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BRIEF REPORT

Prone positioning for mechanically ventilated patients with coronavirus disease 2019: the experience of an Irish regional hospital intensive care unit

Nicholas Di Mascio[1] · Siobhan Clarke[1] · Gillian de Loughry[1] · Wahid Altaf[1]

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Abstract

Background The benefits of prone positioning in acute respiratory distress syndrome (ARDS) have been known for many years. While some controversy exists regarding whether coronavirus disease 2019 (COVID-19) pneumonia should be treated with the same therapeutic strategies as for non-COVID ARDS, the Surviving Sepsis Campaign still provide a weak recommendation to utilise prone positioning in this setting.

Aims The aims of this study are to ascertain if prone positioning improves oxygenation significantly in mechanically ventilated patients with severe COVID-19 ARDS and to describe the feasibility of frequent prone positioning in an Irish regional hospital intensive care unit (ICU) with limited prior experience.

Methods In this retrospective, observational cohort study, we investigate if the PaO_2/FiO_2 ratio and ventilatory ratio improve during and following prone positioning, and whether this improvement correlates with patient baseline characteristics or survival.

Results Between March 2020 and 2021, 12 patients underwent prone positioning while mechanically ventilated for severe COVID ARDS. Sixty-six percent were male, mean age 60.9 (± 10.5), mean BMI 33.5 (± 6.74) and median APACHE II score on admission to ICU was 10.5 (7.25–16.3). Further, 83% were proned within 24 h of being intubated due to refractory hypoxaemia. PaO_2/FiO_2 ratio improved from 11.6 kPa (9.80–13.8) to 15.80 kPa (13.1–19.6) while prone, $p < 0.0001$.

Conclusions We found prone positioning to be a safe method of significantly improving oxygenation in mechanically ventilated patients with severe COVID-19 ARDS. We did not find a relationship between patient baseline characteristics nor illness severity and degree of PaO_2/FiO_2 ratio improvement, nor did we find a relationship between degree of PaO_2/FiO_2 ratio improvement and survival.

Keywords Acute respiratory distress syndrome · COVID-19 · Intensive care · Ireland · Oxygenation · Prone positioning

Introduction

Coronavirus disease 2019 (COVID-19) is global pandemic caused by infection with severe acute respiratory syndrome coronavirus 2. The spectrum of severity of COVID-19 is wide, and although the vast majority experience only mild illness, approximately 5% will require intensive care unit (ICU) admission [1]. At time of writing, the mortality rate of patients admitted to ICU with COVID-19 stands at 35.5%, which has decreased from 41% in 2020 [2]; however, this number is higher in mechanically ventilated patients at 45% [1].

Acute respiratory distress syndrome (ARDS) is a syndrome of diverse aetiologies, defined by oxygenation deficit of acute onset, with bilateral radiographic infiltrates that cannot be solely attributed to a cardiovascular cause [2]. The severity of ARDS is classified by the ratio of the arterial partial pressure of oxygen (PaO_2) to the inspired fractional concentration of oxygenation (FiO_2)—the PaO_2/FiO_2 ratio. By this broad definition, hypoxaemic patients with COVID-19 and bilateral chest X-ray infiltrates easily meet the criteria for ARDS. As such, 20–67% of hospitalised COVID-19 patients are diagnosed with ARDS based on these criteria, and this number increases to 100% in mechanically ventilated patients [3].

✉ Nicholas Di Mascio
ndm3010@yahoo.com

1 Department of Anaesthesia, University Hospital Waterford, Dunmore Road, Co Waterford X91 ER8E, Ireland

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Lung protective ventilation and prone positioning have, in a subset of ARDS patients, not only been proven to benefit ventilation but also shown to decrease mortality [4]. The benefits of prone positioning on lung mechanics have been known for many years and include alveolar recruitment, improved ventilation-perfusion matching, decreased ventilator-induced lung injury, facilitation of lung protective ventilation and improved haemodynamics. So far, however, only the PROSEVA trial has demonstrated significantly lower mortality through prone positioning [4]. More recent studies have shown that prone positioning for COVID ARDS also results in improved oxygenation, with several such studies demonstrating associated overall better outcomes [5–7].

Several editorials, opinion pieces and small studies have stated that COVID ARDS is a unique, atypical form of ARDS, that although fits the Berlin criteria for hypoxaemia may differ considerably with regard to lung compliance and mechanics and consequently may not necessarily benefit from usual ARDS management. At the time of writing, the Surviving Sepsis Campaign provides only a “weak recommendation” to utilise prone positioning for mechanically ventilated COVID-19 patients with moderate to severe ARDS. While it has already been shown that oxygenation improves significantly with prone positioning in COVID-19 ARDS as with non-COVID ARDS, the clinical significance and real-life benefit of this remains elusive.

Our ICU is based in a 500-bed regional university hospital which provides tertiary level care to a population of 500,000 people. It has 6 ICU beds, 4 high dependency beds and admits roughly 700 patients per annum. Admissions to the ICU are diverse; however, in the year prior to the COVID-19 pandemic, only 3 patients were proned. During the pandemic, there were 48 confirmed COVID-19 patients admitted to the ICU from March 2020 to March 2021. A formal proning policy had been in place since 2016 (online supporting information file S1).

In this retrospective, observational, cohort study, we examined the effects of prone positioning in our mechanically ventilated COVID-19 ARDS patients from March 2020 to March 2021. Specifically, we sought to investigate if respiratory physiology (as measured by change in PaO_2/FiO_2 ratio and ventilatory ratio [VR]) improved during and following prone positioning, and whether this improvement could be correlated with patient baseline characteristics (age, body mass index [BMI], APACHE II score). We also examined if this change in respiratory physiology was associated with improved survival, as noted in previous studies [5–7].

Furthermore, as a way of comparing our own practice to that described in international literature, we looked at complication rate, duration of proning sessions, time to first proning session and ICU length of stay.

Methods

Design

This retrospective, observational study was approved by the Research Ethics Committee in University Hospital Waterford.

Inclusion criteria

All patients admitted to the ICU in University Hospital Waterford with laboratory confirmed COVID-19 requiring invasive mechanical ventilation and prone positioning between March 2020 and March 2021.

COVID-19 was confirmed via polymerase chain reaction of nasopharyngeal aspirate.

Exclusion criteria

None.

Protocol

Multidisciplinary proning teams ($n = 7$) led by the ICU trainees were established to complete all proning and supinating sessions. An educational video was circulated amongst the prone positioners to ensure consistent prone positioning technique (online supporting information video file S2). Proning protocols and checklists were instituted (online supporting information files S1 and S3) based on best available evidence. Drawing from the PROSEVA trial, prone positioning was considered for intubated patients with ARDS when the PaO_2/FiO_2 ratio was < 20 kPa (150 mmHg), PEEP $>/= 10$ cmH_2O and $FiO_2 >/= 0.6$; however, ultimately the decision was based on the clinical judgement of the ICU team. Prone positioning was maintained for at least 16 h. Termination of prone positioning was decided by the ICU team based on clinical response. Patients were paralysed for the duration of the proning session.

Data collection

Data was collected through a combination of chart review, local hospital laboratory software (iLab) and our national imaging system (NIMIS). Subject characteristics including age, body mass index (BMI), sex and pre-existing comorbidities were recorded. Charlson comorbidity index was calculated and APACHE II score was derived from laboratory findings on admission to the ICU. Arterial blood gas samples were used to calculate patients’ PaO_2/FiO_2 ratios at time points corresponding to immediately before, mid-way during and 4–8 h after prone positioning. Ventilator settings at these time points were also noted and used to calculate ventilatory ratio. Complications of the proning sessions were documented.

Patients' length of stay, duration of mechanical ventilation and survival were recorded. Patients were followed up until death or discharge from the ICU.

Outcome measures

Primary outcome:

- Oxygenation; measured by the PaO_2/FiO_2 ratio
- Ventilation; measured by ventilatory ratio

Secondary:

- Time to tracheal intubation
- Time to first prone manoeuvre
- Duration of proning sessions
- Complications related to proning
- Mortality
- Length of ICU stay

Statistical analysis

Continuous variables were expressed as mean (Standard deviation [SD]) or median (interquartile range [IQR]) depending on their distribution. The changes in oxygenation and ventilatory ratio were compared pre-prone, during prone positioning and following supine repositioning via Friedman test or repeated measures analysis of variables. Continuous variables were compared pre- and post-prone positioning using the *t* test or Wilcoxon signed rank test.

Categorical variables were compared using Fisher's exact or Chi-square. Comparisons between two groups were analysed using the Mann–Whitney *U* test or the independent *t* test and for more than two groups via the Kruskal–Wallis analysis of variance or repeated measures analysis of variance.

Correlation statistics were performed using Pearson correlation coefficient or spearman's rank correlation.

Data analysis was conducted using Prism 5.

Results

Subject characteristics

Between March 2020 and March 2021, 23 patients underwent mechanical ventilation in the ICU for COVID-19 ARDS, equating to 48% of the COVID-19 ARDS ICU patient cohort. Of these, 12 (52%) underwent prone positioning (Fig. 1). Of these 12 patients, 66% of were male, mean age 60.9 (± 10.5), mean BMI 33.5 (± 6.74). Median APACHE II score on admission to the unit was 10.5 (7.25–16.3) and median CCI 3.5 (1.0–5.0) (Table 1).

Patients were commenced on mechanical ventilation due to refractory hypoxaemia on day 14.0 (9.25–16.5) from symptom onset and 83% were proned within 24 h of tracheal intubation. Individuals underwent 2.5 (1.25–3.75) prone positioning sessions for 17 h (16–19.25). Three subjects (25%) required more than 3 proning sessions.

Primary outcome

PaO_2/FiO_2 ratio

PaO_2/FiO_2 ratio improved overall from 11.6 kPa (9.80–13.8) pre-prone to 15.80 kPa (13.1–19.6) while prone, $p < 0.0001$. Following repositioning supine, significant improvement in PaO_2/FiO_2 ratio persisted to 4–8 h with PaO_2/FiO_2 ratio 12.88 (11.4–16.9) $p = 0.023$, and 24 h $p = 0.042$; however, by 48 h, the improvement in PaO_2/FiO_2 ratio had become non-significant.

Ventilatory ratio

No significant change was noted in overall ventilatory ratio before, during or after the manoeuvre (pre-prone 2.24 [1.76–2.57], during 2.12 [1.78–2.63], supine 2.09 [1.78–2.40], $p = 0.941$).

We found no correlation between severity of respiratory compromise in terms of PaO_2/FiO_2 ratio on admission and patient age, BMI, APACHE II score, or CCI. Likewise, there was no association between these baseline patient characteristics and the degree of PaO_2/FiO_2 ratio improvement during

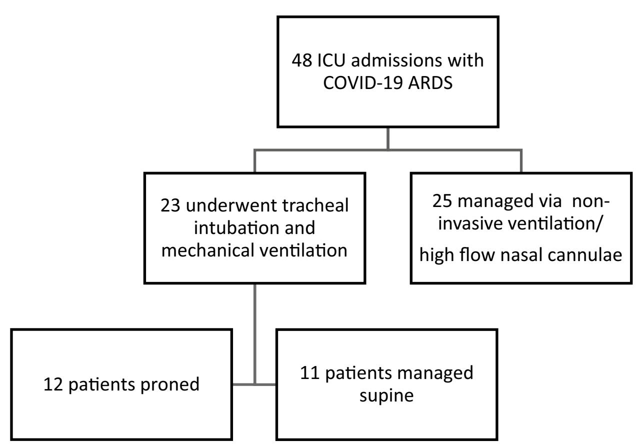

Fig. 1 Management of patients admitted to the Intensive Care Unit (ICU) with COVID-19 Acute Respiratory Distress Syndrome (ARDS) between March 2020 – March 2021

Table 1 Characteristics and respiratory function at baseline, and of those dead vs. alive. Data expressed as mean (SD) or median (IQR)

	Total ($n=12$)	Alive ($n=6$)	Dead ($n=6$)	P value
Age	60.9 (± 10.5)	57.2 (± 7.63)	64.7 (± 12.2)	0.231
BMI	33.5 (± 6.7)	31.9 (± 9.2)	35.0 (± 3.4)	0.449
Sex		M 3 F 3	M 5 F 1	0.54
CCI	3.5 (1.0–5)	2.50 (0.750–5.75)	4.5 (1–5.75)	0.625
APACHE II	10.5 (7.3–16.3)	15.50 (12.3–20.8)	7.50 (6.75–10.3)	0.010
PaO2/FiO2 ratio kPa (baseline)	11.3 (9.25–14.6)	12.2 (8.13–17.3)	11.3 (9.30–12.6)	0.557
Change in PaO_2/FiO_2 ratio kPa (baseline-prone)	4.0 (1.7–7.7)	2.90 (–0.20–8.80)	4.52 (2.04–7.63)	0.78
VR (baseline)	2.22 (1.6–2.65)	2.304 (1.57–2.53)	1.96 (1.59–3.40)	1
Change in VR (baseline–prone)	0.07 (–0.3–0.5)	–0.165 (–0.542–0.659)	0.123 (–0.199–0.493)	0.389

BMI body mass index, *M* male, *F* female, *kPa* kiloPascals, *CCI* Charlson comorbidity index, *VR* ventilatory ratio

prone positioning (Table 2). Finally, we found no significant association between change in PaO_2/FiO_2 ratio and survival (Table 1). Likewise, we observed no significant association between change in VR and survival (Table 1).

Minor complications were documented in 60% of cases; these included facial oedema and endotracheal tube leak. A total of six patients survived to discharge from ICU (50%), the remaining six died in intensive care. Patients were mechanically ventilated for 177 h (62.5–267) and required intensive care for 14.5 days (10–23).

Discussion

In this study, we examined the physiological response to prone positioning as measured by PaO_2/FiO_2 ratio and ventilatory ratio in patients with severe COVID-19 ARDS. Prone positioning has been used as a therapeutic strategy for ARDS for several decades, and in concert with lung protective ventilation has been shown to reduce mortality in patients with moderate to severe disease. The effect of prone positioning on lung mechanics is complex and not consistent across trials [8]; however, some of the known benefits include alveolar recruitment, improved ventilation-perfusion matching, decreased risk of ventilator-induced lung injury (VILI), and consequent facilitation of lung-protective ventilation [9]. Prone positioning allows for a more homogenous distribution of lung stress and strain due to a more uniform distribution of tidal volume, as well as reduced cyclical alveolar opening and closing [10]. With a more even spread of transpulmonary pressure, the likelihood of overdistension due to high PEEP is reduced [10]. Put simply, prone positioning makes the lungs mechanically more homogenous, thus reducing the uneven distribution of stress and strain that accentuates the risk of VILI.

So far, only the PROSEVA trial has demonstrated significantly lower mortality through prone positioning [4], with a 16% 28-day mortality in the prone group vs. 32.8% in the supine group [11]. Of note, this trial used the lowest tidal volumes of all major studies and had near universal use of neuromuscular blockade, while maintaining prone positioning for 17 ± 3 h. The authors also note that no correlation was found between degree of oxygenation response and patient survival [12]. Therefore, the beneficial effect of proning is believed to be due to factors other than oxygenation alone.

Many studies have shown similar significant improvements in PaO_2/FiO_2 ratio in COVID ARDS as for non-COVID ARDS with prone positioning [5–7, 13, 14]; however, sparse few found this improvement to translate to improved survival in COVID ARDS [5–7].

In our study, mean age of our patient cohort was 60.9 (± 10.5), mean BMI 33.5 (± 6.7) and median CCI 3.5,

Table 2 Magnitude of PaO2/FiO2 ratio response (baseline vs while prone) and baseline characteristics, values are mean (SD) or median (IQR)

	No response	0–50%	> 50–100%	> 100%	P value
Age	58.2 (10.4)	58.47 (9.75)	64.57 (10.1)	60.8 (6.46)	0.539
BMI	34.1 (8.2)	32.2 (6.39)	32.9 (4.85)	35.5 (8.53)	0.789
CCI	2 (0.5–6.5)	5 (1–7.25)	5 (1–8)	3 (1.5–4)	0.81
APACHE II	17 (10.5–22.5)	11 (7.75–17)	7 (7–11)	14 (11.5–20)	0.077

BMI body mass index, *CCI* Charlson comorbidity index indicating a younger, more obese patient cohort with fewer comorbidities than in previous non-COVID ARDS studies [8]. Median PaO_2/FiO_2 ratio prior to first proning session was 11.3 kPa (85.5 mmHg), indicating a very severe level of hypoxaemia, even by COVID standards [5, 7, 9, 11].

We found that in COVID-19 patients who were mechanically ventilated and proned for severe ARDS, PaO_2/FiO_2 ratio improved significantly over a series of time points from initial proning up to and including 24 h post final proning session. Overall, PaO_2/FiO_2 ratio improved 36% from 11.6 kPa (9.8–13.8) to 15.8 kPa (13.1–19.6) while prone ($p < 0.0001$). The most dramatic improvement in PaO_2/FiO_2 ratio was observed following the first proning session (11.3 kPa to 18.4 kPa), in keeping with current literature [5]. Following repositioning supine, significant improvement in PaO_2/FiO_2 ratio persisted to 24 h; however, by 48 h, the improvement had become non-significant. Only one patient did not experience any improvement in PaO_2/FiO_2 ratio on initial proning, while 75% of patients experienced a greater than 20% improvement. There was no association between change in PaO_2/FiO_2 ratio and patients' baseline characteristics, consistent with other studies [7].

We did not observe a significant association between change in PaO_2/FiO_2 ratio and survival in our study. Existing literature is conflicting in this area, with several studies reporting a survival benefit in "O_2 responders" or "prone success" groups for both COVID and non-COVID ARDS [5–7, 9]. Some authors [6] suggest that if respiratory physiology has not improved substantially by the end of the first proning session, then alternative therapeutic options should be sought. Contrary to this, the PROSEVA investigators argue that the mechanisms underlying improvement in clinical outcomes are complex and not limited to improvement in gas exchange alone, and therefore proning should be continued even in the absence of a notable improvement in PaO_2/FiO_2 ratio [10]. Guerin et al. state that the primary explanation for decreased mortality associated with prone positioning is due to less overdistension of non-dependent lung regions and less cyclical opening/closing in dependent regions, i.e., facilitation of lung protective ventilation and reduced VILI [10].

The ventilatory ratio, which can be easily calculated from routine bedside variables, correlates positively with pulmonary dead space in ARDS [15]. Pulmonary dead space fraction in turn has been shown to be an independent predictor of mortality in ARDS [15]. A normal value in healthy lungs is 1. In keeping with recent studies [7], although there was a trend toward reduced ventilatory ratio with prone positioning (Table 1), it was not significant.

The retrospective, single-centre, observational nature of this study and the very small sample size are major limitations. As such it is not possible to draw firm conclusions on the relationship between response to prone positioning and outcome. The decision to utilise prone positioning was not standardised and ultimately was based on the clinical judgement of the ICU team. Similarly, although lung-protective ventilation was the goal it was not achieved in all cases. Other limitations include the lack of retrospective accessibility to static compliance and plateau pressure measurements, thus precluding their inclusion in the study.

One finding of this study worthy of note is that prone positioning was used very frequently and early in our ICU once patients were mechanically ventilated. Fifty-two percent of severe COVID ARDS patients underwent at least one proning session while mechanically ventilated, and the median time spent prone per session was 17 h. This compares favourably with the PROSEVA and LUNGSAFE studies.

Furthermore, this study represents the experience of an Irish regional university hospital ICU, which prior to the COVID-19 pandemic had never experienced such demand on its staff and resources. As noted above, this patient cohort represents a particularly severe subset of ARDS. In response to this unprecedented demand, on-call proning teams encompassing all manner of healthcare workers were formed, and a proning demonstration video was created and disseminated within the hospital. The proning procedure soon became smooth and efficient, regardless of time of day, as attested to by the absence of serious adverse complications.

Conclusion

In summary, we found prone positioning to be a safe method of significantly improving oxygenation as measured by the PaO_2/FiO_2 ratio in our cohort of mechanically ventilated patients with severe COVID-19 ARDS. We did not find a relationship between patient baseline characteristics or illness severity and degree of PaO_2/FiO_2 ratio improvement, nor did we find a relationship between degree of PaO_2/FiO_2 ratio improvement and survival. Due to the limited sample size and retrospective nature of the study, drawing definitive conclusions from this data is not possible. However, we still believe it to be valuable in that it demonstrates the experience of regional hospital ICU, and how it can adapt quickly and effectively to unexpected challenges in the public health landscape.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11845-022-03085-9.

Author contribution Authors Dr Di Mascio and Dr Clarke contributed equally to this work. All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Dr Nicholas Di Mascio, Dr Siobhan Clarke and Dr Gillian de

Loughry. The first draft of the manuscript was written by Dr Nicholas Di Mascio and Dr Siobhan Clarke. All authors read and approved the final manuscript.

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Declarations

Competing interests The authors declare no competing interests.

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