# Critically Ill Patients with COVID-19: A Narrative Review on Prone Position

Syeda Kashfi Qadri ( ✉ syeda.kashfi.qadri@singhealth.com.sg )

KK Women's and Children's Hospital    https://orcid.org/0000-0003-4713-6872

**Priscilla Ng**

Duke NUS Medical School

**Theresa Shu Wen Toh**

KK Women's and Children's Hospital

**Sin Wee Loh**

KK Women's and Children's Hospital

**Herng Lee Tan**

KK Women's and Children's Hospital

**Cheryl Bin Lin**

KK Women's and Children's Hospital

**Eddy Fan**

University of Toronto

**Jan Hau Lee**

KK Women's and Children's Hospital

---

---

# Abstract

*Introduction:* Prone position improves mortality in patients with acute respiratory distress syndrome (ARDS). The impact of prone position in critically ill COVID-19 patients remains to be determined. In this review, we describe mechanisms of action of prone position, systematically appraise current experience of prone position in COVID-19 patients and highlight unique considerations for prone position practices during this pandemic.

*Methods:* For our systematic review, we searched PubMed, Scopus and EMBASE from January 1, 2020 to April 16th 2020. After completion of our search, we became aware of four relevant publications during article preparation that were published in May and June 2020 and these studies were reviewed for eligibility and inclusion. We included all studies reporting clinical characteristics of patients admitted to hospital with COVID-19 disease who received respiratory support with high flow nasal cannula, non-invasive or MV and reported the use of prone position. Full text of eligible articles was reviewed and data regarding study design patient characteristics, interventions and outcomes were extracted.

*Results:* We found 7 studies (total 1899 patients) describing prone position in COVID-19. Prone position has been increasingly used in non-intubated patients with COVID-19; studies show high tolerance, improvement in oxygenation and lung recruitment. Published studies lacked description of important clinical outcomes (e.g., mortality, duration of mechanical ventilation).

*Conclusions:* Based on the findings of our review, we recommend prone position in patients with moderate to severe COVID-19 ARDS as per existing guidelines. A trial of prone position should be considered for non-intubated COVID-19 patients with hypoxemic respiratory failure, as long as this does not result in a delay in intubation.

# Introduction

The coronavirus disease of 2019 (COVID-19) has infected almost 18 million people worldwide with nearly 700,000 deaths (case fatality rate of 4.8%)(1). Case fatality rates were reported to be approximately 50% among critically ill patients.(2) A significant proportion of patients admitted to the intensive care unit (ICU) had severe hypoxemic respiratory failure requiring mechanical ventilation (MV). (3, 4) Given the current lack of definitive treatments for COVID-19, supportive care with MV remains the cornerstone of intensive care management in these patients.(5, 6) One of the main adjunctive strategies in patients with ARDS who required MV is prone position. Given the benefits of prone position in moderate to severe ARDS (7), the Surviving Sepsis Campaign's and World Health Organization (WHO) guidelines (8, 9) recommend prone position for 12 to 16 hours for adults and children with severe COVID-19 ARDS.

The main aims of this narrative review are: (1) describe the mechanisms of action and summarize the current evidence for prone position in severe respiratory failure, in particular ARDS; (2) systematically review the current collective experience in prone position in critically ill COVID-19 patients; and (3) highlight unique considerations for prone position practices during the COVID-19 pandemic.

## Mechanism of Action and Benefit of Prone Position

In ARDS, prone position improves oxygenation through changes in the distribution of alveolar ventilation and blood flow, improved matching of local ventilation and perfusion, and reduction in regions of low ventilation/perfusion ratios (Figure 1).(10-12) In addition, prone position may reduce the risk of ventilator-induced lung injury (VILI) and promote the complementary benefits of high PEEP.(13, 14)  Prone position leads to a decrease in barotrauma and atelectrauma via a few mechanisms: reduction in hyperinflation; mitigation of overdistension of well-ventilated alveoli during the use of PEEP; and reduction regional shear strain from cyclical opening and closing of small airways.  (13, 14)

Early trials (15-17) showed no mortality benefit with prone position in adults with ARDS but provided valuable information for the targeted application for prone position. This culminated in a landmark PROSEVA randomized controlled trial (RCT) (18) which showed a reduction in 28-day mortality in patient with severe ARDS treated with prone positioning and lung protective ventilation strategies [16% (38/237) vs. 33% (75/229) in the prone and supine groups, respectively (P<0.001)]. Following this, three meta-analyses showed a reduction in mortality with the use of prone position (19) particularly in those with early implementation (20), prolonged adaption of at least 12 hours (11, 20) and in patients with severe hypoxemia (20) or moderate to severe ARDS (11). These studies have resulted in a strong recommendation (7) for prone position for more than 12 hours per day for adults with severe ARDS. These recommendations are currently echoed in WHO (9), Surviving Sepsis (8) guidelines and expert opinion (21) in the management of COVID-19 ARDS.

## Systematic Review of Current Use of Prone Position in COVID-19 Patients

In this subsection, we examine the association between use of prone position and clinical outcomes (e.g., mortality and duration of MV) and physiological changes (e.g., improvement in oxygenation, lung recruitability) that have been reported in patients with COVID-19.

# Methods

## Search strategy and selection criteria

We included all studies of patients with COVID-19 who received respiratory support with high flow nasal cannula (HFNC), non-invasive ventilation (NIV) or MV and reported the use of prone position and our primary outcome, mortality. We limited our search to January 1, 2020 (the day after the first cases were reported to WHO) to April 16th 2020. After the search was completed, we became aware of four relevant publications that were published in May and June 2020; these studies were reviewed for eligibility and inclusion. We did not use language restrictions, but we excluded articles which were unpublished, had not been peer reviewed, case reports and case series with fewer than 10 patients, expert guidance, commentaries, guidelines and protocols for management. We searched the following major medical databases (PubMed, Scopus and EMBASE) with the following keywords: "SARS-CoV-2" OR "SARS-CoV2" OR "SARSCoV-2" OR "SARSCov2" OR "Coronavirus disease 2019" OR "Novel coronavirus" OR "Novel

coronavirus 2019" OR "2019 nCoV" OR "COVID-19" OR "Wuhan coronavirus" OR "Wuhan pneumonia" OR "2019-nCoV" OR "COVID-19" OR "covid19" OR "covid 19". We used text keywords rather than MeSH and Emtree terms as the indexing of the varied terms to COVID-19 was still in progress at the time. Two authors independently reviewed all abstracts and at least one author reviewed the full text for inclusion. Any disagreements were resolved by consensus with a third reviewer. Articles were selected for full text review if the abstract contained keywords such as "critically ill", "intensive care", "respiratory support" "high flow nasal cannula" "non-invasive ventilation" and "mechanical ventilation". Covidence Systematic Review Software, Veritas Health Innovation, Melbourne, Australia was used to identify and remove duplicates (available at www.covidence.org).

## Data Analysis

At least one of the authors reviewed full text of eligible articles and extracted data on study design, patient characteristics [e.g., age, number of females, $PaO_2/FiO_2$ ratio, oxygenation index (OI), oxygen saturation index (OSI), clinical severity scores including Sequential Organ Failure Assessment (SOFA) and Acute Physiology And Chronic Health Evaluation II (APACHE II) score], interventions (respiratory support, $FiO_2$, ventilator parameters, use of prone position, duration and timing of prone position, extracorporeal membrane oxygenation (ECMO), outcomes (mortality, duration of MV) and adverse events associated with prone position. *A priori*, provided there were sufficient studies, we planned to perform a meta-analysis to assess the association of prone positioning with improvement in $PaO_2/FiO_2$ ratio, duration of MV and mortality.

# Results

We retrieved 8675 references (Figure 2); of which 4236 were duplicates. Of the remaining 4439 unique abstracts, we identified 7 articles (22-29) describing prone position in COVID-19 patients receiving respiratory support with HFNC, NIV or MV (Table 1). Six of 7 studies were observational (22-28) while 1 study was a prospective feasibility study (29). Six studies (22, 23, 25, 27-29) included only adult patients, and 5 were single center (22, 25, 27-29). Three studies included ICU patients alone (22, 25, 26), 3 included only non-intubated patients outside the ICU setting (27-29) and one study included both ICU and non-ICU patients(23). Six of 7 studies involved a small number of adult patients (22, 23, 25, 27-29) (Table 1). Only 1 study (26) included a large cohort of 1591 patients and included adult and pediatric patients. Included studies were clinically heterogenous and there is a paucity of description of clinical outcomes in relation to prone position, precluding us from performing a meta-analysis and providing a pooled effect estimate of the impact of prone position on clinically important outcomes

*Outcomes*

Three of 7 studies (27-29) reported high tolerance of prone position in awake non-intubated patients (63 – 83.9%).

Three studies showed improvement in oxygenation with prone position (27-29). In a single center study of 24 awake non intubated patients with hypoxemic acute respiratory failure (27), 6/24(25%) patients showed greater than 20% increase in $PaO_2$ (compared with baseline) during prone position. Similarly, in a study of 15 patients with poor response to NIV (PEEP 10 cm $H_2O$ and $FiO_2$ of 0.6) all patients showed improvement in SpO2 and $PaO_2$/FiO2 (p<0.001) with prone position.(28) In a third study of 56 patients on oxygen supplementation or continuous positive airway pressure support, oxygenation substantially improved from supine to prone positioning (PaO2/FiO2 ratio 180·5 mm Hg [SD 76·6] vs. 285·5 mm Hg [112·9] in supine and prone positions, respectively; P<0·0001). In 2 studies, improvement in oxygenation was maintained after resupination in half of those who showed improvement with prone position (27, 29) although this change was not significant when compared with oxygenation prior to prone position.

An improvement in lung recruitability was seen with prone position (25). In 12 mechanically ventilated patients, prone position performed over periods of 24 hours when PaO2/FiO2 was persistently lower than 150mmHg resulted in higher proportion of patients of achieved lung recruitment (13/36 vs. 1/17 in the prone and non-prone groups, respectively, P=0.02).(25) The investigators also reported an increase in $PaO_2$/$FiO_2$ ratio though this was not statistically significant (182 ± 140 in prone vs. 120 ± 61 in supine).

Two studies did not report clinical characteristics and outcomes of patients treated specifically with prone position (22, 26). Only 4 of 7 studies (24, 25, 28, 29) reported mortality in patients treated with prone position. Reported mortality rates ranged from 6.7 – 100%.(24, 25, 28, 29) However, these studies which reported mortality lacked control groups and did not adjust for clinically significant patient characteristics or severity of illness. One study reported no difference in the subsequent need for intubation in patients who responded to those who responded to prone position compared with those who did not. (29) None of the studies examined prone position with duration of MV. No serious adverse events were reported in any of the included studies.(22, 24-29)

## Increasing Use of Prone Position in Awake Non-Intubated Patients

There is an increasing use of prone position in non-intubated patients with and without COVID-19. COVID-19 patients are often treated with NIV or HFNC as the initial modality for respiratory support.(22, 30) The benefits of prone position should theoretically apply to spontaneously breathing, non-intubated patients, with improvement in oxygenation while delaying or even avoiding the need for intubation. Collective evidence and physiological basis of prone position in ARDS have encouraged several ICUs to incorporate prone position into their management of non-intubated COVID-19 patients.(8, 31)  Indeed, we became aware of 4 studies that were published after completion of our search that described the use of prone position in non-intubated COVID-19 patients (27-29, 32). Three studies met our inclusion criteria and were included in our systematic review (27-29) .  The fourth study did not fit the inclusion criteria of our review as patients were on low flow or non-rebreather mask oxygen therapy alone (32) reported use of prone position in 25 adult COVID-19 patients with severe hypoxemic respiratory failure. In this latter study, 19/25 (76%) patients responded to prone position with improvement in SpO2 > 95% within one hour(32). Additionally, patients who showed improvement in SpO2 > 95% with prone position, showed a lower

intubation rate of 37% (n = 7) compared with 83% (n = 5) in those whose SpO2 remained < 95% one hour after prone position (mean difference in intubation rate was 46% (95% CI, 10% − 88%). (32)

Studies conducted in non-COVID-19 patients with acute respiratory failure showed similarly promising results although the effect on important clinical outcomes such as mortality and ventilator free days remain unexplored (33-35). A retrospective study (33) comparing oxygenation ($PaO_2/FiO_2$) pre, during, and post (6 to 8 hours) prone position in 15 non-intubated adult patients with non-COVID-19 associated hypoxemic acute respiratory failure showed oxygenation was significantly higher during prone position with the same PEEP and $FiO_2$ throughout the entire duration of prone position (Pao2/Fio2 124±50 mmHg, 187±72 mmHg, and 140±61 mmHg, during PRE, PRONE, and POST steps, respectively, P<0.001). However, the oxygenation improvement did not persist after being returned to supine position, and this was postulated to be secondary to unstable recruitment of dorsal lung regions. Tolerance rate was high (41/43 prone position procedures, 95%) with no significant adverse effects. In a prospective observational study of 20 patients with non-COVID-19 associated moderate to severe ARDS (34), 11/20 (55%) patients avoided intubation when treated with a short duration of prone position (1.8h ± 0.7, mean of 2.4± 1.5 times/day) combined with NIV and HFNC, compared with the expected intubation rate of 75% in patients with moderate to severe ARDS from prior published studies, although this reduction was not statistically significant and did not meet the pre-determined threshold of 40% reduction set by the authors. Of this cohort, 8 patients (73%) had moderate and 3 (27%) had severe ARDS and the addition of prone position to HFNC and NIV resulted in a 25 to 35mmHg increment of $PaO_2/FiO_2$. A few case reports also demonstrated similar findings of improved oxygenation in non-intubated patients post lung transplantation. (35, 36) .

Adverse effects such as pressure sores and tube obstruction associated with prone position in ventilated patients (11, 37) were not seen in the aforementioned studies in non-intubated patients with same level of hypoxemia. However, it is important to note that studies on non-intubated patients utilized a much shorter duration of prone position [median 3 hours (33), at least 30 minutes (34)] than what is recommended in patients with severe ARDS (7). While collective prior studies suggest that prone position in non-intubated patients with acute respiratory failure can result in improved oxygenation and reduced need MV, whether this strongly applies to non-intubated COVID-19 patients remains to be determined as only 4 descriptive studies (27-29, 32), till date, have been published and further trials in non-intubated prone position in COVID-19 patients (NCT04383613, NCT04350723) are underway.

## Choosing the Right Patient to Prone in COVID-19

Despite limited evidence for prone position in COVID-19, certain radiological features in this disease suggest that prone position may benefit these patients. Radiological features distinct to COVID-19 include bilateral multifocal lung involvement with ground glass opacities with predilection for peripheral or posterior lung fields (38) and vascular thickening. (39, 40) As the infection progresses, lung findings progress from unilateral multifocal opacities (in the subclinical stage) to rapidly evolving to bilateral diffuse ground glass opacities (in one week) followed by transition to a consolidative pattern by the

second week of symptoms (41). Maximal lung involvement on radiological imaging has been found to peak 10 days from onset of symptoms (42). Given the predilection for posterior lung lobes and bilateral involvement in COVID-19 pneumonia, prone position may allow recruitment of the diseased posterior lobes and may be potentially beneficial in this viral pneumonia. However it is important to keep in mind that COVID-19 ARDS presents as a spectrum of clinical phenotypes with varying degrees of lung infiltrates, lung recruitability and compliance and hence heterogenous respiratory mechanics (16), with some patients more or less likely to respond to prone positioning.

Given this clinical heterogeneity, electrical impedance tomography (EIT), a non-invasive imaging tool that can assess lung recruitment in patients with ARDS may be a useful technique to guide patient selection for prone position. Studies on adult populations have shown efficacy of EIT as a bedside tool to evaluate regional ventilation and effectiveness of lung recruitment strategies (43, 44).  However, more research on respiratory mechanics, utility of EIT and the effect of prone position in COVID-19 patients is required in order for definitive management guidelines to be established.

## Limitations and Alternatives to Prone Position

It is important to consider the feasibility and practicality of prone position, particularly given the resource constraints of the current pandemic. Absolute contraindications to prone position include unstable spinal or pelvic fractures, open chest or abdomen, central cannulation for ECMO or ventricular assist devices. Relative contraindications include raised intracranial or intraocular pressure, uncontrolled seizures, recent cardiac arrhythmias, precarious central line or ECMO cannulae, pregnancy in the second or third trimester as well as hemodynamic instability or significant coagulopathy. (45, 46) Systematic reviews of prone position have demonstrated a higher incidence of pressure sores, tracheal tube obstruction and dislodgement of thoracostomy tubes with prone position (19, 20). However, implementation by an experienced team with an adequate number of personnel(18) and the use of standardized protocols can minimize adverse events and occupational injuries to healthcare staff (18, 45, 47). Additionally, many of the contraindications are unlikely in awake non-intubated patients who may be able to prone and then un-prone themselves either independently or with minimal assistance. During the current pandemic, where resource limitations have compromised the delivery of health care, this simple and inexpensive intervention, particularly when delivered in a standardized manner with appropriate patient selection and with dedicated proning teams and strict protocols for patient selection, may prove to be a safe and effective way to reduce the need for MV and perhaps reduce mortality as well.

One case report described the use of "supine chest compression" in two adults with severe ARDS in whom prone position could not be performed: a 34 year old man with polytrauma and a 45 year old man with maxillofacial injury and head injury (48). Supine chest compression was performed as an alternative to prone position by placing 2-kg weight (in the form of iron bars or water bags) on bilateral chest wall while the patients were in supine position as a new concept to compress the anterior chest wall. Both patients saw an improvement in $PaO_2/FiO_2$ within 6 hours of chest wall compression without major adverse effects and serious complications. The authors postulated that the impediment of the more compliant

ventral chest wall by chest compression technique would result in redistribution of ventilation in favor of the highly perfused dorsal area, hence increasing ventilation perfusion ratio, similar to the respiratory mechanics of prone position.

Supine chest compression might be an interesting alternative to prone position particularly during the COVID-19 pandemic as it may not require dedicated manpower or an increase in use of sedatives and paralysis, and has a potentially lower risk of adverse events like ventilator disconnection and endotracheal. Future clinical studies are needed to evaluate the clinical benefits and adverse effects of supine chest compression in patients with ARDS and also in subgroups such as the pediatric population and COVID-19 patients. There is an ongoing clinical trial evaluating the effects of supine chest compression on hemodynamics and respiratory parameters in patients with moderate to severe ARDS (49).

## Discussion

Since the start of the pandemic, prone position has gained importance as an adjunctive treatment modality which may not only improve short-term outcomes but also lessen the burden on health care resources by improving oxygenation and hence reducing or delaying the need for intubation. However, our systematic review revealed that there was a paucity of rigorous data on the potential efficacy of prone position in COVID-19 patients. As such, recommendations to utilize prone position in COVID-19 patients has been extrapolated from previous ARDS studies. Preliminary collective experience seems to suggest that prone position was associated with improvement in lung recruitability in prone position (25) as well as improved oxygenation (27-29, 32). No significant adverse events were reported with prone position in any of the studies. However, the level of evidence remains low: studies in our review had small sample sizes, were observational in design, and had no comparator groups. As such, there remains a gap in the current evidence for the use of prone position in COVID-19 patients, particularly in non-intubated patients as well as in relation to clinically significant outcomes such as need for intubation, mortality and duration of MV. For now, in COVID-19 patients who require MV and meet the criteria for ARDS (50), we recommend the use of prone position as per the Surviving Sepsis Campaign's and WHO guidelines (8) (9). In addition, in our opinion, given the current evidence, a trial of prone position, with close monitoring of clinical parameters, oxygenation and tolerance should be considered for awake, non-intubated COVID-19 patients with hypoxemic respiratory failure, as long as they can be appropriately rescued with intubation and MV if this trial fails as delay in intubation is in itself associated with increased mortality.(51)

COVID-19 disease has resulted in significant and unprecedented demands on healthcare systems around the world. As healthcare systems adapt to the pandemic, it would be timely to design and conduct both high-quality observational studies and RCTs that can elucidate the role of low-cost interventions such as prone position, in both intubated and non-intubated patients. At present there are at least 20 studies registered (https://clinicaltrials.gov) which aim to investigate the role of prone position in COVID-19. An intervention such as this is especially important to investigate as it is simple, does not require additional

costly equipment, and has the potential to help resource poor facilities to improve clinical outcomes and prevent mortality.

# Declarations

## Author Contributions

SKQ conducted the search of relevant databases for the systematic review. SKQ, PN, SWL, TSWT and CBL reviewed abstracts and full text for inclusion and performed data extraction for the systematic review. SKQ, HLT, SWL, TSWT, CBL and JHL drafted the manuscript. LJH and SKQ contributed to study conception and design, search strategy development, data analysis and revision of the manuscript. EF contributed to idea generation, revision of manuscript and feedback.

## Funding source

## Potential Conflicts of Interest

Dr. Fan has received personal fees from ALung Technolgies, Fresenius Medical Care, and MC3 Cardiopulmonary outside the submitted work. All other authors have no conflicts to declare

# References

1. WHO. Coronavirus disease (COVID-19) Situation Report - 195 2020 [Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200802-covid-19-sitrep-195.pdf?sfvrsn=5e5da0c5_2.
2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020.
3. Grasselli G, Pesenti A, Cecconi M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. JAMA. 2020.
4. Deng Y, Liu W, Liu K, Fang YY, Shang J, Zhou L, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study. Chin Med J (Engl). 2020.
5. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med. 2020.
6. Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. JAMA. 2020.
7. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine

Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med. 2017;195(9):1253-63.

8. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19). Crit Care Med. 2020.

9. World Health Organization, "Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance", [online] https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf Accessed 6th April 2020.

10. Johnson NJ, Luks AM, Glenny RW. Gas Exchange in the Prone Posture. Respir Care. 2017;62(8):1097-110.

11. Munshi L, Del Sorbo L, Adhikari NKJ, Hodgson CL, Wunsch H, Meade MO, et al. Prone Position for Acute Respiratory Distress Syndrome. A Systematic Review and Meta-Analysis. Ann Am Thorac Soc. 2017;14(Supplement_4):S280-S8.

12. Guérin C. Prone positioning acute respiratory distress syndrome patients. Ann Transl Med. 2017;5(14):289.

13. Scholten EL, Beitler JR, Prisk GK, Malhotra A. Treatment of ARDS With Prone Positioning. Chest. 2017;151(1):215-24.

14. Gattinoni L, Taccone P, Carlesso E, Marini JJ. Prone position in acute respiratory distress syndrome. Rationale, indications, and limits. Am J Respir Crit Care Med. 2013;188(11):1286-93.

15. Gattinoni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med. 2001;345(8):568-73.

16. Gattinoni L. et al. COVID-19 pneumonia: different respiratory treatment for different phenotypes? (2020) Intensive Care Medicine; DOI: 10.1007/s00134-020-06033-2.

17. Taccone P, Pesenti A, Latini R, Polli F, Vagginelli F, Mietto C, et al. Prone positioning in patients with moderate and severe acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2009;302(18):1977-84.

18. Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159-68.

19. Sud S, Friedrich JO, Adhikari NK, Taccone P, Mancebo J, Polli F, et al. Effect of prone positioning during mechanical ventilation on mortality among patients with acute respiratory distress syndrome: a systematic review and meta-analysis. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2014;186(10):E381-90.

20. Bloomfield R, Noble DW, Sudlow A. Prone position for acute respiratory failure in adults. Cochrane Database Syst Rev. 2015(11):Cd008095.

21. Matthay MA, Aldrich JM, Gotts JE. Treatment for severe acute respiratory distress syndrome from COVID-19. The Lancet Respiratory medicine. 2020.

22. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory medicine. 2020.

23. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(5):846-8.

24. Ruan Q, Yang K, Wang W, Jiang L, Song J. Correction to: Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med. 2020;46(6):1294-7.

25. Pan C, Chen L, Lu C, Zhang W, Xia JA, Sklar MC, et al. Lung Recruitability in COVID-19-associated Acute Respiratory Distress Syndrome: A Single-Center Observational Study. Am J Respir Crit Care Med. 2020;201(10):1294-7.

26. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020.

27. Elharrar X, Trigui Y, Dols AM, Touchon F, Martinez S, Prud'homme E, et al. Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure. JAMA. 2020.

28. Sartini C, Tresoldi M, Scarpellini P, Tettamanti A, Carcò F, Landoni G, et al. Respiratory Parameters in Patients With COVID-19 After Using Noninvasive Ventilation in the Prone Position Outside the Intensive Care Unit. JAMA. 2020.

29. Coppo A, Bellani G, Winterton D, Di Pierro M, Soria A, Faverio P, 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.

30. Wang K, Zhao W, Li J, Shu W, Duan J. The experience of high-flow nasal cannula in hospitalized patients with 2019 novel coronavirus-infected pneumonia in two hospitals of Chongqing, China. Ann Intensive Care. 2020;10(1):37.

31. Meng L, Qiu H, Wan L, Ai Y, Xue Z, Guo Q, et al. Intubation and Ventilation amid the COVID-19 Outbreak: Wuhan's Experience. Anesthesiology. 2020.

32. Thompson AE, Ranard BL, Wei Y, Jelic S. Prone Positioning in Awake, Nonintubated Patients With COVID-19 Hypoxemic Respiratory Failure. JAMA Intern Med. 2020.

33. Scaravilli V, Grasselli G, Castagna L, Zanella A, Isgrò S, Lucchini A, et al. Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: A retrospective study. J Crit Care. 2015;30(6):1390-4.

34. Ding L, Wang L, Ma W, He H. 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(1):28.

35. Feltracco P, Serra E, Barbieri S, Persona P, Rea F, Loy M, et al. Non-invasive ventilation in prone position for refractory hypoxemia after bilateral lung transplantation. Clin Transplant. 2009;23(5):748-50.

36. Feltracco P, Serra E, Barbieri S, Milevoj M, Michieletto E, Carollo C, et al. Noninvasive high-frequency percussive ventilation in the prone position after lung transplantation. Transplant Proc. 2012;44(7):2016-21.

37. Mora-Arteaga JA, Bernal-Ramírez OJ, Rodríguez SJ. The effects of prone position ventilation in patients with acute respiratory distress syndrome. A systematic review and metaanalysis. Med Intensiva. 2015;39(6):359-72.

38. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus Disease 2019 (COVID-19): A Systematic Review of Imaging Findings in 919 Patients. AJR Am J Roentgenol. 2020:1-7.

39. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.

40. Bai HX, Hsieh B, Xiong Z, Halsey K, Choi JW, Tran TML, et al. Performance of radiologists in differentiating COVID-19 from viral pneumonia on chest CT. Radiology. 2020:200823.

41. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis. 2020;20(4):425-34.

42. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. Radiology. 2020:200370.

43. Yun L, He HW, Moller K, Frerichs I, Liu D, Zhao Z. Assessment of Lung Recruitment by Electrical Impedance Tomography and Oxygenation in ARDS Patients. Medicine (Baltimore). 2016;95(22):e3820.

44. Putensen C, Wrigge H, Zinserling J. Electrical impedance tomography guided ventilation therapy. Curr Opin Crit Care. 2007;13(3):344-50.

45. Dirkes S, Dickinson S, Havey R, O'brien D. Prone positioning: is it safe and effective? Crit Care Nurs Q. 2012;35(1):64-75.

46. Bamford P, Denmade C, Newmarch C, Shirley P, Singer B, Webb S, et al. Guidance for: Prone Positioning in Adult Critical Care 2019 [Available from: https://www.ficm.ac.uk/sites/default/files/prone_position_in_adult_critical_care_2019.pdf.

47. Oliveira VM, Piekala DM, Deponti GN, Batista DCR, Minossi SD, Chisté M, et al. Safe prone checklist: construction and implementation of a tool for performing the prone maneuver. Rev Bras Ter Intensiva. 2017;29(2):131-41.

48. Samanta S, Soni KD. Supine chest compression: alternative to prone ventilation in acute respiratory distress syndrome. Am J Emerg Med. 2014;32(5):489.e5-6.

49. ClinicalTrials.gov [Internet]. Antonelli (MD): National Library of Medicine (US). 2020 Jan - . Identifier NCT03719937, ArtificiaL Increase in chesT Wall Elastance as an alteRnative to PRONE Positioning in Moderate-to-severe ARDS: a Physiological Study The ALTERPRONE Study . Available from: https://clinicaltrials.gov/ct2/show/record/NCT03719937?view=record.

50. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307(23):2526-33.

51. Kangelaris KN, Ware LB, Wang CY, Janz DR, Zhuo H, Matthay MA, et al. Timing of Intubation and Clinical Outcomes in Adults With Acute Respiratory Distress Syndrome. Crit Care Med. 2016;44(1):120-9.

# Tables

Table 1: Included studies that described prone position in patients with COVID-19, clinical characteristics and outcomes of patients

| Author Date of Publication Sample size (n) | Study outcomes | Age | Respiratory support | | | ECMO[a] | Prone position | Mortality (Overall) | Mortality (Prone) |
|---|---|---|---|---|---|---|---|---|---|
| | | mean (SD[b]) | HFNC[c] n (%) | NIV[d] n (%) | MV[e] n (%) | n (%) | n (%) | (n, %) | n |
| Yang et al 21st Feb 2020 n = 51 | Primary: 28-day mortality Secondary: need for MV, ARDS[f], shock | 59.7 (13.3) | 33 (63) | 29 (55) | 22 (42) | 6 (12) | 6 (12) | 32 (62) | NA[g] |
| Ruan et al 3rd March 2020 n = 150 | Clinical predictors of outcomes in mild and severe disease | 57.7 (NA) | 41 (27) | 51 (34) | 25 (17) | 7 (5) | 3 (2) | 68 (45) | 3 |
| Pan et al 23rd March 2020 n = 12 | Respiratory mechanics | 59 (9) | 9 (75) | | 9 (75) | 3 (25) | 7 (58) | 3 (25) | 1 |
| Grasselli et al 6th April 2020 n = 1591 | Clinical response in first 6-24 hours following ICU[h] admission | 63 (56-70) * | 0 | 137 (9) | 1150 (72) | 5 (0.3) | 240 (15) | 405 (25) | NA |
| Elharrar et al 15th May 2020 n = 24 | Primary: proportion of responders (PaO$_2$ increase ≥20% between before and during PP[i]) Secondary: PaO$_2$[j], PaCO$_2$[k], variation before, during and after; feasibility, tolerance, persistent responders | 66.1 (10.2) | 19 (79) | 0 | 5 (20) | 0 | 24 (100) | 0 | 0 |
| Sartini et al 15th May 2020 n = 15 | Respiratory parameters Other: 14-day outcomes (discharged, still treated with prone or intubated) | 59 (6.5) | 0 | 15 (100) | 0 | 0 | 15 (100) | 1 (7) | 1 |
| Coppo et al 19th June 2020 n = 56 | Primary: Variation in oxygenation PaO$_2$/FiO$_2$[l] between baseline and resupination Secondary: safety and feasibility of prone position | 57.4 (7.4) | NA | 44 (79%) | 0 | 0 | 56 (100) | 5 (9) | 5 |

Abbreviations: [a]ECMO extracorporeal membrane oxygenation; [b]standard deviation, [c]high frequency nasal cannula; [d]non-invasive ventilation; [e]mechanical ventilation; [f]acute respiratory distress syndrome; [g]not available; [h]intensive care unit prone position; [i]prone position; [j]PaO$_2$ (partial pressure of oxygen); [k]PaO$_2$ (partial pressure of carbon dioxide); [l]fractional concentration of oxygen in inspired air                    *Median (interquartile range).
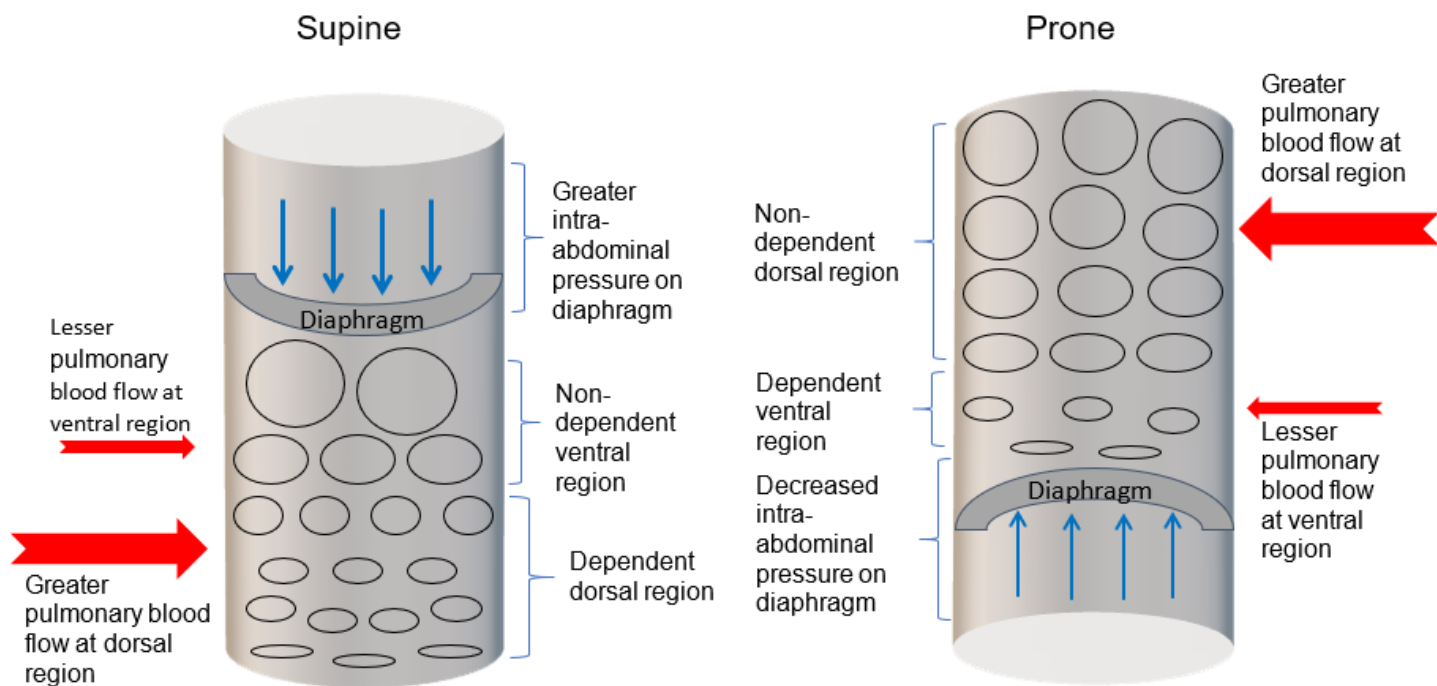
# Figures

**Figure 1**

Schematic showing the changes in ventilation and perfusion in supine and prone position
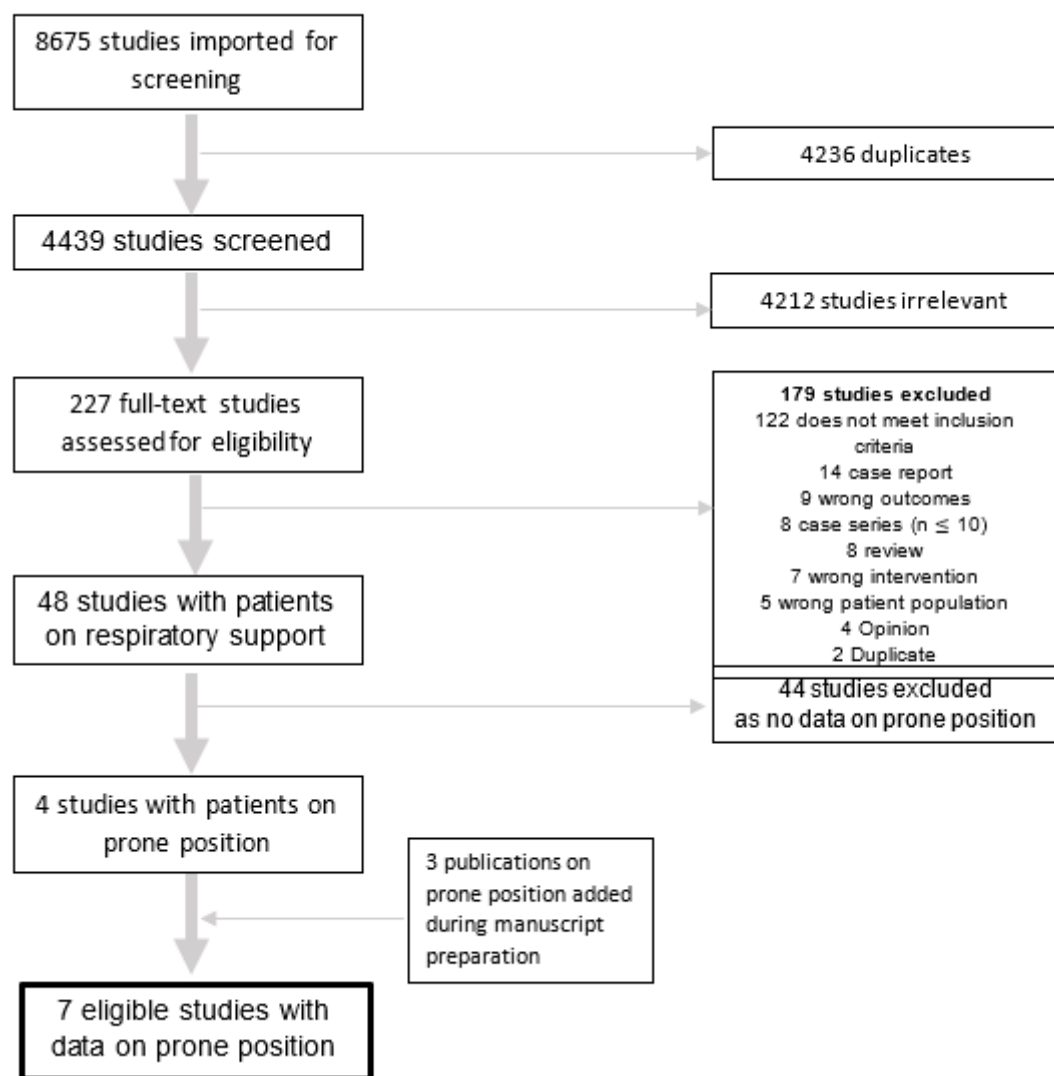
**Figure 2**

Study Selection for Systematic Review of Prone Position in COVID-19 patients