Application of the prone position during COVID-19 pandemic (PROCOV). An international survey of clinicians

Kevin Benavente, Stephanie Yoshimura, James Davis, Achal Dhupa, Ehab Daoud

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Abstract:

Background

Benefits of the prone position in ARDS are well established, and the evidence of its benefits for the COVID-19 patients are growing. However, the clinical utilization of such a maneuver is less established. We attempted to analyze the clinician's utilization and attitude of the prone position and what is the main drive for its usage.

Methods

An international survey of eight questions. The questionnaire was anonymous and included the country of practice, percentage of patients with COVID-19 they have placed in the prone position while undergoing mechanical ventilation, most important factor that determined the need for the prone position (SpO_2, PaO_2:FiO_2, FIO_2, PEEP), duration of prone position in hours/day, use of neuro-muscular blocking agents, body position (flat, trendelenburg, reverse trendelenburg), the use of a specific protocol for the prone position, if they believe that prone position is beneficial, and if their practice will change or not. The survey was active for five months.

Statistical analysis included frequencies of each response, as well as subgroup analyses designed to identify potential correlates of longer or shorter proning durations. The questionnaire assessed clinicians optimism regarding the continuing use of proning in the future, and how different cutoffs for proning initiation may be associated with attitudes towards proning. Associations between categorical variables were analyzed using Fisher's exact test. A P-value of < 0.05 was considered statistically significant. Results are expressed in Means ± Standard Deviation (SD)

Results

294 questionnaires were collected from 35 countries with 78% of responders from the USA. Median duration of proning was 14.8 ± 2.8 hours per day. 74% of clinicians utilized an established protocol for proning their patients. The decision to initiate proning was non-significant and split between the use of oxygen saturation SpO_2 (30%) mean 92.44 ± 5.61, PaO_2:FiO_2 ratio (28%) mean 188.44 ± 57.36, FiO_2 mean 78.6 ± 15.65, PEEP mean 12.96 ± 4.66, or immediate prone positioning following intubation (22%).

41.2% of surveyed utilize the prone position in 25-50%, average percent patients proned calculated at 7.1%. Estimated 77% of respondents reported prone positioning to be helpful in 50% or less of cases. 91% of responders used NMB either always or frequently, and there was statistical significance between the use of NMB and perceived benefits of proning ($P < 0.001$). 74% of those surveyed use a protocol for proning, the use of protocol and the perceived benefits of proning was statistically significant ($P < 0.001$).

Conclusion

There are few agreements between clinicians on the duration of the proning sessions and use of NMB and using a protocol for proning. There was no agreement on the trigger of the prone position or the belief of its usefulness. This ambiguity should trigger an evidence-based ARDS management using the prone position in COVID-19 patients.

Keywords: Prone position, COVID-19, ARDS, Survey, Neuromuscular blockers

Authors
1. Kevin Benavente MD, Medical resident, JABSOM, University of Hawaii, USA
2. Stephanie Yoshimura MD, Medical resident, JABSOM, University of Hawaii, USA
3. James Davis, Associate Specialist, Quantitative Health Sciences, University of Hawaii, USA
3. Achal Dhupa MD, FACP, FCCP. Section Chief Pulmonary/Critical Care Medicine, Scripps Memorial Hospital -La Jolla San Diego, California, USA
4. Ehab G Daoud, MD, FACP, FCCP. Associated professor of Medicine, John A Burns School of Medicine, Hawaii, USA

Corresponding author: kevinb33@hawaii.edu
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Introduction

The prone position has been applied to patients with acute respiratory failure since the mid-70s of the last century showing improved oxygenation. [1,2]

Over the last four decades, many studies [3,4,5,6] have added to our understanding of the mechanisms and benefits of the prone position but lacked data on mortality to compare differences between the prone and supine position in the Acute Respiratory Distress Syndrome (ARDS). Post hoc analysis of some of those studies demonstrated mortality benefits. However, not until 2013 with the publication of the PROSEVA trial [7] was the prone position shown to improve mortality in moderate-severe cases.

Documented benefits have led the prone position to be included in the recommendations of the "Surviving Sepsis Campaign" [8] and the American Thoracic Society (ATS)/European Society of Intensive Care Medicine (ESICM) [9] for moderate to severe ARDS, recommending more than 12 hours daily.

The physiologic changes that lead to the improvements in oxygenation, ventilation, and mortality are summarized in many reviews. [10,11,12] Lung inflation and ventilation are more evenly dispersed in the prone than in the supine position, whereas perfusion is similar in both conditions, the ventilation–perfusion ratios are more homogeneously distributed in the prone position with homogeneous distribution of stress and strain. Dorsal alveolar recruitment prevails over ventral derecruitment, leading to increased lung compliance. Theses improve ventilation to perfusion matching and perhaps the reduction of dead space ventilation.

Evening the distribution of transpulmonary forces may reduce the incidence of Ventilator Induced Lung Injury (VILI).

In addition, other mechanical factors that contribute to the benefits of the prone position include: enhanced airway drainage, reduction of atelectasis induced by the weight of the heart and abdominal organs on the dorsal alveoli, possible reduction in pneumonia, as well as improvement in the right heart function and pulmonary circulation.

The above benefits have led to increased utilization of the prone position during the SARS-CoV-2 pandemic for both mechanically and non-mechanically ventilated patients. The data on improved oxygenation are more robust, however the data on mortality has been conflicting. [13,14,15]

Prone positioning can be performed by using a special proning bed, but with the supply shortage inflicted by the COVID-19 pandemic, protocols were initiated with nurses and respiratory therapists trained to perform manual proning.

Despite the documented benefits and guidelines, studies have shown that the prone position is utilized in only a fraction of the moderate-severe ARDS [16] and COVID-19 ARDS patients. [17]

In this study, we attempted to identify the attitude of clinicians worldwide regarding their utilization of the prone position for the COVID-19 patients.

Materials and Methods

We designed an eight-question questionnaire and posted it on the "Society of Mechanical Ventilation" website and advertised it in the monthly newsletter and

in different social media platforms. The survey was active for five months from August to December 2021.

The questionnaire was anonymous and asked the country of practice, the percentage of patients with

COVID-19 the respondent placed in the prone position while undergoing mechanical ventilation, the most important factor that determined the need for proning (SpO_2, PaO_2:FiO_2, FiO_2, PEEP), duration of prone position employed in hours, the use of neuro-muscular blocking agents (NMB) during proning, the body position used (flat, trendelenburg, reverse trendelenburg), the use of a specific protocol for proning, if the respondent believed that prone position is beneficial, and if their proning practice will change in the future or not.
No IRB application was filled because the survey was anonymous with patient or institutional identifiers.

Statistics

Statistical analysis included frequencies of each response, as well as subgroup analyses designed to identify potential correlates of longer or shorter proning durations. The questionnaire assessed clinicians optimism both for COVID-19 and ARDS patients regarding continuing to use of proning in the future, and how different cutoffs for proning initiation may be associated with attitudes towards proning. Associations between categorical variables were analyzed using Fisher's exact test. A P-value of < 0.05 was considered statistically significant. Results are expressed in Means ± SD.

Results

294 questionnaires were ultimately included in the study from clinicians who completed the survey. Respondents from 35 countries/territories were represented, with the majority from the United States of America (78%). Table 1 summarizes the geographical locations of the responders.

Country of Practice	Responses (%)
North America	234 (79.9)
Asia	29 (9.9)
Europe	20 (6.8)
Africa	9 (3.1)
South America	1 (0.3)

Table 1: Clinician Geographic Origin of Practice

Clinicians kept their patients in the prone position for a mean of 14.8 ± 2.8 hours daily, with a range between 8 and 24 hours. 74% of clinicians utilized an established protocol for proning their patients.

91% of respondents reported use of NMB agents when initiating the prone positioning with at least some of their patients, while only 8.8% of clinicians never used these agents.

Body position preference while prone was largely split between flat (40%) and head tilted up in the reverse trendelenburg position (48%), while minority (12%) placed the patients with the head tilted down in the trendelenburg position.

Regarding the most important parameter used to initiate proning, practice patterns were non-significantly split between use of oxygen saturation SpO_2 (30%), the PaO_2:FiO_2 ratio (28%), or immidiately following intubation (22%). 4.4% of clinicians responded they never prone their patients. These findings are summarized in table 2.

In terms of the specific cutoffs clinicians use to initiate proning, for those with a preference for relying on the fraction of inspired oxygen, most clinicians applied an FiO_2% of 70%, with a slightly higher median and average cutoff when taking into account all respondents from this subgroup (77.5% and 78.3% respectively)

For clinicians who instead utilize SpO_2%, an oxygen saturation between 95-100% was used by a majority of respondents (45.3%) to initiate prone positioning, followed by a saturation of 85-90% (24.4% of clinicians).

In terms of the PaO_2:FiO_2 ratio, most clinicians utilized a cutoff of 100-150 (27.5%), followed closely behind by a cutoff of <300 (25.3%), and 150-200 (22.5%).

The specific PEEP settings utilized by clinicians to initiate the prone position varied, however in 82.3% of respondents, a PEEP >10 cmH_2O was sufficient to use as a cutoff for when prone positioning should be initiated. A smaller number of respondents (52.9%) relied on higher PEEP setting >15 cmH_2O to initiate prone positioning. Those findings are summarized in table 3.

Characteristic	N = 294
Mean Hours Prone Per Day, Median (IQR)	15.0 (13.0, 16.0)
Use of Muscle Paralytics, n (%)	
Always	71 (24%)
Never	26 (8.8%)
Sometimes	197 (67%)
Body Position, n (%)	
Flat	117 (40%)
Head tilted down	35 (12%)
Head tilted up	142 (48%)
Perceived Benefit of Prone Positioning, n (%)	
In 25-50% of Cases	132 (45%)
In 50-75% of the cases	53 (18%)
In less than 25% of the cases	79 (27%)
In more than 75% of the cases	15 (5.1%)
No benefit	15 (5.1%)
Expected use of Prone Positioning in Non-COVID Patients, n (%)	
Expect to Decrease Use	76 (26%)
Expect to Increase Use	62 (21%)
Stay the same	156 (53%)
Most Important Parameter used to Initiate Prone Positioning, n (%)	
FiO_2	26 (8.8%)
Immediately after intubation	65 (22%)
PaO2:FiO_2 ratio	83 (28%)
PEEP	19 (6.5%)
SPO_2% (O_2Sat)	87 (30%)
Never Prone	14 (4.8%)

Table 2 Clinicians practice and preference using the prone positioning

Most of our respondents (45%) believed prone positioning to be beneficial in only 25-50% of their patient population. Cumulatively, we calculated that 77% of respondents who reported prone positioning to be helpful in 50% or less of their cases.

Furthermore, given their experience with prone positioning in COVID patients, most clinicians (53%) reported that their use of this technique in non-COVID ARDS patients would likely stay the same.

Most clinicians reported utilizing prone positioning in between 25-50% of their patients (41.2%). However, by calculating an approximate estimation, using averaged totals of the percent of patients placed prone and the corresponding percent of clinicians who responded, our cohort of clinicians placed 7.1% of patients in the prone position during their hospitalization. (Table 4).

Table 3: Cutoffs for initiation of prone position

FiO_2 Cutoff, n=26 (%)	
Mean FiO_2 ± SD	78.6 ± 15.65
SpO_2 Cutoff, n=86 (%)	
Mean SpO2 ± SD	92.44 ± 5.61
PaO_2:FiO_2 Cutoff, n=80 (%)	
Mean PaO_2:FiO_2 ± SD	188.44 ± 57.36
PEEP Cutoff, n=17	
Mean PEEP ± SD	12.96 ± 4.66

When categorizing respondents between those who found a modest or greater benefit to proning (defined as prone positioning being helpful in >25% of their patient population) versus those who found little to no benefit (<25% of patients), a statistically significant difference (P <0.001) between these two groups was demonstrated when comparing either absolute use/disuse of NMB vs only occasional use of NMB.

Clinicians who reported little to no benefit with proning were more likely to use paralytic agents in either all, or none, of their patients, compared to those who found modest or greater benefit (40% vs 23% respectively for universal paralytic use, 33% vs 7.5% for completely absent paralytic use). In contrast, patients who found higher benefit with proning more frequently reported only sometimes using NMB, compared to those who found little benefit (69% vs 27% respectively). The difference between these groups reached statistical significance, P <0.001 (Table 5).

In terms of the correlation between having a pre-established proning protocol, and perceived benefit of prone positioning, of the 279 clinicians who admitted at least modest benefit of proning, defined as benefiting at least 25% or more of their patients, 77% of them reported having an established protocol at their institution. This contrasts with the 15 clinicians that found proning to be effective in less than 25% of patients, where an established protocol was present only 27% of the time. This difference reached statistical significance, p value <0.001 (Table 6).

Position	Number of Clinicians Responding Yes	Percent of Clinicians	Fraction of COVID Patients Placed Prone	Percentage of Patients Placed in Prone Position
I never prone	13	4.4	0	0.0
< 25%	89	30.3	0.125	3.8
25-50%	121	41.2	0.375	15.4
50-75%	52	17.7	0.625	11.1
> 75%	19	6.5	0.875	5.7

Table 4: Approximate percentage of patients placed in prone position during the COVID outbreak. Percentage of patients placed in the prone position is percent of clinicians times fraction of patients placed in the prone position

Model	Respondent use of NMB	Perceived benefit of Proning, n (%)		P value[1]
		High benefit	Low benefit	
Model 1	Always	65 (23)	6 (40)	P < 0.001
	Never	21 (7.5)	5 (33)	
	Sometimes	193 (69)	4 (27)	
Model 2	Always	65 (76)	6 (55)	P = 0.16
	Never	21 (24)	5 (45)	
Model 3	Never	21 (9.8)	5 (56)	P < 0.001
	Sometimes	193 (90)	4 (44)	

Table 5: Use Neuro Muscular Blockers (NMB) either all of the time, some of the time, or none of the time, and corresponding perceived benefit of prone positioning categorized as either low benefit (<25% of patients) or high benefit (>25% of patients). [1] Fisher's exact test

Characteristic	Low Perceived Benefit, n= 15	High Perceived Benefit, n = 279	P value
Prone Positioning Protocol Available, n (%)	4 (27)	214 (77)	P <0.001

Table 6: Benefit of Prone Positioning by Established Protocol Availability. High benefit defined as being helpful in >25% of patients, low benefit described as being helpful in less than 25% of patients.

Discussion

Our results show wide variation in practice patterns between most of the variables surveyed. In our opinion that reflects the state of confusion and the lack of strong evidence-based guidelines or recommendations on using the prone position in ARDS in general and in COVID-19 specifically.

Our findings are consistent with the hypothesis that there is no agreement in clinical practice on when to initiate the prone position or what triggers clinicians' to place their patients in the prone position.

The PROSEVA [7] trial protocol used PaO_2:FiO_2 of less than 150 with FiO_2 above 60% for 16 hours, the current societies guidelines [8,9] give vague recommendation for the prone position "For adults with sepsis-induced moderate-severe ARDS, we recommend using prone ventilation for greater than 12 hr daily". With the lack of more specific evidence-based guidelines, clinicians find themselves choosing indications that they believe is the best.

The duration of the prone position (mean of 14.8 ± 2.8 hours) in our study was most consistent with the PROSEVA protocol.

The majority of those surveyed stated that they use a protocol for proning in their institutions which has shown to be beneficial for COVID-19 patients. [18] This is further supported in our study by the fact that having an established protocol was associated with greater perceived benefit of proning, stressing the importance of implementing a regimented protocol whenever prone positioning is expected to be used extensively.

Though 22% of responders reported that they place their patients in the prone position, from our results, we estimate that only about 7.19% on average of mechanically ventilated patients with COVID-19 were placed in the prone position. This is much smaller than a recent study from the UK [17] where they showed that prone positioning was not applied to 76% of patients with moderate hypoxemia and 45% of those with severe hypoxemia with a big missed opportunity to use the prone position in those who did not survive. Those numbers are less than other studies where the incidence of proning was about 30% [19] in the first 2 days. However our survey did not specify the severity of respiratory failure or ARDS as mild, moderate to severe, or the timing from intubation precisely or for how many days on average patients were placed in the prone position. Other smaller studies [20] showed much higher rate of the application of the prone position about 70%.

Our results and the results of the above cited articles raise the question of why there is much hesitancy to use the prone position for patients with ARDS or COVID-19 ARDS. Though hypothetical, the shortage of clinicians [21] could limit the manpower needed given the multiple personnel required to place patients in the prone position. The shortage of personal protection equipment that occurred especially early in the pandemic might have added another layer of limitation to the manpower required. [22] Another plausible explanation could be the fear of possible adverse events of the prone position including loss of the artificial airway, pressure ulcers, and peripheral nerve damage. [23]

Lack of education on the benefits of the prone position might be a factor. A recent study [24] has shown that the increased education has led to an increased application of the prone position.

The use of neuromuscular blockers for severe ARDS has shown improved outcomes in ARDS [18] but their efficacy during the prone position is less studied. A small study in one center showed no difference in the efficacy or safety between those who were on muscle paralytics versus those who were on no paralytics. [25] This issue remains unknown and unclear if the combined use of neuromuscular blockers during proning is superior to each one alone. [26]

Our results reveal that those who use NMB in at least some of their patients were more likely to report higher benefit of proning compared to those who never use NMB. This may suggest the potential role NMB has in either facilitating the efficacy of prone positioning, or in improving outcomes regardless of prone or supine positioning. Nonetheless, paralytic agents should likely be

considered on a case-by-case basis for COVID patients. More studies to establish if the combined treatment with NMB and proning is beneficial and to establish better evidence-based guidelines are needed.

To our knowledge, there are no specific guidelines for sedation or use of muscle paralytics for the COVID-19 patients, unlike for the existing guidelines for sedation/analgesia in ARDS [27] or guidelines for using neuromuscular blockers in the adult critically ill patients. [28]

Another interesting finding is the body position during the prone position of whether patients are placed in the reverse trendelenburg (body tilted up) or flat or reverse trendelenburg (body tilted down), though the results were not significant statistically, the majority of those surveyed place the patient in the reverse trendelenburg or flat position, almost 12% selected trendelenburg position. Most clinicians place the prone patients in the reverse trendelenburg positions based on small studies of the benefits of this position on oxygenation and the possible reduced risk of aspiration. [29,30]

A recent observational study by our group in COVID-19 proned patients showed that when placing the patient in the trendelenburg position, the tidal volume and the respiratory compliance markedly improved. [31]

Regarding the perceived benefits of the prone position for the COVID-19 patients, our results again showed no statistically significant agreement with a majority of those surveyed (45%) who claimed the maneuver is beneficial in 25%-50% of cases but wide variety of perception from the extremes of no benefits or highly beneficial in more than 75% of the cases. Those results reflect the current literature of unknown mortality benefits for COVID-19 patients. [13,14,15] We did not define the benefits in our survey in regard to oxygenation or mortality.

Limitations

Our study has some limitations, the uneven number between geographical locations with North Americas made up almost 80% of responders. We did not collect information about the clinical experience or places they practice for example academic vs. nonacademic, rural or urban of those surveyed.

We did not include the SpO_2:FiO_2 in the questionnaire as a possible trigger for placing patients in the prone position. This ratio has been increasingly utilized for assessing hypoxemia and correlates well with the PaO_2:FiO_2. [32]

We did not ask about the timing between intubation and proning or duration in days patients placed in the prone position.

Despite those limitations, our study adds some information that have not been studied or validated before.

This data was collected using a convenience sample and as such has some notable weaknesses. First, the only respondents were those visiting the website or associated social media announcements. Second, those who had the interest and time to respond may have different choice of practices than those who did not. Third, some of our questions had a wide range of choices for example 25%-50% and thus less specific.

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