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Review

Effect of awake prone positioning in COVID-19 patients- A systematic review

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Background: Prone positioning is known to reduce mortality in intubated non-COVID-19 patients suffering from moderate to severe acute respiratory distress syndrome (ARDS). However, studies highlighting the effect of awake proning in COVID-19 patients are lacking. We aim to conduct a systematic review of the available literature to highlight the effect of awake proning on the need for intubation, improvement in oxygenation and mortality rates in COVID-19 patients with ARDS.
Method: — A systematic search of 2 medical databases (PubMed, Google Scholar) was performed until July 5, 2020. Thirteen studies fulfilled the inclusion criteria, and 210 patients were included for the final analysis.
Result: —Majority of the patients were above 50 years of age with a male gender predominance (69%). Face mask (26%) was the most common interface used for oxygen therapy. The intubation and mortality rates were 23.80% (50/210) and 5.41% (5/203) respectively. Awake proning resulted in improvement in oxygenation (reported by 11/13 studies): improvement in SpO_2, P/F ratio, PO_2 and SaO_2 reported by 7/13 (54%), 5/13 (38%), 2/13 (15%) and 1/13 (8%) of the studies. No major complications associated with prone positioning were reported by the included studies.
Conclusion: Awake prone positioning demonstrated an improvement in oxygenation of the patients suffering from COVID-19 related respiratory disease. Need for intubation was observed in less than 30% of the patients. Thus, we recommend early and frequent proning in patients suffering from COVID-19 associated ARDS, however, randomized controlled trials are needed before any definite conclusions are drawn.

Contents

Abbreviations: ARDS, acute respiratory distress syndrome; PP, prone positioning; CPAP, continuous positive airway pressure; HFNO, high flow nasal oxygen; COT, conventional oxygen therapy; HFNC, high flow nasal cannula; NIV, noninvasive ventilation; ICU, intensive care unit.

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1. Introduction

The COVID-19 pandemic has resulted in a significant increase in the number of cases with respiratory failure. With the progress of the COVID-19 pandemic, resources like ventilators and intensive care beds are going to be the rate-limiting step in the treatment of these patients. Hence, strategies to prevent intubation and mechanical ventilation are urgently needed. Acute respiratory distress syndrome (ARDS) is one of the main complications of COVID-19 occurring in 20–40% of patients with severe disease [1,2]. Evidence has demonstrated that prone positioning (PP) can improve oxygenation and reduce the 28-day mortality from 32.8% to 16% ($p < 0.001$) in non-COVID-19 related ARDS [3]. The improvement in oxygenation in the prone position is the result of better ventilation-perfusion matching. The dorsal portion of the lung reopens as they are not compressed by mediastinum or abdominal cavity resulting in the recruitment of more gas exchanging pulmonary alveoli [4,5]. The Surviving Sepsis Campaign COVID-19 guidelines have recommended the prone positioning to be one of the treatment option in COVID-19 related ARDS [6–8]. Various clinicians around the world have tried prone positioning in awake, normally breathing patients receiving noninvasive ventilation, continuous positive airway pressure, or conventional oxygen therapy [9–11]. They have reported that prone positioning appears to improve oxygenation and may decrease respiratory effort as well as lung injury and the need for intubation [12]. The reduced need for intubation and ICU admission may prove to be helpful, especially in a resource-limited setting. Our aim was to conduct a systematic review of the available literature on awake proning in COVID-19 patients with an emphasis to highlight the effect of awake proning on the need for intubation, improvement in oxygenation and mortality rates in COVID-19 patients with ARDS.

2. Materials and method

2.1. Search strategy and inclusion criteria

Two authors (Abhishek Singh and Sachit Anand) systematically searched PubMed and Google Scholar databases published till July 5, 2020. The keywords searched were ((prone position) OR (proning) OR (prone positioning) OR (prone)) AND ((COVID-19 OR SARS-CoV-2 OR Coronavirus)). We retrieved all studies where prone positioning was done in awake and non-intubated patients having a confirmed diagnosis of COVID-19. The inclusion criteria for studies included: *Patients*: All non-intubated COVID-19 patients, where diagnosis is made with RT-PCR using oropharyngeal/nasal/nasopharyngeal swab; *Intervention*: Prone positioning; *Comparison*: Patients nursed in supine position; *Outcome*: proportion of patients requiring intubation, improvement in oxygenation and mortality rates. Explicit reporting of parameters of oxygenation was not considered in the inclusion criteria. A total of 279 studies were identified at the outset. After screening, 14 studies were eligible for the review. The studies that met our inclusion criteria were separately screened by two authors (Puneet Khanna and Madhurjya). Any ambiguity was resolved by mutual discussion and consensus. Out of these 14 studies, one study was excluded as it dealt with prone positioning in 25-weeks pregnant COVID positive mother. A detailed PRISMA flow diagram of the search strategy is included in Fig. 1.

2.2. Data extraction

After screening the article, data were extracted by two authors (Sachit Anand and Abhishek Singh) independently. Information on the author, type of study, number of patients, gender, age, disease severity, clinical manifestation, type of intervention, duration of intervention, and outcome were extracted by the above two authors in the designed data extraction table (Table 1).

2.3. Statistical analysis

The statistical analysis was performed using SPSS 20.0 (IBM Corp, Armonk, NY). The continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as a percentage. The student t-test was used for continuous while chi-square or fishers exact for categorical variables. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patient characteristics

A total of 220 patients from 13 included studies were included in this review. The proportion of patients who were males was 69% (151/220). Coppo et al. [19] have reported that prone positioning was not feasible in nine children (patients were not able to maintain the prone position for at least 3 hours), and one child had incomplete data. Therefore, 210 patients were included in the final review. Although the average age at presentation was not mentioned in all studies, the mean age at presentation of patients

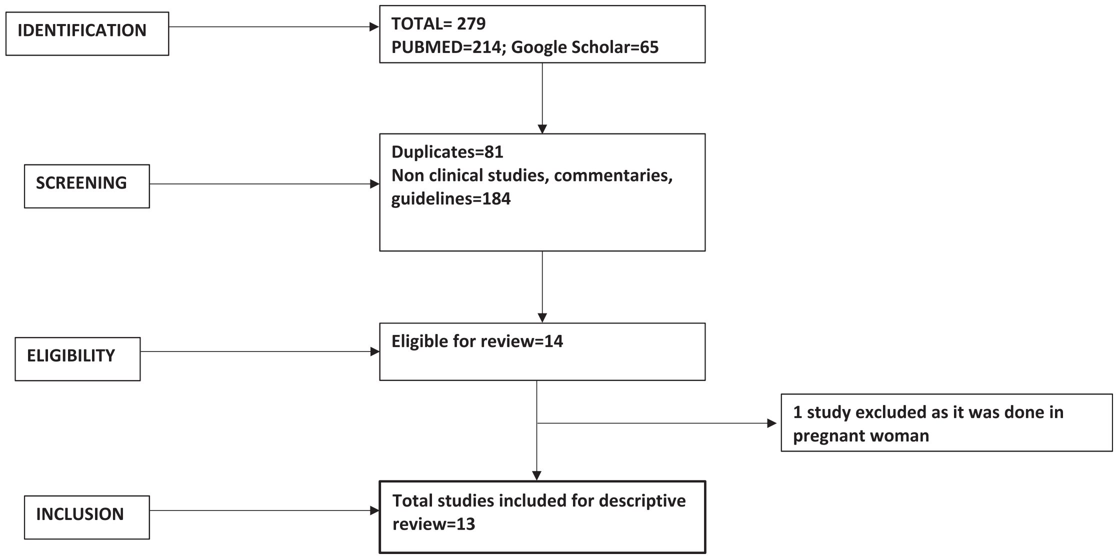

Fig. 1. PRISMA flow diagram of the search strategy.

Table 1
Articles included in the final analysis and data extraction.

S. No	Author	Study type	N	Gender (M)	BMI (kg/m^2) Mean (SD)	Age Mean (SD)	Data on comorbidities	Time between admission and proning	Duration of proning
1	Coppo et al.	Prospective Cohort	56[#]	44	27.5 (3.7)	57.4 (7.4)	Yes	Mean (SD) = 3.5 (3.1)	Atleast 3 hours
2	Caputo et al.	Prospective Cohort	50	30	–	59 (13.7)	No	Within 24 hours	–
3	Elharrar et al.	Prospective Cohort	24	16	*	66.1 (10.2)	Yes	Median (IQR) = 1 (0–1.5)	–
4	Thompson et al.	Prospective Cohort	25	18	–	63.7 (7.8); 67.5 (10.4)	Yes	Median (range) = 3 (1–12)	1–24 h
5	Xu et al.	Case series	10	5	–	50.2 (9.1)	Yes	–	>16 hours per day
6	Ziqin et al.	Case series	10	8	–	60.6 (9.1)	No	–	1 hour sessions, 5-times/day
7	Damarla et al.	Case series	10	7	–	57.7 (12.9)	No	Median (IQR) = 5 (2.3–13.3) hours	**Day**: Prone-supine every 2 hourly **Night**: Prone
8	Golestani-Eraghi et al.	Case series	10	0	–	–	No	–	Mean: 9 hours
9	Sartini et al.	Cross-sectional	15	13	24 (3.4)	59 (6.5)	No	Median (IQR) = 9 (7.5–14)	Median (IQR): 3 (1–6) hours
10	Despres et al.	Case series	6	6	26.5 (3.2)	[**]54.4 (11.8)	No	–	Mean (range): 5 (1–16) hours
11	Sztajnbok et al.	Case series	2	2	–		No	–	10 and 8 hours
12	Slessarev et al.	Case report	1	1	–		No	–	16–18 hours/day
13	Elkattawy et al.	Case report	1	1	–		Yes	–	>12 hours/day

[#] 46 out of 56 children were included in analysis.
[*] BMI of >30 was seen in 23% of patients.
[**] Mean (SD) age of patients in studies no. 10–13 calculated collectively.

from all studies was above 50 years of age. Of the available data, the youngest patient in whom prone positioning was attempted was 31 years old and was reported by Xu et al. [23] Information about fever at the time of presentation was limited to two studies (including three children) only [11,13]. A total of ninety comorbidities (with some patients having more than one comorbidity) were reported by the authors from five studies only. These included cardiovascular (congestive heart failure, hypertension, previous myocardial infarction, vascular disease), respiratory (chronic bronchopulmonary disease), diabetes mellitus, hyperlipidemia, liver disease, chronic kidney disease, and malignancy.

3.2. Details on proning

a) Time between admission and proning

The timing of initiating the prone positioning was variable in the five studies in which it was mentioned. It was started within a few hours by Damarla et al., while it took a median (IQR) duration of 9 (7.5–14) days by Sartini et al.

b) Duration of proning

Table 2
Showing types of Oxygen delivery interface.

Oxygen delivery interface	N (%)
Helmet CPAP	44 (21%)
Reservoir mask	9 (4%)
Face mask	55 (26%)
Venturi mask	9 (4%)
Nasal cannula	36 (17%)
HFNC	24 (11%)

The duration of proning was also variable among the various included studies. Coppo et al. [19] had followed a stringent criterion of at least 3 hours of proning, and excluding those in whom it was not feasible. Proning duration of as long as 24 hours was encouraged by Thompson et al. [22] Similar lengthy durations of prone posturing were seen in some other studies as well [23,26,28–31]. Prone posturing in multiple sessions was adopted in studies by Ziqin et al. [24] and Damarla et al. [25] In the study by Caputo et al. [20], primary and secondary outcomes were assessed at 5 min and 24 hours respectively post proning. However, they have not mentioned the duration of proning. Elharrar et al. [21] had also evaluated the feasibility of prone posturing at 1 hour and 3 hours but not mentioned the mean/median or total duration.

3.3. Outcomes

Awake proning resulted in improvement in oxygenation (reported by 11/13 studies): improvement in SpO_2, P/F ratio, PO_2 and SaO_2 reported by 7/13 (54%), 5/13 (38%), 2/13 (15%) and 1/13 (8%) of the studies (Table 3). Only 23% (3/13) of the studies expressed more than parameter of oxygenation [19,27,29]. The intubation and mortality rates after prone positioning were 23.80% (50/210) and 5.41% (5/203) respectively (Table 4). A subjective improvement in the symptoms was also observed in the remaining non-intubated survivors. All these patients were shifted to a step down unit or discharged from the hospital. Data on the duration of hospital/ICU stay is also limited, with only three studies highlighting it [11–13]. Information on complications and adverse events associated with prone-posturing was reported by 31% (4/18) of the studies [1,3,7,8]. None of these studies had reported major adverse events. Back pain was reported in 42% of patients by Elharrar et al. [3].

3.4. Oxygen delivery interface

Different oxygen delivery interface was used in different studies. Out of all, face mask (26%) was most commonly used. Helmet CPAP, nasal cannula, and high flow nasal cannula (HFNC) were used in 21%, 17%, and 11% of patients, respectively (Table 2). Thompson et al. [22] have highlighted the use of a nasal cannula or non-rebreather face mask but exact numbers are not mentioned. Similarly, Despres et al. [28] have described the use of either high flow nasal oxygen (HFNO) or conventional oxygen therapy (COT). A total of nine prone-posturing sessions, four combined with HFNO and five with COT, were instituted in their study.

4. Discussion

Clinicians throughout the world are fighting an uphill battle of managing the enormous COVID-19 patient load. Further, a sudden spurt in the ICU admissions of COVID-19 patients with varying degree of respiratory failure is worrisome, especially in resource challenged nations. Aerosol generation potential of non-invasive ventilation strategies has precluded their use in COVID-19 patients and has resulted in a low threshold for intubation [13]. In this critical situation, any respiratory support modality which can conserve critical healthcare resource and reduce intubation should be carefully evaluated.

There is convincing evidence regarding prone positioning in mechanically ventilated patients suffering from moderate to severe ARDS [14], but limited evidence exists regarding the effect of prone positioning in awake spontaneously breathing patients. In 2003, Valter et al. reported that awake proning quickly improved oxygenation and allowed the prevention of intubation in 4 patients [9]. Feltracco et al. [15,16] successfully demonstrated the resolution of refractory hypoxemia in 5 lung transplant recipients who underwent awake proning with noninvasive ventilation. Similarly, a retrospective study on 15 non intubated patients who underwent prone positioning procedures, demonstrated significant improvement in PaO_2 when the patient was positioned from supine to prone with PaO_2 coming back to baseline after 6 hours of repositioning [10]. Ding et al. conducted a recent study to assess the effect of prone position along with high flow nasal cannula or noninvasive ventilation in 20 patients suffering from moderate to severe ARDS [11]. They concluded that the addition of prone positioning has contributed to the prevention of intubation in 11 out of 20 patients, and they had a significantly higher Pao 2/Fio2 ratio.

4.1. Oxygenation

In the present systematic review, we explored the effect of prone positioning on oxygenation in non-intubated spontaneously breathing patients suffering from COVID-19 related pneumonia. Majority of the patients (11/13 studies including 199 patients) showed significant improvement in oxygenation after prone positioning. Promising results were observed when the proning session was started early. One of the reasons for this outcome was the availability of a higher proportion of potentially recruitable alveoli in the early stages of ARDS [17]. The other explanation was the improvement is ventilation-perfusion matching. Although, the improvement in oxygenation after awake proning was not long-lasting in few studies [19,21], there was a definite reduction in the requirement for oxygen therapy [23,25,26,29,31] and intubation rates [24,28]. Subjective improvement in the symptoms after initiation of prone posturing was also observed in the patients [27,30].

4.2. Need for intubations

The intubation rate in our study was 23.80%, which does not seem to be high for a cohort of patients suffering from ARDS. Studies published during the initial months of the pandemic suggest an intubation rate of 32% [32]. However, we are well aware that this proportion has decreased over time and is subjected to a further decline as the pandemic progresses. This is because, the requirement for invasive mechanical ventilation among the COVID-19 patients primarily depends on the severity of illness [33]. With the beefed-up testing strategy of the present times, there is an early recognition of the COVID-19 positive cases. Therefore, strategies such as non-invasive ventilation (NIV), awake prone positioning and restrictive fluid resuscitation are started early. When instituted timely, these strategies have shown to reduce the need for IMV drastically [34]. Although, the intubation rate as per the current review depicts a beneficial effect of awake prone positioning, we cannot exclude the fact that the included studies were published at different timepoints during the pandemic. Thus, one might not get enthusiastic as these rates can be a reflection of the difference in the clinical presentation of patients diagnosed at different juncture during the pandemic. In fact, parameters such as oxygen saturation (by pulse oximetry) at presentation can be really helpful to

Table 3
Showing improvement in oxygenation and intubation rates of each study.

	Oxygenation improvement												Intubations
	SaO_2 (S)	SaO_2 (P)	p	SpO_2 (S)	SpO_2 (P)	p	P/F (S)	P/F (P)	p	PO_2 (S)	PO_2 (P)	p	
Coppo et al.	**97.2**	**98.4**	**<0.0001**	**97.2**	**98.2**	**0.01**	**180.5**	**285.5**	**<0.0001**				**13/46 (28%)**
Caputo et al.	-	-	-	**84**	**94**	**0.001**	-	-	-	-	-	-	**13/50 (26%)**
Elharar et al.	-	-	-	-	-	-	-	-	-	**72.8**	**91**	**0.006**	**5/24 (21%)**
Thompson et al.	-	-	-	*	*	-	-	-	-	-	-	-	**12/25 (48%)**
Xu et al.	-	-	-	-	-	-	**Significant elevation of P/F after prone position**			-	-	-	**0**
Ziqin et al.[#]	-	-	-	-	-	-	-	-		-	-	-	**1/10 (10%)**
Damarla et al.	-	-	-	**94**	**98**	-	-	-	-	-	-	-	
Golestani-Eraghi et al.	-	-	-	-	-	-	-	-	-	**46.3**	**62.5**	-	**2/10 (20%)**
Sartini et al.	-	-	-	-	-	**<0.001**	**58–117**	**114–122**	**<0.001**	-	-	-	**1/15 (7%)**
Despres et al.	-	-	-	-	-	-	**183**	**168**		-	-	-	**3/6 (50%)**
Sztajnbok et al. (Case 2)	-	-	-	**94**	**96**	-	**198**	**238**	-	-	-	-	**0**
Slessarev et al.	-	-	-	-	-	-	-	-	-	-	-	-	**0**
Elkattawy	-	-	-	**<88%**	**>95%**	-	-	-	-	-	-	-	**0**

** Out of nine proning sessions in six patients, an improvement in P/F ratio was expressed in four sessions only.
* Mentioned the range SpO_2 improvement i.e. 1%–34% (median [SE], 7% [1.2%]; 95% CI, 4.6%–9.4%).
# Nine patients were successfully weaned off oxygen after a median duration of 8 days.

Table 4
Cumulative intubation rate and death.

Outcome	N	n	Percentage
Intubation	210	50	23.80%
death	203**	11	5.41%

** - Depress et al. and Elkattawy et al. - No outcome data was available.

investigate the success of non-intubation strategy. In the present study, a detailed discussion regarding this was not possible due to paucity of data, as only seven studies (54%) had presented information on this variable.

4.3. Complications and mortality

Although data on complications was limited and was highlighted by less than one-third (30%) of the included studies, no major complications were associated with prone positioning. Mortality rate among the COVID-19 patients with ARDS who were subjected to awake prone positioning was 5.4%.

Maneuvers which safely improve oxygenation without the need for sophisticated instruments and healthcare resource are of immense importance during this COVID-19 pandemic [18]. We believe that awake proning is one such modality. It is simple, cost-effective, easy to initiate and does not require an additional workforce. A concern associated with the risk of aerosolization and transmission of the virus while using additional respiratory support during prone positioning like HFNC or NIV can be mitigated by using personal protective equipment by all the professionals involved in the patient-care and by strictly following hospital infection control guidelines.

4.4. Need for guidelines and protocol

Till now, no official guidelines has been developed for proning non intubated patients. Patients are advised by the clinician to remain in prone position for as long as possible. Development of a proning protocol will not only help to improve compliance but will also provide guiding principle for implementing proning maneuver. It should include time of initiation, number of proning sessions per day, average time to be spent on each position (prone, right and left lateral decubitus, and supine position), proning in negative pressure room, early identification of complications, etc. Additionally, a protocol for close monitoring of the parameters depicting the success of non-intubation strategy for e.g. oxygen saturation by pulse oximetry and precautions for preventing complication and infection are needs to be constructed.

Promoting compliance for awake proning is a major concern for clinicians. Poor compliance to awake proning is mainly seen in obese patients and in those having history of back pain. These patients will benefit from a shorter proning session and a dedicated proning team will certainly improve compliance and reduce complication during the entire proning session.

4.5. Precautions

All the proned patients must be monitored closely. Use of sedative or anxiolytic may improve compliance to proning, but they should be used only if the ward is equipped with close monitoring of hemodynamics and oxygenation status of the patient. Every effort should be made to avoid displacement of oxygenation adjunct during proning as this may have life threatening consequences. The development of a pressure ulcer in awake patients is a rare possibility but all pressure points should be adequately padded, which will help to increase patient comfort and compliance.

4.6. Limitations

Our study has several limitations. Firstly, most of the studies were case reports and case series. Hence the low-evidence of the included studies cannot be overlooked. Secondly, majority of these studies lacked the control population, and the sample size was small. Thirdly, patient discomfort following prone positioning was not evaluated in these studies. Of concern, a comprehensive data including all the parameters was not reported/lacking. Finally, the follow-up data was not mentioned in all the studies. We are also aware that the literature on COVID-19 is very dynamic and growing at a fast pace. Therefore, additions/revisions/changes in the outcomes reported in the present study are expected.

5. Conclusion

Awake prone positioning is a low cost, less resource utilizing, and easy to implement strategy, particularly in low and middle-income countries with limited healthcare infrastructure. Our study clearly demonstrates that awake proning is a feasible option for patients suffering from COVID-19 related ARDS. Majority of the patients showed improvement in oxygenation and respiratory symptoms with little patient discomfort during prone positioning. The intubation rates in this review also depict a beneficial role of awake proning. Since case reports and case series form the majority of the included studies, a well-structured randomized controlled trial is needed to define which COVID-19 patients will benefit the most from awake proning. This will not only avoid unnecessary intubations, but will conserve essential medical resources during times of pandemic. However, it should be evaluated against the risk of delaying unavoidable intubation in sick patients.

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None.

Declaration of competing interest

None.

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Participated in Research design- AS, PK, SA, MB.
Participated in writing paper- AS, MB, SA.
Participated in research work- AS, PK, SA, MB.
Participated in Data Analysis- AS, SA.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tacc.2020.09.008.

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