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Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajemThe
American Journal of
Emergency Medicine

Early, awake proning in emergency department patients with COVID-19

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ARTICLE INFO

Article history:

Received 16 May 2020

Received in revised form 27 November 2020

Accepted 27 November 2020

Available online xxxxx

Keywords:

Proning

COVID-19

Feasibility

ABSTRACT

Objective: Proning has been shown to improve oxygenation and mortality in certain populations of intubated patients with acute respiratory distress syndrome. Small observational analyses of COVID-19 patients suggest awake proning may lead to clinical improvement. Data on safety and efficacy is lacking. We sought to describe the effect of proning on oxygenation in nonintubated COVID-19 patients. We also evaluated feasibility, safety, and other physiological and clinical outcomes associated with this intervention.

Methods: We conducted a prospective, observational cohort study of nonintubated patients with COVID-19 who underwent proning per an Emergency Department (ED) clinical protocol. Patients with mild to moderate respiratory distress were included. We calculated change in oxygenation by comparing the oxygen saturation to fraction of inspired oxygen ratio (SpO₂:FiO₂) during the five minutes prior to proning and first 30 min of proning. We also captured data on respiratory rate, duration of proning, need for intubation, intensive care unit admission, survival to discharge.

Results: Fifty-two patients were enrolled. Thirty were excluded for not meeting protocol inclusion criteria or missing baseline oxygenation data, leaving 22 for analysis. The SpO₂:FiO₂ ratio increased by a median of 5 (IQR: 0–15) in the post-proning period compared to the pre-proning period (median: 298 (IQR: 263–352) vs 295 (IQR: 276–350), $p = 0.01$). Respiratory rate did not change significantly between time periods. No immediate adverse events occurred during proning. Five patients (23%) were intubated within 48 h of admission.

Conclusion: Early, awake proning may be feasible in select COVID-19 patients and was associated with improved oxygenation.

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1. Introduction

Proning is a maneuver that has been well-described in mechanically ventilated patients with acute respiratory distress syndrome (ARDS) in the intensive care unit and has been demonstrated to improve oxygenation and mortality in certain patient populations [1–4]. The technique, which involves placing a patient prone (face down), is thought to have various physiologic effects including improving the ability for more homogenous oxygenation of the severely injured lungs [5]. While the vast majority of data on proning comes from the mechanically ventilated ARDS patient population, there have been reports of proning in non-intubated patients. Scaravilli et al. performed a retrospective analysis on fifteen non-intubated, awake patients and suggest that proning is feasible in this population and was associated with improved oxygenation [6].

The SARS-CoV – 2 pandemic has rapidly overwhelmed many elements of the United States healthcare system and is posing unprecedented challenges for physicians on the front lines managing these deteriorating patients. While severe respiratory disease in COVID–19 has been postulated to have similar characteristics to other forms of ARDS, the physiology of this virus also has some unique features and our knowledge of its behavior is evolving. Specifically, at least one phenotype has been reported as having substantial hypoxia (ventilation perfusion mismatching) while maintaining relatively good lung compliance, although others have challenged this assessment [7,8]. Anecdotal reports on the news, other media, and free online access medical education forums suggest that awake proning improves oxygenation and potentially averts or delays the need for mechanical ventilation [9–14]. Whether or not performing this maneuver early improves hypoxemia, work of breathing, and need for intubation remains unknown. Recent small, prospective cohorts of patients with COVID-19 suggest immediate benefit in oxygenation in this population [15,16].

The Emergency Department (ED) at Beth Israel Deaconess Medical Center initiated an awake proning protocol for non-intubated patients

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with COVID-19 respiratory disease as part of the clinical pathway for management of these patients. The primary objective of this study was to determine if implementation of a clinical protocol to prone awake, non-intubated COVID-19 positive patients with mild to moderate respiratory distress was associated with an improvement in oxygenation. Secondary objectives included evaluating the feasibility, safety, and other physiological and clinical outcomes associated with this intervention.

2. Methods

2.1. Study design and setting

This was a prospective, observational cohort study of adult ED patients 18 years of age or greater presenting with respiratory illness from confirmed COVID-19 who were enrolled in an awake proning clinical protocol. This study adhered to the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [17]. This study was reviewed by the institutional review board at our medical center and determined to be exempt.

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2.2. Protocol development and implementation

An early awake protocol was developed by members of the ED operational team and physicians boarded in emergency medicine and pulmonary critical care at our institution based on the best available evidence and consensus. Further input was obtained from ED nursing leadership and the protocol was modified for feasibility. The protocol is displayed in the online supplementary appendix (Fig. A.1).

2.3. Selection of participants

ED patients with respiratory symptoms at Beth Israel Deaconess Medical Center, an urban tertiary care center with an ED annual volume of approximately 55,000 were enrolled in the protocol if they met the following inclusion criteria: confirmed COVID-19 positive diagnosis or high suspicion for COVID-19 respiratory disease (e.g. patients with a history of respiratory or other COVID-19 symptoms and physician discretion based on any other historical, exam, or diagnostic testing results in the ED) dependent on supplemental oxygen via nasal cannula or nonrebreather to maintain an oxygen saturation of $>93\%$, normal mentation, ability to follow commands, and able to safely change position with minimal assistance. Patients were excluded if there was low suspicion for COVID-19 by the emergency physician, the patient was not being tested for COVID-19, the patient demonstrated rapidly deteriorating respiratory status at time of protocol or needed immediate intubation and mechanical ventilation, the patient was unable to safely change position with minimal assistance (e.g. had a fracture that impairs ability to prone, spinal instability, vomiting, confusion, inability to cooperate with staying in a prone position), or the patient had a variable fraction of inspired oxygen (FiO_2) during the pre-proning period which limited accurate calculation of oxygen saturation to fraction of inspired oxygen ($SpO_2:FiO_2$) ratio. Patients who subsequently tested negative for COVID-19 were excluded from the analysis.

Patients enrolled in the pathway were identified by screening and tracking all subjects for whom an electronic order or electronic acknowledgement of entering this pathway was performed. Our electronic tracking system included a notification to the physician team to order the protocol for possible patients. The physicians could also order this if a notification was not sent but the patient was believed to have met inclusion criteria. Ordering of the protocol was left to the discretion of the physician. Patients with a documented proning start time in the nursing notes, who were able to prone either face down or in the lateral position, and who had complete documentation of heart rate, blood pressure, and oxygen saturation during their ED stay were included. Patients who subsequently tested negative for COVID-19 by

polymerase chain reaction (PCR) nasal swab or would not have made oxygenation inclusion criteria for the protocol were excluded. Patients were enrolled in the protocol from April 4, 2020 through April 26, 2020. Our ED tracking system records oxygen saturation and respiratory rate by the minute from telemetry monitoring for all ED patients. Once patients were identified, a trained research assistant abstracted the other variables of interest from the ED and inpatient online medical record.

2.4. Measurements

Data on patients' vital signs including heart rate, blood pressure, respiratory rate, oxygen saturation, and oxygen support requirements were reported immediately prior to proning and for the duration of the ED stay. Additionally, oxygen saturation and respiratory rate were collected every minute during the remainder of the ED stay after the proning protocol was initiated. Respiratory rates recorded by the monitor which were below 8 or above 50 were considered to be spurious and were not included for data analysis. Outcome information was solicited through hospital discharge or death.

2.5. Outcomes

Our primary outcome measure was the $SpO_2:FiO_2$ ratio during the 5 min before proning compared to the $SpO_2:FiO_2$ from 5 to 35 min after the initiation of proning. Data from the first 5 min immediately after proning was initiated were excluded. We quantified the number of enrolled patients who tolerated the protocol and any immediate events after initiation of the protocol leading to cessation of the protocol (e.g. vomiting, respiratory decompensation, immediate need for intubation, death). We also determined the duration of proning in the ED, need for intubation, time on a ventilator, need for intensive care unit admission, oxygen requirements for non-intubated patients, and survival to hospital discharge, all during the duration of the patient's hospitalization.

2.6. Analysis

Given the lack of any large trials assessing oxygenation in COVID-19 patients at this time, we calculated our power from a cohort of septic patients. Using baseline $SpO_2:FiO_2$ information from a trial in septic shock, we assumed a mean baseline $SpO_2:FiO_2$ of 303 and a standard deviation of 112 [18]. Since the data in this study is paired, we assumed an increase of 15% with a correlation of 0.8. Given an alpha of 0.05, 22 patients would be required to have 80% power.

The analysis population included all patients who tolerated the proning protocol between April 4, 2020, and April 26, 2020 and had data on oxygenation from both before and during proning. Change in oxygen saturation (divided by FiO_2 in order to account for changes in supplemental oxygen) and respiratory rate were evaluated using the median value from 5 min prior to proning compared to the median value from minutes 5–35 of proning using a Wilcoxon signed rank test. The median difference in medians between groups were quantified by calculating a change score (value from proning period - value from pre-proning period) for each patient and taking the median of the change. As a subgroup analysis, we restricted our population to patients with no change in oxygen delivery in order to control for changes that might be dictated by physician discretion (i.e. a subjective decision to change the oxygen delivery). Descriptive statistics were used to quantify the secondary outcomes; no hypothesis testing was performed for these outcomes. Descriptive statistics were presented as counts with percentages or medians and interquartile ranges (IQRs). When analyzing differences in baseline demographics between included and excluded patients, Wilcoxon rank-sum, Chi Square, and Fisher's exact tests were used, as appropriate. All analyses were conducted with

Stata software, version 14.2 (College Station, TX) and a p -value of <0.05 was used for significance.

3. Results

3.1. Characteristics of study subjects

In total, 52 patients with a confirmed positive COVID-19 PCR test were enrolled in the proning protocol. Thirty patients (58%) were excluded for reasons noted in Fig. 1. The one patient who was excluded due to inability to tolerate the protocol was unable to lay prone due to abdominal discomfort with the position but did not have any vital sign changes when proning was attempted. There were no significant differences between the patients who were included and those that were excluded in terms of measured baseline characteristics (Table 1). Of the 22 remaining patients included in this analysis, 14 patients (64%) were men, the age range was 23 to 85 years, and the median age was 61 (IQR: 50, 65) years. Additional demographics are in Table 1. All 22 patients completed at least 30 min of proning. The median duration of proning in which vitals were collected was 109 (IQR: 65–159) minutes with a range of 19 to 294 min. None of the patients experienced immediate vomiting, respiratory decompensation, immediate need for intubation, or death upon proning.

3.2. Main results

The SpO₂:FiO₂ ratio significantly increased in patients in minutes 5–35 of proning compared to the 5 min before initiation of the protocol with a median increase of 5 (IQR: 0–15), median 295 (IQR: 276–350) vs 298 (IQR: 263–352), $p = 0.01$. In the 20 patients (91%) with respiratory rate information, the respiratory rate did not change significantly prior to compared to during the proning protocol: median 26 (IQR: 23–30) vs 25 (IQR: 23–38), $p = 0.36$. More information can be found in Table 2. These results were similar in the subgroup analysis restricted to patients with no oxygenation changes (Table 3).

Table 1
Patient Demographics and Baseline Characteristics

	Included (n = 22)	Excluded (n = 30)	p-value
Median age	61 (IQR: 50, 65)	60 (IQR: 50, 70)	0.95
Male sex	14 (64)	15 (50)	0.40
Race			0.87
White	5 (23)	9 (30)	
Black	11 (50)	14 (47)	
Other/unknown	6 (27)	7 (23)	
Ethnicity			>0.99
Hispanic	7 (33)	11 (37)	
Not Hispanic	13 (59)	17 (57)	
Unknown	2 (9)	2 (7)	
Median body mass index ^a	31.6 (IQR: 29.3, 35.1)	33.2 (IQR: 28.0, 36.3)	0.84
Past medical history			
Coronary artery disease	2 (9)	1 (3)	0.57
Cancer	2 (9)	6 (20)	0.44
Congestive heart failure	0 (0)	1 (3)	>0.99
Chronic obstructive pulmonary disease	2 (9)	1 (3)	0.57
Dementia/Alzheimer's	0 (0)	1 (3)	>0.99
Diabetes	8 (36)	11 (37)	>0.99
Alcohol abuse	1 (5)	0 (0)	0.42
Cardiac Arrhythmia	2 (9)	2 (7)	>0.99
Hypertension	10 (45)	14 (47)	0.93
Hyperlipidemia	7 (32)	8 (27)	0.76
Obesity	4 (18)	8 (27)	0.53
Renal disease	1 (5)	4 (13)	0.38
Stroke	0 (0)	1 (3)	>0.99
Thyroid disease	2 (9)	0 (0)	0.17
Tobacco use	2 (9)	3 (10)	>0.99
HIV/AIDS	0 (0)	1 (3)	>0.99
Asthma	3 (14)	6 (20)	0.72
FiO ₂ at baseline	31.5 (IQR: 27, 36)	n/a	n/a

Values in parentheses represent percentages unless otherwise noted.

Abbreviations: FiO₂ = fraction of inspired oxygen.

^a 13 values were missing: 3 in the patients who were included; 10 in the patients who were excluded.

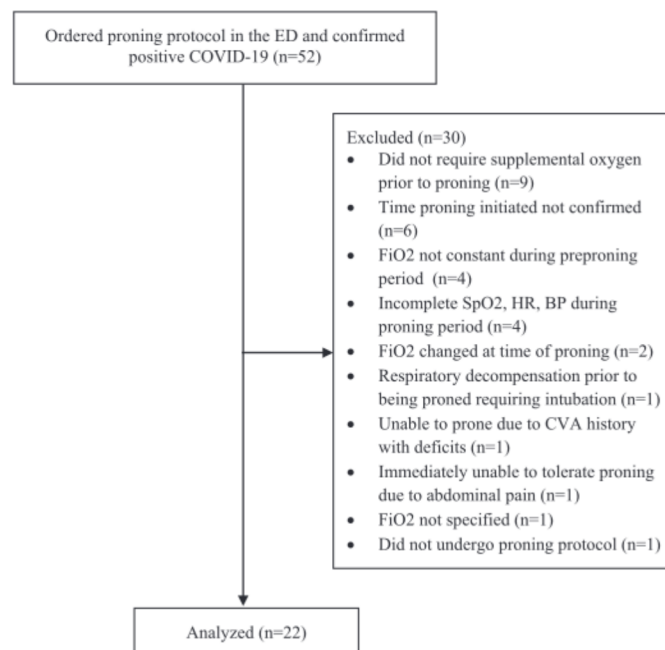


Fig. 1. Flow Chart of Patient Selection for ED Proning Protocol.

Table 2
Primary and Key Secondary Outcomes

	5 min prior to proning	Minutes 5–35 of proning protocol	Median difference	p-value
Median SpO ₂ /FiO ₂ ratio	298 (IQR: 264, 352)	295 (IQR: 279, 350)	5 (95% CI: 0, 15)	0.01
Median SpO ₂	94% (IQR: 92, 96)	96% (IQR: 95, 97)	1 (95% CI: 0, 3)	0.01
Median FiO ₂	31.5 (IQR: 27, 36)	33 (IQR: 27, 33)	0 (95% CI: 0, 0)	0.58
Median respiratory rate ^a	26 (IQR: 23, 30)	25 (IQR: 23, 28)	-2 (95% CI: -5, 3)	0.36

Abbreviations: SpO₂ = oxygen saturation, FiO₂ = fraction of inspired oxygen.

^a 20/22 patients had respiratory data in the time frame analyzed.

Five patients (23%) were intubated in the first 48 h following ED admission. Two additional patients were intubated after 48 h, resulting in a total of seven patients intubated during their hospitalization. The reason for intubation for all patients was progressive respiratory failure and/or inability to maintain an airway. Of the patients who were intubated, the median number of days they remained on a ventilator was 19 (IQR: 15–21) days. Nine patients (41%) were admitted to the ICU during their hospital admission. Two patients died and 20 (91%) survived to hospital discharge (Table 4). Fifteen patients did not require intubation, one of which signed an advanced directive as Do Not Intubate (DNI) and declined ICU transfer. The maximum supplemental oxygen therapy for one patient (6.7%) was a non-rebreather mask at 15 l flow and for three patients (20.0%) was an oxymizer at a median of 10 l flow.

4. Discussion

The results of our study suggest feasibility and safety of an early proning protocol of non-intubated patients with COVID-19. Compared to the immediate pre-proning time period, both the SpO₂:FiO₂ and oxygen saturation increased during the first 30 min of proning. Only a single patient enrolled in the pathway was unable to tolerate proning due to abdominal discomfort and no immediate adverse events were noted for any subjects. While the current study lacked a control group for comparison, the immediate temporal association with improved oxygenation is suggestive that proning may be causally related to this maneuver. We intentionally included a five-minute washout period immediately after the patient proned to account for any erroneous data during the proning process and to allow for the physiological effects of proning to stabilize. The possibility remains that the associative change occurred by chance or the natural progression of disease. However, arguing against this is the intuitive notion that patients do not typically improve oxygenation over a short period of time in critical illness without some intervention. Nonetheless, the possibility for confounding exists and our findings remain associative with randomized trials necessary to prove causation.

To date, there have been several published datasets on awake proning in the COVID-19 population. In an observational study of 50 hypoxic COVID-19 patients who underwent awake, self-proning in a single ED, Caputo et al. found that SpO₂ increased from 84% (IQR 75–90) pre-proning to 94% (IQR 90–95) 5 min post-proning [14]. Our results demonstrate this transient increase extends beyond the immediate initial proning period, to at least 30 min. In addition, and in contrast

Table 4
Other Outcomes

	N = 22
Duration of proning in the ED (minutes)	109 (IQR: 65, 159)
Intubation during first 48 h	5 (23)
Intubation during hospital admission	7 (32)
Median days of ventilator support	19 (IQR 15, 21)
Admission to the ICU	9 (41)
Survival to hospital discharge	20 (91)

Values in parentheses indicate percentages unless otherwise noted.

Abbreviations: ED = emergency department, ICU = intensive care unit.

to Caputo et al., we incorporated the concept of accounting for FiO₂ both pre- and post-proning as this could potentially impact an associative change with oxygen saturation. In the current study, we also found that the SpO₂:FiO₂ ratio was higher in the post-proning period. Moreover, we performed a sensitivity analysis in those receiving the same FiO₂ before and after proning and found that SpO₂ was improved. Caputo et al. report higher increases in oxygen saturation compared to the current study, however these could potentially be accounted for, in part, by the provision of oxygen (i.e., increased FiO₂) as opposed to proning per se.

In an observational study of 25 non-intubated COVID-19 patients in which a constant FiO₂ was maintained, Thompson et al. found an increase in median SpO₂ of 7% (95% CI: 4.6–9.4) in COVID-19 patients who were proned for at least 1 h [15]. Another, similar 25 patient sample found that 63% of patients were able to tolerate awake proning beyond 3 h with an increase in oxygenation of 25% [16]. The results of our study support this notion that there is feasibility and improvement in oxygenation beyond the immediate five minutes. Future studies using longer time periods are needed to determine how long these effects may be observed.

Published data for proning non-intubated patients in disease states other than COVID-19 is also sparse. In one prospective, observational cohort of twenty non-intubated patients with ARDS initially treated with noninvasive oxygenation measures, Ding et al. found patient proning was well tolerated. They demonstrated that the ratio of partial pressure of arterial oxygen (PaO₂) to the FiO₂ in the high flow nasal cannula (HFNC) plus proning group was significantly higher in those who did not require intubation (125 ± 41 mmHg vs 119 ± 19 mmHg, *P* = 0.043) [19]. While this patient population and supplemental oxygen delivery modalities were different than those in our cohort, proning was found to have a positive correlation with oxygenation. Because of our

Table 3
Oxygenation Changes in Patients with a Constant FiO₂

N = 19	5 min prior to proning	Minutes 5–35 of proning protocol	Median difference	p-value
Median SpO ₂ /FiO ₂ ratio	297 (IQR: 264, 352)	300 (IQR: 267, 350)	4 (95% CI: 0, 13)	0.01
Median SpO ₂	94% (IQR: 92, 96)	96% (IQR: 95, 97)	2 (95% CI: 0, 4)	0.00
Median FiO ₂	33 (IQR: 27, 36)	33 (IQR: 27, 36)	n/a	>0.99
Median respiratory rate ^a	26 (IQR: 23, 30)	25 (IQR: 23, 29)	-1 (95% CI: -3, 3)	0.56

Abbreviations: SpO₂ = oxygen saturation, FiO₂ = fraction of inspired oxygen.

^a 17/19 patients had respiratory data in the time frame analyzed.

institution's policy on the use of HFNC at the time this study was conducted, none of our patients received this oxygen delivery modality. HFNC has been shown to have a significant mortality benefit [20] and therefore may augment any benefit or proning. Furthermore, while these authors found improvement in oxygenation in this group, it is possible these patients were more hypoxic at baseline as they required positive pressure. Future studies are needed to investigate a potential benefit in oxygenation using greater FiO₂ and positive pressure in COVID-19 patients.

Optimal respiratory support strategies in COVID-19 patients with hypoxemia is an area of active debate and investigation. In a March 30 letter to the editor, Gattitoni et al. suggest that COVID-19 pneumonia does not lead to the typical ARDS picture in certain phenotypes [7], however this has been contested by others [21]. The threshold and optimal timing of intubation and mechanical ventilation for COVID-19 patients remains controversial and incompletely defined. Both non-invasive ventilation and high-flow oxygen have been used in an effort to prevent intubation in certain populations of respiratory failure though these modalities have been limited in some hospital settings with COVID-19 because of concerns of aerosolization [22,23]. These modalities also remain controversial in terms of overall efficacy and the exact population which may benefit. In contrast, delays to intubation have been noted as a reason for unexpected sudden cardiac arrest in ICU patients and could theoretically lead to worse outcomes if delayed to a point where pulmonary or systemic inflammation worsens without more definitive intervention [24]. Thus, determining the threshold and timing of intubation is a delicate balance that requires experience and expertise. Proning may provide yet another mechanism to improve oxygenation and avoid the need for mechanical ventilation when used alone or in combination with other modalities like high-flow oxygen. While our study suggests oxygenation may improve with proning, whether progression to intubation was decreased or outcomes improved remains unknown and will require randomized trials to better assess.

There are several limitations to this study. This study had a small sample size and as such physicians should use caution when applying these findings in clinical practice. Given minimal data on awake proning in COVID-19 patients, however, this study demonstrates feasibility for future analyses in this population. While we did find a positive association with oxygenation, our study lacked a control group and therefore whether this may have occurred in the absence of proning remains unknown. We did however allow for a five-minute washout period to account for any possible fluctuations that occur with immediate repositioning and our statistical analysis plan measured changes in each individual patient, thereby allowing for each patient to be his or her own control. Additionally, we measured SpO₂ as a marker of oxygenation, which is less accurate than the partial pressure of oxygen in arterial blood (PaO₂). Patients were also given the option of face down or lateral proning, based on their own personal preference and comfort, and it is therefore plausible that the type of proning may have affected our outcomes. It is also possible some patients were missed in the enrollment, as ordering of the protocol at the discretion of the treating emergency physician and this may have introduced selection bias. Finally, we cannot make any conclusions about how proning affects patient with a higher oxygen requirement or how it affects morbidity and mortality in the long term as these true rates in the general COVID-19 population are in flux and the study did not have a separate control group for comparison.

5. Conclusion

The results of our study suggest feasibility and safety of an early, awake proning in patients with COVID-19 respiratory illness in the ED. In this population, we found that proning was associated with an increase in oxygenation as measured by the SpO₂:FiO₂ ratio. Further

controlled studies are needed to determine the efficacy of this technique in patients with COVID-19.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Michael W. Donnino MD is supported, in part, by grants from the National Heart, Lung, and Blood Institute of the National Institutes of Health (R01HL13670504, K24HL12710106).

Declaration of Competing Interest

None.

Acknowledgements

We would like to acknowledge Garrett Thompson MPH, Jacob Boise BS, Lethu A. Ntshinga AB, Shivani Mehta BA, Emma Hershey BA, and Mahmoud S. Issa MD for their help with data collection.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajem.2020.11.074>.

References

- [1] Guerin C, Reignier J, Richard J, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med*. 2013;368:2159–68. <https://doi.org/10.1056/NEJMoa1214103>.
- [2] Gattinoni L, Carlesso E, Taccone P, et al. Prone positioning improves survival in severe ARDS: a pathophysiologic review and individual patient meta-analysis. *Minerva Anestesiol*. 2010;76:448–54.
- [3] Valesky W, Chow L. Prone positioning for acute respiratory distress syndrome in adults. *Acad Emerg Med*. 2020. <https://doi.org/10.1111/acem.13948>.
- [4] Dickinson S, Park PK, Napolitano LM. Post-position therapy in ARDS. *Crit Care Clin*. 2011;27:511–23. <https://doi.org/10.1016/j.ccc.2011.05.010>.
- [5] Gattinoni L, Taccone P, Carlesso E, Marini JJ. Prone position in acute respiratory distress syndrome. Rationale, indications, and limits. *Am J Respir Crit Care Med*. 2013;188:1286–93. <https://doi.org/10.1164/rccm.201308-1532CL>.
- [6] Scaravilli V, Grasselli G, Castagna L, et al. Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: a retrospective study. *J Crit Care*. 2015;30:1390–4. <https://doi.org/10.1016/j.jcrc.2015.07.008>.
- [7] Gattinoni L, Coppola S, Cressoni M, Busana M, Chiumello D. Covid-19 does not lead to a “typical” acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2020;201:1299–300. <https://doi.org/10.1164/rccm.202003-0817LE>.
- [8] Gattinoni L, Chiumello D, Camporota, et al. COVID-19 pneumonia: different respiratory treatment for different phenotypes? *Intensive Care Med*. 2020. <https://doi.org/10.1007/s00134-020-06033-2>.
- [9] Sun Q, Qiu H, Huang M, et al. Lower mortality of COVID-19 by early recognition and intervention: experience from Jiangsu Province. *Ann Intensive Care*. 2020;10:33. <https://doi.org/10.1186/s13613-020-00650-2>.
- [10] Slessarev M, Cheng J, Ondrejicka M, Arntfield R. Patient self-proning with high-flow nasal cannula improves oxygenation in COVID-19 pneumonia. *Can J Anesth*. 2020. <https://doi.org/10.1007/s12630-020-01661-0>.
- [11] EMRAP LIVE: COVID19 Update March 31; 2020 <https://www.youtube.com/watch?v=G1bKyc31XhM&t=3192s>. Accessed March 31, 2020.
- [12] EMRAP LIVE: COVID19 Update April 28; 2020 <https://www.youtube.com/watch?v=rnkQv-cQSiE> Accessed April 29, 2020.
- [13] Weingart SD. COVID-19 – awake pronation (aka the pig roast) a guest write-up by David Gordon, MD EMCrit Podcast April 6; 2020 <https://emcrit.org/emcrit/awake-pronation/> Accessed April 7, 2020.
- [14] Caputo ND, Strayer RJ, Levitan R. Early self-proning in awake, non-intubated patients in the emergency department: a single ED's experience during the COVID-19 pandemic. *Acad Emerg Med*. 2020;27:375–8. <https://doi.org/10.1111/acem.13994>.
- [15] Thompson AE, Ranard BL, Wei Y, Jelic S. Prone positioning in awake, nonintubated patients with COVID-19 hypoxemic respiratory failure. *JAMA Intern Med*. 2020 Jun 17:e203030. <https://doi.org/10.1001/jamainternmed.2020.3030>.
- [16] Elharrar X, Trigui Y, Dols AM, et al. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. *JAMA*. 2020;323:2336–8. <https://doi.org/10.1001/jama.2020.8255>.
- [17] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The strengthening the reporting of observational studies in epidemiology (STROBE)

- statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61:344–9. <https://doi.org/10.1016/j.jclinepi.2007.11.008>.
- [18] Moskowitz A, Yankama T, Andersen LW, et al. Ascorbic acid, corticosteroids, and thiamine in sepsis (ACTS) protocol and statistical analysis plan: a prospective, multi-center, double-blind, randomized, placebo-controlled clinical trial. *BMJ Open*. 2019;9:e034406. <https://doi.org/10.1136/bmjopen-2019-034406>.
- [19] Ding L, Wang L, Ma W, et al. 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;24:28. <https://doi.org/10.1186/s13054-020-2738-5>.
- [20] Frat JP, Thille AW, Mercat A, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372:2185–96 doi:0.1056/NEJMoa1503326.
- [21] Ziehr DR, Alladina J, Petri CR, et al. Respiratory pathophysiology of mechanically ventilated patients with COVID-19: a cohort study. *Am J Respir Crit Care Med*. 2020. <https://doi.org/10.1164/rccm.202004-1163LE>.
- [22] Hui DS, Chow BK, Lo T, et al. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different face masks. *Eur Respir J*. 2019;53:1802339. <https://doi.org/10.1183/13993003.02339-2018>.
- [23] Li J, Fink JB, Ehrmann S, et al. High-flow nasal cannula for COVID-19 patients: low risk of bio-aerosol dispersion. *Eur Respir J*. 2020;55:2000892. <https://doi.org/10.1183/13993003.00892-2020>.
- [24] Bauer PR, Gajic O, Nanchal R, et al. Association between timing of intubation and outcome in critically ill patients: a secondary analysis of the ICON audit. *J Crit Care*. 2017;42:1–5. <https://doi.org/10.1016/j.jcrc.2017.06.010>.