)	.07
Mechanical ventilation	0.46 (0.23–0.95)	.03
Quantitative outcomes*		
ICU length of stay ≥ 9 d	0.46 (0.23–0.94)	.03
Hospital length of stay ≥ 14 d	0.50 (0.24–1.04)	.06

* Considered the median as the cutoff point.

Discussion

In this observational prospective study, we found that prone positioning was safe and feasible in most subjects with acute respiratory failure due to SARS-CoV-2 infection. Our results add to those of other studies.[6,8,14,15] The main causes for interruption of the maneuver were lower back pain, a sustained fall in oxygen saturation (main cause), coughing crisis, abdominal pain, worsening dyspnea, and discomfort during positioning, as confirmed in other studies.[6,8,14,15] In our study, some subjects reported anxiety being treated with medication, a situation that proved to be safe. In our study, there were no adverse events during the maneuver confirmed in the Rosén et al[16] study, where no increase in adverse events with pressure ulcers or cardiorespiratory arrest was identified.

We investigated the factors more common for awake prone maneuver failure, and the outcome of prone positioning, previous comorbidities, age, sex, BMI, and other characteristics studied was not predictive factors of the response to prone maneuver in our study, as demonstrated by Cheriana et al.[17] We found that prone positioning in the responders was associated with an increase in P_{aO_2}, the S_{pO_2}/F_{IO_2} ratio, and a reduction in breathing frequency, as demonstrated by other studies in the literature.[11,14,18,19] The significant increase in S_{pO_2} values during prone positioning could be an indicator to help physicians identify early patients at lower risk for short-term intubation. The use of prone positioning should be limited to less severe patients, and this failure to respond to the prone position can be associated with a short maneuver time. The beneficial impact of prone positioning in patients with ARDS was demonstrated only in the PROSEVA study[1] with durations of prone positioning of 16 h, whereas previous studies with shorter durations of prone positioning showed no beneficial impact. We need further studies to clarify this.

After 12 h of HFNC treatment, the ROX index demonstrated the best prediction accuracy (area under the receiver operating characteristic curve 0.74). A ROX index ≥ to 4.88 measured after 12 h of HFNC was significantly associated with a lower risk for mechanical ventilation.[20] Chandel et al[21] demonstrated that the ROX index was sensitive for the identification of subjects who were successfully managed with HFNC without the subsequent need for endotracheal intubation. Interestingly, in our study, the ROX index was not a predictive factor for the success of the maneuver.

That the early application of awake prone positioning, together with an HFNC or NIV, may help avoid endotracheal intubation was demonstrated in our study and by Ding et al.[15] The latter study revealed that early awake prone positioning together with NIV/HFNC made endotracheal intubation redundant in > 50% of subjects (11/20), similar to our study results. Sun et al[22] provided evidence for the early recognition and treatment of subjects with COVID-19 with ARDS and pneumonia using an HFNC, together with awake prone positioning and restrictive fluid resuscitation, and showed a decrease in the invasive mechanical ventilation rate. Finally, we showed that subjects who responded to prone positioning did not require intubation in the first 48 h after the prone maneuver; although the results were not statistically significant, this may be due to the small sample size. The responders had fewer deaths, more days free of mechanical ventilation, more days outside of the ICU, and fewer days in the hospital as demonstrated in a meta-analysis.[23,24] In Coppo et al[12] and Rósen et al,[16] the response to prone positioning showed no significant difference in the rate of intubation compared with nonresponders.

To our knowledge, this study is the largest prospective trial to analyze prone positioning in awake subjects, specifically in those with COVID-19-related pneumonia. This procedure in awake subjects with COVID-19 has been reported in a limited number of case reports and cohort studies.[7-10] The data collected are of high quality and complete. The external validity of our study is strengthened by the subjects being enrolled in various clinical settings every day, although the need for therapeutics to prevent intubation and consequently conditions to place awake patients in prone positioning can differ widely from one hospital to another and from one country to another.

Our study has several limitations. The lack of a control group (and randomization) does not allow inference regarding patient-centered outcomes, and the enrollment of nonconsecutive subjects might have led to selection bias. Another limitation of our study is that it is a single-center study; thus, it might not be generalizable, and the sample size was small. Another limitation, intubation, is a clinical decision, and the clinical practice of the authors may be different from that of other clinicians.

Conclusions

We found that prone positioning in awake, spontaneously breathing subjects was well tolerated. We observed

RESPIRATORY CARE Paper in Press. Published on November 23, 2021 as DOI: 10.4187/respcare.08982

that the group that responded to the maneuver had lower mortality and shorter lengths of stay in the ICU and the hospital.

REFERENCES

1. Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368(23):2159-2168.
2. Cornejo RA, Díaz JC, Tobar EA, Bruhn AR, Ramos CA, González RA, 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.
3. Bamford P, Bentley A, Dean J, Whitmore D, Wilson-Baig N. ICS guidance for prone positioning of the conscious COVID patient 2020. Intensive Care Society. Available at: https://emcrit.org/wp-content/uploads/2020/04/2020-04-12-Guidance-for-conscious-proning.pdf.
4. Telias I, Katira BH, Brochard L. Is the prone position helpful during spontaneous breathing in patients with COVID-19? JAMA 2020;323(22):2265-2267.
5. Slessarev M, Cheng J, Ondrejicka M, Arntfield R; Critical Care Western Research Group. Patient self-proning with high-flow nasal cannula improves oxygenation in COVID-19 pneumonia. Can J Anaesth 2020;67(9):1288-1290.
6. Elharrar X, Trigui Y, Dols AM, Touchon F, Martinez S, Prud'homme E, Papazian L. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. JAMA 2020;323(22):2336-2338.
7. Caputo ND, Strayer RJ, Levitan R. Early self-proning in awake, nonintubated patients in the emergency department: a single ED's experience during the COVID-19 pandemic. Acad Emerg Med 2020;27(5):375-378.
8. Solverson K, Weatherald J, Parhar KKS. Tolerability and safety of awake prone positioning COVID-19 patients with severe hypoxemic respiratory failure. Can J Anaesth 2021;68(1):64-70.
9. Xu Q, Wang T, Qin X, Jie Y, Zha L, Lu W. Early awake prone position combined with high-flow nasal oxygen therapy in severe COVID-19: a case series. Crit Care 2020;24(1):250.
10. Sartini C, Tresoldi M, Scarpellini P, Tettamanti A, Carcò F, Landoni G, Zangrillo A. Respiratory parameters in patients with COVID-19 after using noninvasive ventilation in the prone position outside the intensive care unit. JAMA 2020;323(22):2338-2340.
11. Thompson AE, Ranard BL, Wei Y, Jelic S. Prone positioning in awake, nonintubated patients with COVID-19 hypoxemic respiratory failure. JAMA Intern Med 2020;180(11):1537-1539.
12. Coppo A, Bellani G, Winterton D, Pierro M, Soria A, Faverio P, et al. Feasibility and physiological effects of prone positioning in nonintubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. Lancet Respir Med 2020;8(8):765-774.
13. Brochard L, Slutsky A, Pesenti A. Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. Am J Respir Crit Care Med 2017;195(4):438-442.
14. Scaravilli V, Grasselli G, Castagna L, Zanella A, Isgrò S, Lucchini A, et al. Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: a retrospective study. J Crit Care 2015;30(6):1390-1394.
15. Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. Crit Care 2020;24(1):28.
16. Rosén J, von Oelreich E, Fors D, Jonsson Fagerlund M, Taxbro K, Skorup P, et al; PROFLO Study Group. Awake prone positioning in patients with hypoxemic respiratory failure due to COVID-19: the PROFLO multi-center randomized clinical trial. Crit Care 2021;25(1):209.
17. Cherian SV, Li C, Roche B, Reyes SA, Karanth S, Lal AP, et al. Predictive factors for success of awake proning in hypoxemic respiratory failure secondary to COVID-19: a retrospective cohort study. Respir Med 2021;181:106379.
18. Tu GW, Liao YX, Li QY, Dong H, Yang LY, Zhang XY, et al. Prone positioning in high-flow nasal cannula for COVID-19 patients with severe hypoxemia: a pilot study. Ann Transl Med 2020;8(9):598.
19. Damarla M, Zaeh S, Niedermeyer S, Merck S, Niranjan-Azadi A, Broderick B, Punjabi N. Prone positioning of nonintubated patients with COVID-19. Am J Respir Crit Care Med 2020;202(4):604-606.
20. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard JD, Masclans JR. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: the utility of the ROX index. J Crit Care 2016;35:200-205.
21. Chandel A, Patolia S, Brown AW, Collins AC, Sahjwani D, Khangoora V, et al. High-flow nasal cannula therapy in COVID-19: using the ROX Index to predict success. Respir Care 2021;66(6):909-919. june no
22. Sun Q, Qiu H, Huang M, Yang Y. Lower mortality of COVID-19 by early recognition and intervention: experience from Jiangsu Province. Ann Intensive Care 2020;10(1):33.
23. Tan W, Xu DY, Xu MJ, Wang ZF, Dai B, Li LL, et al. The efficacy and tolerance of prone positioning in nonintubation patients with acute hypoxemic respiratory failure and ARDS: a meta-analysis. Ther Adv Respir Dis 2021;15:17534666211009407.
24. Cardona S, Downing J, Alfalasi R, Bzhilyanskaya V, Milzman D, Rehan M, et al. Intubation rate of patients with hypoxia due to COVID-19 treated with awake proning: a meta-analysis. Am J Emerg Med 2021;43:88-96.