Clinical benefits of prone positioning in the treatment of non-intubated patients with acute hypoxic respiratory failure: a rapid systematic review

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ABSTRACT

Background The COVID-19 pandemic has led to a surge in critically unwell patients with type 1 respiratory failure. In an attempt to reduce the number of patients requiring mechanical ventilation, prone positioning (PP) of non-intubated patients has been added to many hospital guidelines around the world. We set out to conduct a systematic review of the evidence relating to PP in the non-intubated patient with type 1 respiratory failure secondary to COVID-19 and other causes.

Methods The review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. A literature search of major databases and grey sources was conducted. Studies were assessed for inclusion by two authors according to prespecified criteria. Data collection processes, analysis and risk of bias assessment were planned.

Results 31 studies were included for analysis. These consisted of prospective and retrospective case series, cohort studies and case reports. None of the studies included a comparison group. No statistical analysis was performed. Descriptive data of included studies and narrative synthesis are presented.

Conclusions No high-quality randomised controlled trials were found and thus evidence in relation to PP as a treatment for non-intubated patients with type 1 respiratory failure is lacking.

INTRODUCTION

Acute respiratory failure is a leading reason for endotracheal intubation, mechanical ventilation and referral to the intensive care unit (ICU). Patients have traditionally been cared for in a recumbent or semirecumbent position. Prone positioning (PP) refers to the practice of positioning patients on their ventral surface. Theoretically, the reasons why PP might convey substantial physiological benefit include improved gas exchange via more homogeneous matching of ventilation and perfusion, increased cardiac output from optimisation of right ventricular preload and afterload, and improved drainage of secretions via the general dorsal lung to ventral trachea drainage vector.[1–3]

In 2013, the Prone Positioning in Severe Acute Respiratory Distress Syndrome (PROSEVA) Trial demonstrated that PP, for a minimum of 16 hours continuously, conveyed a mortality benefit at 28 days, for mechanically ventilated patients with moderate to severe acute respiratory distress

Key messages

What is already known on this subject
► Prone positioning (PP) in intubated, mechanically ventilated patients has been demonstrated to reduce mortality, particularly in patients with severe acute respiratory distress syndrome (ARDS).
► PP has been used extensively during the COVID-19 pandemic in awake, non-intubated patients despite the lack of robust evidence of benefit.

What this study adds
► In this systematic review, we found no high-quality evidence that PP in awake, non-intubated patients reduces rates of subsequent intubation or decreases mortality.
► There was some signal that PP may improve hypoxia.
► However, randomised controlled trials are needed to assess whether PP in awake, non-intubated patients confers patient benefit.

syndrome (ARDS) (ie, P/F ratio <150 mm Hg). Prior to the publication of PROSEVA, several trials demonstrated no significant benefit in clinically relevant outcomes when PP was applied across a broader group of patients. This is despite evidence that PP improved oxygenation across all groups of mechanically ventilated patients with ARDS. This contrast demonstrates the importance of randomised controlled trials (RCTs) in determining whether improvement in physiological markers translates to improvement in patient-oriented outcomes, as well as in determining specific protocols that are effective, and which patient groups stand to benefit.

PP in patients who are not intubated has been less well studied. The capacity for awake patients to modulate their own position, cough and exercise voluntary control makes them a physiologically distinct population from heavily sedated intubated patients. Therefore, it is not clear that the benefit conveyed by PP on intubated patients is transferable. Potential harms of PP in non-intubated patients are yet to be elucidated but may include dislodged venous access or O_2 delivery devices, delay to intubation and pressure injuries. Tolerance

of PP, especially for prolonged periods, is considerably more variable in awake patients than in those who are deeply sedated.

The current COVID-19 pandemic has resulted in hospitals and ICUs being overwhelmed with patients in respiratory failure. COVID-19 is a viral pneumonia caused by SARS-CoV-2 infection often leading to severe hypoxia, ARDS and respiratory failure.[4] About 15% of patients with COVID-19 require oxygen therapy and about 5% require mechanical ventilation.[5] Despite a lack of strong supporting evidence, PP in non-intubated patients has been recommended in guidelines and advocated by influential FOAMed sites as a means to avoid endotracheal intubation for COVID-19-associated respiratory failure.[6]

If PP is shown to be beneficial in non-intubated patients, this cost-effective intervention could have a substantial impact on preserving hospital resources. Despite the pressures the COVID-19 pandemic has placed on healthcare systems, it remains important to ensure that this intervention is supported by quality evidence.

The objective of this review was to identify and synthesise the evidence related to PP in non-intubated patients with type 1 respiratory failure from all aetiologies.

METHODS

The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The protocol was prospectively registered on the PROSPERO website (PROSPERO 2020 CRD42020184705).

Outcomes

The primary outcome was endotracheal intubation due to progressive respiratory failure. Secondary outcomes included change in oxygenation (PaO_2/FiO_2), need for escalation of respiratory support without requiring intubation, admission to ICU, mortality, adverse effects of PP, length of hospital stay and ventilator-free days.

Patient and public involvement

Patients and the public were not involved in the design, evaluation or dissemination of this research.

Literature search

A literature search was designed with the assistance of a medical librarian and performed on 14 August 2020. The following databases were searched:

1. PubMed.
2. Google Scholar.
3. WHO COVID-19 database.
4. Cochrane Clinical Trials Register.
5. Grey sources.

The search was conducted from inception of databases to 14 August 2020 and had no language restriction. Grey sources included Google and Google Scholar, FOAMed sites, reference lists of articles, clinical trial registries and conference abstracts. Titles and abstracts were reviewed, and full text of relevant and potentially relevant articles were obtained. The search strategy for MEDLINE is included as online supplemental appendix 1.

Inclusion and exclusion criteria

Articles for inclusion were limited to those available in English, with no restrictions on the country of origin. Studies included were those conducted on adult patients with acute type 1 respiratory failure, who were spontaneously breathing, and who underwent PP of any duration as a therapeutic intervention. Studies on paediatric patients, or on patients intubated at study commencement, were excluded.

Controlled trials and observational studies that included a comparison group were to be included in the final quantitative review. Case series and cohort studies were also reviewed for their narrative value. Editorials, commentaries and opinion pieces were excluded.

Study selection, data extraction and synthesis

Studies were screened for relevance and independently reviewed by two authors who assessed the studies against the inclusion/exclusion criteria. Arbitration was provided by a third author when required.

An electronic tool was designed to facilitate data extraction by two independent investigators. We also planned to assess the quality of included studies using the Cochrane risk of bias tool by two authors independently, with arbitration by a third author if required.

Analysis

Descriptive data about study characteristics are presented. Our plan for statistical analysis was to use RevMan, V.5.4, The Cochrane Collaboration, 2020, presenting risk ratios for the dichotomous outcomes (eg, primary outcome of endotracheal intubation) and difference in means (or standardised mean difference) for continuous outcomes. We planned to use the inverse variance approach to meta-analysis with either fixed or random effects meta-analysis. Heterogeneity was to be assessed with I^2.

Changes from protocol

Small changes were required from the published protocol. The original search was conducted from 1995 to present; however, this was subsequently extended to the inception of databases. No meta-analysis was performed as no suitable studies were identified. The planned quality assessment was changed from the Cochrane risk of bias tool to the methodological index for non-randomised studies (MINORS) tool,[7] a validated tool for non-randomised studies, as this was better suited to the types of studies found.

RESULTS

The PRISMA flow diagram is presented in figure 1. The search strategy identified 725 records. After removing duplicates, 561 abstracts were screened. We obtained 57 full-text articles for detailed review. Thirty-one records were agreed to have data that could contribute value to the review.[8–38] Excluded full-text articles are listed in online supplemental appendix 2. No identified studies included an appropriate comparator and therefore no statistical analysis was performed.

The articles reviewed and their major findings are summarised in online supplemental table 1 and 2. The design of the studies reviewed is summarised in table 1.

The nine cohort studies identified were assessed for methodological quality with the MINORS tool[7] (table 2). Only two studies scored higher than 10 of a maximum 16 for non-comparative studies.

Heterogeneity of design and methodology was evident across all the included studies. For the larger studies, patients were selected via convenience sampling or cross-sectional survey. Protocols for PP varied with regard to level of ergonomic support and supervision. Some protocols combined PP with
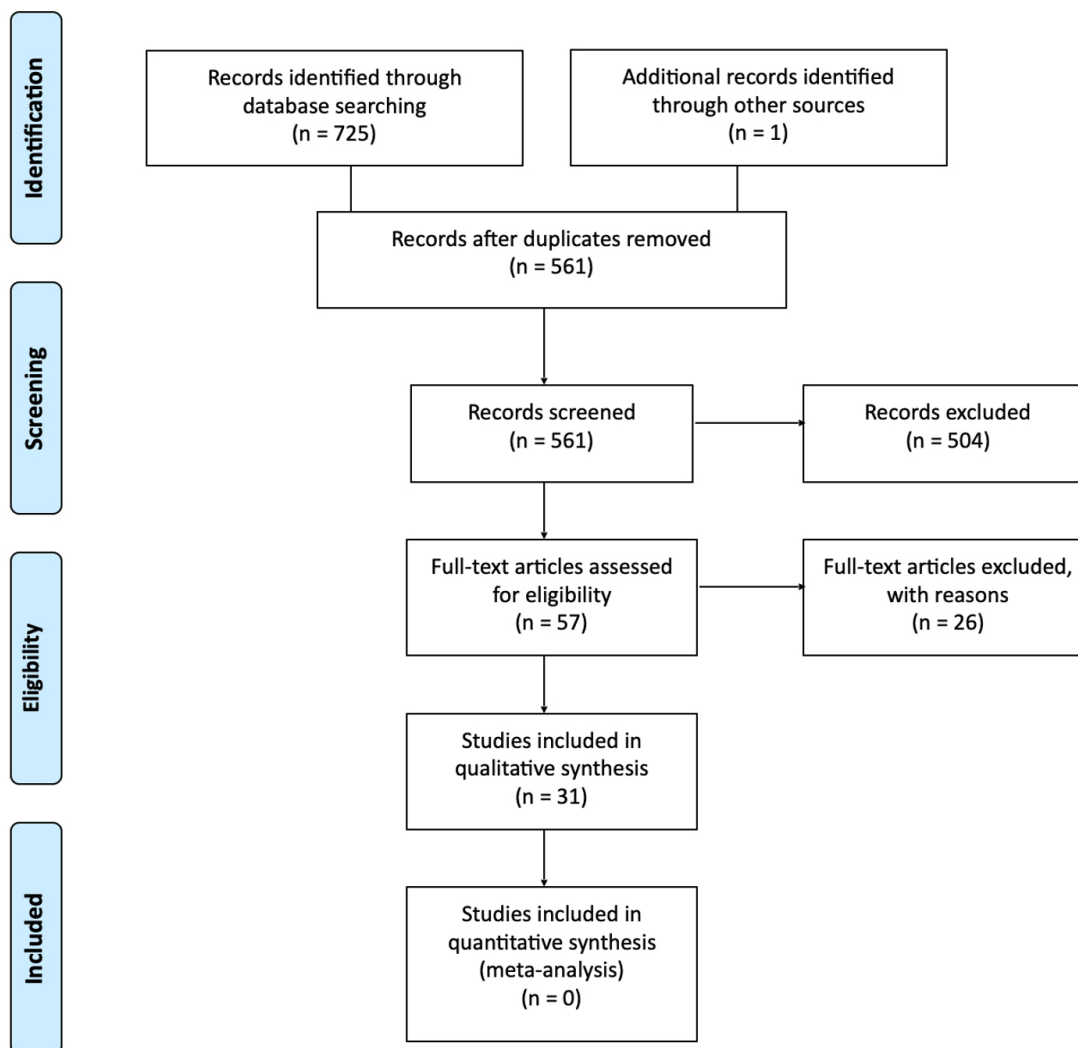
Figure 1 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

other postures. Duration and frequency also varied, and in some protocols was very limited due to poor patient tolerance. The devices used for respiratory support included standard nasal cannulae, Hudson masks, non-rebreather masks, high flow nasal cannulae, mask non-invasive ventilation and helmet continuous positive airway pressure (CPAP). In some studies, the mode of respiratory support was changed with the initiation of PP. The most common outcome measure was oxygenation (PaO_2/FiO_2). Other outcome measures included rate of intubation, dyspnoea, respiratory rate, haemodynamic parameters, tolerance, comfort and mortality. Some of the studies included data on adverse events. Limited documentation and missing data were noted in several studies.

Protocols for capturing data also differed between studies. To illustrate, SPO_2 and PaO_2/FiO_2 were measured at different times depending on the study, with examples including 5 min post PP,

intervals from 10 to 60 min, post return to the supine position or as a single daily measurement. Rates of intubation were occasionally reported. Only a few studies reported time-to-event outcomes such as mortality or hospital discharge.

Although meta-analysis was not possible, some comments can be made in relation to the available data. Of note, it appeared that PP resulted in improved oxygenation in many patients across the studies. This was observed as a consistent before-and-after effect following initiation of PP. While some patients maintained improved oxygenation with resupination, most did not. The findings in terms of other respiratory parameters like respiratory rate, work of breathing and dyspnoea were noted to either improve or remain unchanged.

Two studies[22][28] reported lower than anticipated rates of intubation in patients prescribed PP, but in the absence of true comparator groups, no real conclusions can be drawn. Coppo et al noted that there was no difference in the rate of intubation between patients who responded to PP with improved oxygenation relative to non-responders.[16]

Nine studies reported on the outcome of tolerance. Two reported no intolerance (or 100% tolerance). In other studies, intolerance ranged from 8% to 40%. Only Coppo et al delineated reasons for intolerance—five for discomfort, one for coughing, one for non-cooperation and two for worsening of

Table 1 Design of included studies

Study design	COVID-19 studies	Non-COVID-19 studies
Prospective observational cohort studies	5	1
Retrospective observational cohort studies	3	0
Case series/single case studies	16	6

Table 2 MINORS score for the identified PP cohort studies

Criteria	Burton-Papp et al[17]	Caputo et al[18]	Coppo et al[16]	Ding et al[22]	Dong et al[23]	Elharrar et al[24]	Lawton et al[28]	Retucci et al[32]	Sartini et al[34]
1. A clearly stated aim	1	1	2	2	1	2	1	2	1
2. Inclusion of consecutive patients	1	2	0	1	0	2	1	2	0
3. Prospective collection of data	0	2	2	2	0	2	0	2	1
4. Endpoints appropriate to the aim of the study	1	1	2	2	1	1	1	1	1
5. Unbiased assessment of the study endpoint	1	1	1	1	1	1	0	1	1
6. Follow-up period appropriate to the aim of the study	2	1	2	1	1	1	2	0	1
7. Loss to follow-up less than 5%	1	1	1	1	0	1	2	1	1
8. Prospective calculation of study size	0	0	2	2	0	0	0	0	0
9. An adequate control group	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
10. Contemporary groups	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
11. Baseline equivalence of groups	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
12. Adequate statistical analysis	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total score	7	9	12	12	4	10	7	9	6

Each criteria is scored either: 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The ideal score is 16 for non-comparative studies and 24 for comparative studies.
PP, prone positioning.

respiratory parameters (from 56 patients enrolled).[16] Of the two studies that reported 100% tolerance, one prescribed PP sessions of 1-hour duration and excluded patients requiring FiO_2 >50%.[29] The other specified no standardised duration of PP.[34] Burton-Papp et al reported that poor tolerance seemed to correlate with increased risk of intubation.[17] No other adverse events were reported.

DISCUSSION

Our systematic review found no high-quality evidence to support the use of PP in the management of awake, non-intubated, adult patients with respiratory failure, in terms of clinically relevant outcome measures. Despite this, the available data suggest that PP may improve oxygenation and appears to be sufficiently safe for further study.

Our review found that 24 of the 31 studies published on PP in non-intubated patients have been conducted during the COVID-19 pandemic. The context for these studies has been one of system overwhelm, need for innovation and diversion of resources to support the clinical workload. PP is distinguished from other therapies in that it is a cheap, non-pharmacological, behavioural intervention, conducted with the necessary cooperation of the patient. The same features that make PP attractive as a therapy make it difficult to study and more likely to be prescribed, even when high-quality evidence is lacking. These contextual factors may explain why we did not find any RCTs or uncontrolled observational trials with appropriate comparator groups which we could include in a quantitative analysis. The included papers consisted solely of case studies, case series and observational cohorts for qualitative or narrative review.

As is the nature of observational study design, the included studies were vulnerable to selection bias, favouring the inclusion of patients able to tolerate PP. Such patients are likely to be younger, less sick, have fewer comorbidities and better physiological reserve, thus inflating the apparent effectiveness of the intervention. For example, in one of the largest cohort studies of patients with COVID-19 in Italy, the included convenience sample was, on average, 10 years younger than that of patients not enrolled.[15] Age is known to be the most important factor associated with mortality for COVID-19.

Other confounding factors noted in many of the studies included the bundling of PP with cointerventions such as antiviral medications, hydroxychloroquine and steroids. Additionally, there was variation in the mode of respiratory support both within and between studies, including some studies where changing the mode of respiratory support coincided with commencement of PP. Lawton et al found that the relatively early application of mask CPAP and awake PP resulted in a lower than expected rate of ICU admission and intubation. This is despite the study population having a higher burden of risk factors for severe COVID-19 disease than the reference population of the UK ISARIC database, with the exception of age.[28] While the reported outcomes were impressive, the bundling of mask CPAP with PP, lack of detail as to how many patients received PP and the very small amount of PP prescribed limit the conclusions possible from this study. Future trials will ideally examine the effectiveness of PP as a standalone intervention, compared with 'standard care' determined by the broader evidence base at the time.

Significant heterogeneity was noted both across and within studies, in terms of the frequency, timing and duration of PP. Most protocols were designed and applied with a degree of pragmatism and allowed for broad variation in tolerance. For

example, many prescribed a minimum duration and frequency of PP, but no upper limit. At least one study excluded intolerant patients from the study group. Special note is also warranted on the subject of supervision, which likely increases compliance and safety, but also increases resource use. Given the presence of two nurses and a physician in one study, the purported resource savings are likely to have been negated. Researchers protocolising PP for future clinical trials need to consider the importance of cost, reproducibility and tolerance.

Outcome measures differed between studies. Many focused on short-term improvement in oxygenation. Indeed, in the studies that used oxygenation as an outcome measure, many patients exhibited a significant improvement, temporally related to the commencement of PP. In some cases, this improvement persisted after resupination. And yet, when Coppo *et al* then compared these 'responders' to the 'non-responders' in terms of subsequent rate of intubation, they found no difference.[16] This highly relevant observation illustrates the point that physiological endpoints can be poor surrogates for clinically relevant outcomes. Indeed, transient improvements in oxygenation from PP could delay inevitable intubation and lead to worse patient outcomes. Thus, future studies should focus on patient-oriented outcomes, such as avoidance of intubation and mortality.

Just 7 of the 34 reviewed papers looked at the effect of PP in the treatment of patients with respiratory failure from causes other than COVID-19. Aetiologies included bilateral pneumonia, viral pneumonia, drowning, thoracic trauma with pulmonary contusions, lupus pneumonitis, bone marrow transplantation and atelectasis. All these studies reported improvement in oxygenation, temporally associated with the initiation of PP, though again, the lack of comparator groups limits how much can be concluded. The findings do, however, raise the possibility that PP may have utility in respiratory failure due to a broad range of causes.

It is also plausible that any potential benefit of PP in non-intubated patients will be limited to certain subgroups. Indeed, this was revealed in the study of PP for mechanically ventilated patients with ARDS. A Cochrane review on this subject found that benefits were confined to patients with severe hypoxaemia in whom PP was implemented early and applied for a prolonged period.[3] The review found no convincing evidence of benefit nor harm from PP in a broader group of patients.[3] The same subgroup was shown to benefit from PP in the PROSEVA trial, where from 466 included patients, mortality in the prone group was 16.0%, compared with 32.8% in the supine group (p<0.001).[39] In non-intubated patients, there are insufficient data to inform which patients are likely to benefit from PP and which patients may be harmed.

Limitations

The review was restricted to full-text articles written in English. The abstracts of two Japanese case reports were found and not included as time constraints precluded their translation and it was decided they would not have affected our conclusions. Also, this is a fast-moving field and we expect further data to be available soon. It will be imperative to continue to evaluate new evidence to ensure patients are offered interventions that are supported by data.

CONCLUSION

Despite theoretical physiological advantages, we could not find any high level evidence to demonstrate the clinical effectiveness of PP in non-intubated patients with respiratory failure. Although many patients appear to respond to the intervention

with improved respiratory parameters, the absence of any comparator groups limits the conclusions that can be drawn. RCTs or other comparative studies are required to determine if clinical benefits exist and, if they do, which patients will benefit most. Future investigation may also serve to inform the optimisation of protocols and implementation of the intervention.

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REFERENCES

1 Gattinoni L, Taccone P, Carlesso E, *et al*. Prone position in acute respiratory distress syndrome. rationale, indications, and limits. *Am J Respir Crit Care Med* 2013;188:1286–93.

2 Scholten EL, Beitler JR, Prisk GK, *et al*. Treatment of ARDS with prone positioning. *Chest* 2017;151:215–24.

3 Bloomfield R, Noble DW, Sudlow A. Prone position for acute respiratory failure in adults. *Cochrane Database Syst Rev* 2015;11:CD008095.

4 Gibson PG, Qin L, Puah S. COVID-19 ARDS: clinical features and difference to "usual" pre-COVID ARDS. *Med J Aust* 2020.

5 Guan W-J, Ni Z-Y, Hu Y, *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708–20.

6 Weingart S. EMCrit Blog, 2020. Available: https://emcrit.org/emcrit/awake-pronation/ [Accessed 20 Apr 2020].

7 Slim K, Nini E, Forestier D, *et al*. Methodological index for non-randomized studies (minors): development and validation of a new instrument. *ANZ J Surg* 2003;73:712–6.

8 Tulleken JE, van der Werf TS, Ligtenberg JJ, *et al*. Prone position in a spontaneously breathing near-drowning patient. *Intensive Care Med* 1999;25:1469–70.

9 Tu G-W, Liao Y-X, Li Q-Y, *et al*. Prone positioning in high-flow nasal cannula for COVID-19 patients with severe hypoxemia: a pilot study. *Ann Transl Med* 2020;8:598.

10 Sorensen CV, Schonemann NK, Christensen AM. Wake prone position for spontaneously breathing, hypoxic patients with pneumonia. *Intensive Care Med* 2002;28:S124-S.

11 Valter C, Christensen AM, Tollund C, *et al*. Response to the prone position in spontaneously breathing patients with hypoxemic respiratory failure. *Acta Anaesthesiol Scand* 2003;47:416–8.

12 Muralidhar TR. A new concept in severe ARDS: non-invasive ventilation (NIV) in the prone position as a strategy to prevent invasive ventilation. *Indian J Crit Care Med* 2015.

13 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.

14 Bellone A, Basile A. Prone positioning in severe acute hypoxemic respiratory failure in the emergency ward. *Emerg Care J* 2018;14.

15 Bastoni D, Poggiali E, Vercelli A, *et al*. Prone positioning in patients treated with non-invasive ventilation for COVID-19 pneumonia in an Italian emergency department. *Emerg Med J* 2020;37:565–6.

16 Coppo A, Bellani G, Winterton D, *et al*. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. *Lancet Respir Med* 2020;8:765–74.

17 Burton-Papp HC, Jackson AIR, Beecham R, *et al*. Conscious prone positioning during non-invasive ventilation in COVID-19 patients: experience from a single centre. *F1000Res* 2020;9:859.

18 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.

19 Cohen D, Wasserstrum Y, Segev A, *et al*. Beneficial effect of awake prone position in hypoxaemic patients with COVID-19: case reports and literature review. *Intern Med J* 2020;50:997–1000.

20 Damarla M, Zaeh S, Niedermeyer S. *Prone positioning of non-intubated patients with COVID-19*, 2020.

21 Despres C, Brunin Y, Berthier F, *et al*. Prone positioning combined with high-flow nasal or conventional oxygen therapy in severe Covid-19 patients. *Crit Care* 2020;24:1–2.

22 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.

23 Dong W, Gong Y, Feng J. Early awake prone and lateral position in Non-intubated severe and critical patients with COVID-19 in Wuhan: a respective cohort study. *medRxiv* 2020:2020.05.09.20091454.

24 Elharrar X, Trigui Y, Dols A-M, *et al*. Use of prone positioning in Nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. *JAMA* 2020;323:2336.

25 Elkattawy S, Noori M. A case of improved oxygenation in SARS-CoV-2 positive patient on nasal cannula undergoing prone positioning. *Respir Med Case Rep* 2020;30:101070.

26 Froelich S, Mandonnet E, Julla J-B, *et al*. Towards individualised and optimalised positioning of non-ventilated COVID-19 patients: Putting the affected parts of the lung(s) on top? *Diabetes Metab* 2021;47:101167.

27 Jena SK, Pradhan SK, Subhankar S. Awake self-proning in a nonintubated COVID patient: a case report from a tertiary care COVID hospital in eastern India. *IJRC* 2020;9:221–3.

28 Lawton T, Wilkinson KM, Javid R, *et al*. Reduced ICU demand with early CPAP and proning in COVID-19 at Bradford: a single centre cohort. *medRxiv.* 2020.

29 Ng Z, Tay WC, Ho CHB. Awake prone positioning for non-intubated oxygen dependent COVID-19 pneumonia patients. *Eur Respir J* 2020;56. doi:10.1183/13993003.01198-2020. [Epub ahead of print: 23 Jul 2020].

30 Paul V, Patel S, Royse M, *et al*. Proning in Non-Intubated (pini) in times of COVID-19: case series and a review. *J Intensive Care Med* 2020;35:818–24.

31 Pérez-Nieto OR, Guerrero-Gutiérrez MA, Deloya-Tomas E, *et al*. Prone positioning combined with high-flow nasal cannula in severe noninfectious ARDS. *Crit Care* 2020;24:114.

32 Retucci M, Aliberti S, Ceruti C, *et al*. Prone and lateral positioning in spontaneously breathing patients with COVID-19 pneumonia undergoing noninvasive helmet CPAP treatment. *Chest* 2020;158:2431–5.

33 Ripoll-Gallardo A, Grillenzoni L, Bollon J, *et al*. Prone positioning in Non-Intubated patients with COVID-19 outside of the intensive care unit: more evidence needed. *Disaster Med Public Health Prep* 2020;14:e22–4.

34 Sartini C, Tresoldi M, Scarpellini P, *et al*. Respiratory parameters in patients with COVID-19 after using noninvasive ventilation in the prone position outside the intensive care unit. *JAMA* 2020;323:2338.

35 Sztajnbok J, Maselli-Schoueri JH, Cunha de Resende Brasil LM, *et al*. Prone positioning to improve oxygenation and relieve respiratory symptoms in awake, spontaneously breathing non-intubated patients with COVID-19 pneumonia. *Respir Med Case Rep* 2020;30:101096.

36 Thompson AE, Ranard BL, Wei Y. Prone positioning in awake, Nonintubated patients with COVID-19 hypoxemic respiratory failure. *JAMA Intern Med* 2020.

37 Whittemore P, Macfarlane L, Herbert A, *et al*. Use of awake proning to avoid invasive ventilation in a patient with severe COVID-19 pneumonitis. *BMJ Case Rep* 2020;13. doi:10.1136/bcr-2020-236586. [Epub ahead of print: 03 Aug 2020].

38 Xu Q, Wang T, Qin X, *et al*. Early awake prone position combined with high-flow nasal oxygen therapy in severe COVID-19: a case series. *Crit Care* 2020;24:250.

39 Guérin C, Reignier J, Richard J-C, *et al*. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368:2159–68.