# EVIDENCE SUMMARY

## Should side lying position be used in patients with severe to critical COVID-19?

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## Should self-proning be used in non-intubated patients with severe COVID-19?

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## RECOMMENDATIONS

**We suggest self-proning position in non-intubated patients with severe and critical COVID-19** (*Very low certainty of evidence; Weak recommendation)*

*Consensus Issues*
Self-proning in non-intubated patients with severe and critical COVID-19 was suggested despite the lack of significant benefit in terms of mortality, need for endotracheal intubation, and need for intensive care unit stay on the basis that self-proning may still offer some benefit on improving oxygenation citing theoretical effect and personal experience, and taking into consideration the existing recommendations made by various international guidelines as well.

**There is insufficient evidence to recommend the use of side lying in non-intubated patients with severe and critical COVID-19** *(Very low certainty of evidence)*

*Consensus Issues*

There was very limited evidence to recommend side lying for the same subset of patients, although it was recognized that there may be some benefit. This intervention will depend on the physician's prerogative in situations where self-proning is not possible. Potential harm such as patient discomfort and risk of accidental removal of peripheral lines and endotracheal tubes and the need for additional healthcare workers to perform proning in sedated and mechanically ventilated patients should be considered for both patient and health care worker in attempting this intervention.

## PREVIOUS RECOMMENDATION

We suggest self proning to improve oxygenation status of non-intubated hospitalized patients with COVID-19 infection requiring oxygen supplementation. *(Very low quality of evidence; Conditional recommendation)*

*Previous Consensus Issues*
Self-proning is recommended for patients with COVID-19 infection who are not qualified to be intubated. Based on the studies, self proning has no impact on mortality and intubation.

## What's new in this version?

- As of September 20, 2021, 4 new randomized controlled trials (RCTs) were available for review to evaluate proning in COVID-19 patients.
- Recommendation for proning is maintained based on very low quality of evidence with a conditional recommendation.

## Key Findings

Among non-intubated severe patients with COVID 19 with oxygen saturation of at least 90% and oxygen requirement of less than 6 liters per minute, pooled results of 4 randomized controlled trials showed no difference in the duration of proning and outcomes such as mortality, need for intubation and the need for intensive care.

A case series of five patients with COVID-19 associated ARDS showed that side lying accompanied with Positive End Expiratory Pressure (PEEP) titration provided a statistically significant benefit by decreasing the incidence of overdistension and lung collapse. Adverse events were not reported.

The certainty of evidence for both side lying and proning are very low due to serious risk of bias, substantial heterogeneity and imprecision.

## Introduction

Positioning maneuvers such as proning and side lying have been proven to provide benefit in patients with Acute Respiratory Distress Syndrome (ARDS).[1] However, whether these benefits extend to patients with severe to critical COVID-19 is still under clinical investigation. Proning position results in improvement in ventilation-perfusion mismatching in patients with ARDS. Despite studies explaining the proposed pathophysiologic basis for COVID ARDS (CARDS) such as intravascular thrombosis and loss of lung perfusion regulation, retrospective studies have provided some evidence of benefit for positioning maneuvers in severe and critical patients.[2-4]

## Review Methods

A comprehensive literature search was done (date of last search: September 20, 2021) for the 2 clinical questions using Medline, Cochrane Library, Google Scholar and clinicaltrials.gov with the following keywords: "lateral positioning", "side lying" "lateral decubitus", "proning", "prone positioning" "prone position" and "COVID-19" "SARS-COV2". All studies that resulted from the search were reviewed and appraised. Randomized controlled trials and available meta-analysis relating to side lying and proning were included.

## Results

**Proning**

A total of 34 RCTs were screened and evaluated at the time of the search. Of these, only four RCTS (Rosen et al., Kharat et al., Jayakumar et al., and Taylor et al.)[6-9] were found to have completed and published results on proning and COVID-19 while the other 30 RCTs were still in the process of recruitment, final manuscript review or publishing. There were no RCTs available for the use of proning in intubated COVID-19 patients.

Patients included in the studies were adults greater than 18 years old, diagnosed with COVID-19, admitted in the ICU [8] and medical wards [6,7,9], with oxygen saturation of at least 90% [7-9] and oxygen requirement of <6 liters per minute.[7-9] Exclusion criteria were similar among all studies which included pregnant women, patients who were unable to perform proning, those with hemodynamic instability and those who were in need of immediate intubation.

Different protocols on proning were used in the included studies and ranged from 6 to 48 hours. The study of Taylor et al., Kharat et al. and Jayakumar et al. instructed patients on how to perform self-proning (not specified) and were advised to undergo proning for at least 48 hours, 12 hours and 6 hours respectively. On the other hand, the study by Rosen et al. provided illustrations and instructed patients to do self-proning for at least 16 hours. All four studies had assigned teams of nurses and physicians for evaluation and monitoring of patients with no mention of self-monitoring. Similar outcomes were identified such as need for intensive care, mortality and need for intubation. The study of Jayakumar et al. provided data on the effect of proning on oxygenation by measuring the PaO2/FiO2 ratio after 2 hours, which was found to be statistically not significant (p value=0.3). Other outcomes such as change in PaO2, change in SpO2 and change in ROX index were not evident in the studies.

*Need for intubation*

Three randomized controlled trials [6,8,9] with very low evidence have been evaluated in terms of patients needing intubation. The study of Rosen et al. reported their primary outcome of patients on proning needing intubation at 33% while rates taken from Taylor et al. and Jayakumar et al. were at 0 and 20% respectively. A subgroup analysis was done based on duration of proning, which showed no difference between patients who underwent self-proning for 16 hours or more (RR 1.0, 95% CI 0.53-1.90) and those who underwent self-proning for less than 6 hours (RR 1.0, 95% CI 0.56-1.77*).*

*Mortality*

Three studies evaluated mortality as an outcome in patients who underwent proning. The studies of Rosen et al., Taylor et al. and Jayakumar et al. reported a mortality rate of 17%, 0% and 10% respectively. On subgroup analysis, there were no significant differences in mortality for patients who did self-proning for 16 hours or more (RR 2.17, 95% CI 0.58-8.03) and self-proning for 6 hours or less (RR 1.50, 95% CI 0.27-8.34).

*Need for Intensive Care*

All of the four RCTS evaluated the effect of proning and the need for intensive care. Two studies (Rosen et al. and Taylor et al.) who had proning for >16 hours had rates of 75% and 29% respectively while patients who underwent proning for <12 hours (Jayakumar et al. and Kharat et al.) had rate of 13% and 10% respectively. Results from both subgroups with different durations of proning (>16 hours RR 0.96, 95% CI 0.61-1.51 and <12 hours RR 1.58, 95% CI 0.98-2.54) showed no significant difference in the patient's need for intensive care.

**Side Lying**

A total of six studies were screened to review the evidence of side lying in COVID-19. Of the six studies, two were excluded due to the unavailability of outcomes and three were RCTS that were on the process of recruiting participants. The identified and available study was a case series published in 2021 which included five patients on mechanical ventilation.[5] Patients included in the study were adults aged 44-85 years old with COVID-19 associated ARDS, who were mechanically ventilated, sedated, and paralyzed. Lung overdistension and collapse were evaluated using Electrical Impedance Tomography (EIT) accompanied with Positive End Expiratory Pressure (PEEP) titration in 5 patients, initially on supine followed by side lying, as determined by the more aerated lung which would then be positioned down. Lung overdistension and collapse were measured before and after positioning (supine to targeted lateral position) with decremental PEEP titration. Results from this study revealed a statistically significant effect of decreasing overdistension accompanied with PEEP titration in the right lung ($p < 0.0005$) when in side lying and prevention of lung collapse in the left lung [at PEEP 14 ($p = 0.034$), at PEEP 10 ($p = 0.028$), at PEEP 8 ($p = 0.019$), and at PEEP 6 cmH2O ($p = 0.007$)]. No statistical significance was observed in right lung collapse and left lung overdistension. There was no data available for outcomes on mortality, Intensive Care Unit (ICU) admission, initiation of anti-inflammatory treatment and length of hospital stay.

## Evidence to Decision

There is still scarce data on the use of proning and side lying in the management of severe to critical COVID-19 patients. Retrospective cohort studies and other RCTS would recommend these maneuvers but some are still uncertain on its benefit on management.

One of the most common disadvantages of doing proning position especially in intubated patients is the need for a team of health workers to carefully position patients into proning, taking into consideration the discomfort and the risk of removing peripheral lines and tubes.[10, 11]

## Recommendations from Other Groups

Four guidelines on the management of COVID-19 were identified. Their recommendations are summarized in the table below.

| Group/Society/Network | Year | Recommendation | Level of Evidence/Strength of Recommendation |
|---|---|---|---|
| American Thoracic Society [12] | 2020 | For patients with refractory hypoxemia due to progressive COVID-19 pneumonia (ARDS), we suggest prone ventilation | Conditional Recommendation |
| World Health Organization [13] | 2021 | We suggest awake prone positioning of severely ill patients hospitalized with COVID-19 requiring supplemental oxygen (includes high-flow nasal oxygen) or non-invasive ventilation (conditional, low certainty evidence). | Conditional Recommendation |

| | | | |
|---|---|---|---|
| European Respiratory Society [14] | 2021 | Prone positioning may improve oxygenation in non-intubated patient with acute hypoxemic respiratory failure and is widely used for mechanically ventilated patients with COVID-19. | Very Low Conditional Recommendation |
| National Institutes of Health [15] | 2021 | For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, the Panel recommends considering a trial of awake prone positioning to improve oxygenation | CIIa |
| | | The Panel recommends against using awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation | AIII |
| | | For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, the Panel recommends prone ventilation for 12 to 16 hours per day over no prone ventilation | BIIa |

## Research Gaps

There is still limited data on the use of proning and side lying in the management of severe to critical COVID -19 patients. As of now, RCTS are in the process of recruitment and data collection and may further contribute to provide evidence in the management of COVID-19.

## References

[1] Griffiths MJD, McAuley DF, Perkins GD, Barrett N, Blackwood B, Boyle A, et al. Guidelines on the management of acute respiratory distress syndrome. BMJ Open Respir Res. 2019;6(1).

[2] Adeola JO, Patel S, Goné EN, Tewfik G. A Quick Review on the Multisystem Effects of Prone Position in Acute Respiratory Distress Syndrome (ARDS) Including COVID-19. Clin Med Insights Circ Respir Pulm Med. 2021;15.

[3] Attaway AH, Scheraga RG, Bhimraj A, Biehl M, Hatipoğ Lu U. Severe covid-19 pneumonia: Pathogenesis and clinical management. BMJ. 2021;372.

[4] Schifino G, de Grauw AJ, Daniele F, Comellini V, Fasano L, Pisani L. Effects of prone and lateral position in non-intubated patients with 2019 Novel Coronavirus (COVID-19) pneumonia. Pulmonology. 2021;27(2):167–71.

[5] Mlček M, Otáhal M, Borges JB, Alcala GC, Hladík D, Kuriščák E, et al. Targeted lateral positioning decreases lung collapse and overdistension in COVID-19-associated ARDS.

BMC Pulm Med [Internet]. 2021;21(1):1–7. Available from: https://doi.org/10.1186/s12890-021-01501-x

[6] Rosén J, von Oelreich E, Fors D, Jonsson Fagerlund M, Taxbro K, Skorup P, et al. Awake prone positioning in patients with hypoxemic respiratory failure due to COVID-19: the PROFLO multicenter randomized clinical trial. Ann Am Thorac Soc [Internet]. 2021;7(1):00692–2020. Available from: http://dx.doi.org/10.1183/23120541.00692-2020

[7] Kharat A, Dupuis-Lozeron E, Cantero C, Marti C, Grosgurin O, Lolachi S, et al. Self-proning in COVID-19 patients on low-flow oxygen therapy: a cluster randomised controlled trial. ERJ Open Res [Internet]. 2021;7(1):00692–2020. Available from: http://dx.doi.org/10.1183/23120541.00692-2020

[8] Jayakumar D, Ramachandran, DNB P, Rabindrarajan, DNB E, Vijayaraghavan, MD BKT, Ramakrishnan, AB N, Venkataraman, AB R. Standard Care Versus Awake Prone Position in Adult Nonintubated Patients With Acute Hypoxemic Respiratory Failure Secondary to COVID-19 Infection—A Multicenter Feasibility Randomized Controlled Trial. J Intensive Care Med. 2021;36(8):918–24.

[9] Taylor SP, Bundy H, Smith WM, Skavroneck S, Taylor B, Kowalkowski MA. Awake prone positioning strategy for nonintubated hypoxic patients with covid-19 a pilot trial with embedded implementation evaluation. Ann Am Thorac Soc. 2021;18(8):1360–8.

[10] Ghelichkhani P, Esmaeili M. Prone Position in Management of COVID-19 Patients; a Commentary. Arch Acad Emerg Med. 2020;8(1):1–3.

[11] Shelhamer MC, Wesson PD, Solari IL, Jensen DL, Steele WA, Dimitrov VG, et al. Prone Positioning in Moderate to Severe Acute Respiratory Distress Syndrome Due to COVID-19: A Cohort Study and Analysis of Physiology. J Intensive Care Med. 2021;36(2):241–52.

[12] Wilson KC, Chotirmall SH, Bai C, Rello J. COVID-19: Interim Guidance on Management Pending Empirical Evidence. Am Thorac Soc Int Task Force [Internet]. 2020;1–12. Available from: www.thoracic.org/professionals/clinical ‐ %0Aresources/disease ‐ related ‐ resources/covid ‐ 19 ‐ %0Aguidance.pdf

[13] WHO. Clinical management Clinical management Living guidance COVID-19. World Heal Organ. 2021;(January):16–44.

[14] Chalmers JD, Crichton ML, Goeminne PC, Cao B, Humbert M, Shteinberg M, et al. Management of hospitalised adults with coronavirus disease 2019 (COVID-19): A European respiratory society living guideline. Eur Respir J. 2021;57(4).

[15] COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Disponible en: https://covid19treatmentguidelines.nih.gov/. Natl Inst Heal [Internet]. 2020;2019:130. Available from: https://www.covid19treatmentguidelines.nih.gov/

# Appendix 1. Evidence to Decision

Table 1. Summary of initial judgements prior to the panel discussion: side lying, proning (N = 8)

| FACTORS | JUDGEMENT | | | | | RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS |
|---|---|---|---|---|---|---|
| **Problem** | No | Yes (8) | | | | • Despite studies explaining the proposed pathophysiologic basis for COVID ARDS (CARDS) such as intravascular thrombosis and loss of lung perfusion regulation, retrospective studies have provided some evidence of benefit in severe and critical patients |
| **Benefits** | Large (3) | Moderate (1) | Small (2) | Uncertain (2) | | • One observational study provided a significant decrease in overdistension and lung collapse in mechanically ventilated patients accompanied with PEEP titration.<br>• Proning: no significant difference in terms of need of intubation, need for intensive care and mortality regardless of duration of proning |
| **Harm** | Large | Small (8) | Uncertain | | | • Reported adverse effects during proning: pressure ulcers, vomiting and cardiac arrest.<br>• Other harms observed in studies were removal of peripheral lines and possible removal of the endotracheal tube in intubated patients. |
| **Certainty of Evidence** | High | Moderate (2) | Low (2) | Very low (4) | | |
| **Balance of effects** | Favors drug (4) | Does not favor drug (1) | Uncertain (3) | | | • There were no significant difference in terms of need of intubation, mortality and need for intensive care in COVID-19 patients who underwent proning. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Values** | Important uncertainty or variability (1) | Possibly important uncertainty or variability (3) | Possibly NO important uncertainty or variability (3) | No important uncertainty or variability (1) | | | |
| **Resources Required** | Uncertain (3) | Large cost (1) | Moderate Cost (2) | Negligible cost (2) | Moderate savings | Large savings | |
| **Certainty of evidence of required resources** | No included studies (4) | Very low (1) | Low (2) | Moderate (1) | High | | |
| **Cost effectiveness** | No included studies (3) | Favors the comparison | Does not favor either the intervention or the comparison | Favors the intervention (5) | | | |
| **Equity** | Uncertain (3) | Reduced | Probably no impact (3) | Increased (2) | | | |
| **Acceptability** | Uncertain (1) | No | Yes (7) | | | | |
| **Feasibility** | Uncertain (1) | No | Yes (7) | | | | |

# Appendix 2. Search Yield and Results

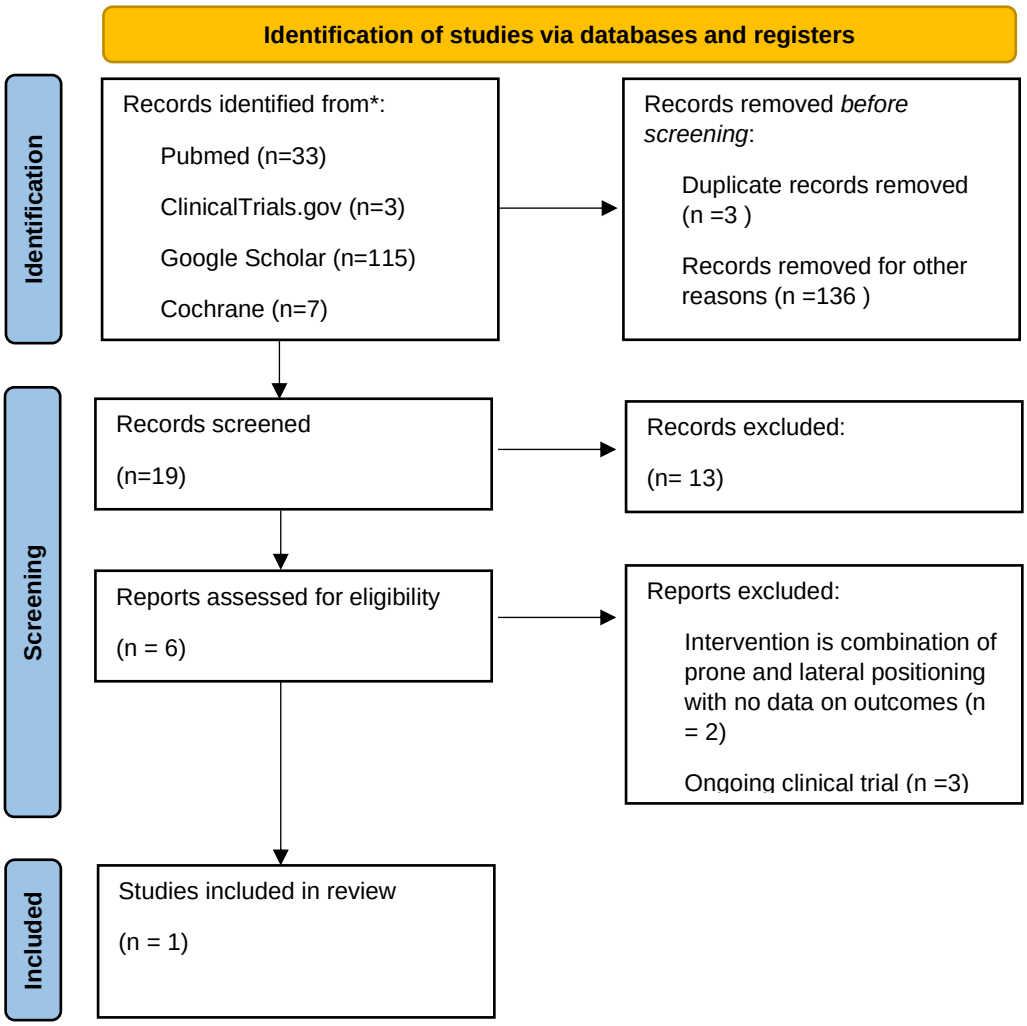


Figure 1: PRISMA flow diagram of Search Yield results for side lying

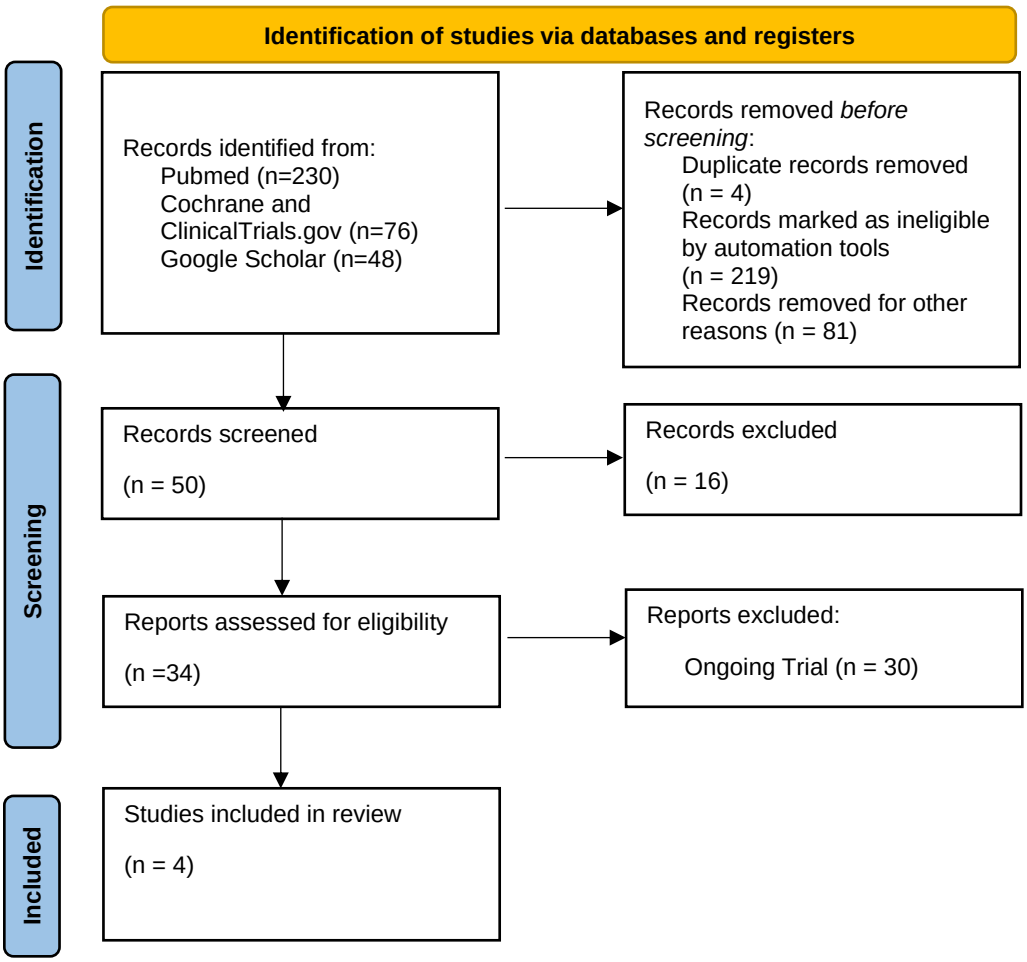


Figure 2: PRISMA flow diagram of Search Yield results for proning

Table 2. Detailed search strategy for side lying

| # | Query | Results |
|---|---|---|
| | Pubmed | |
| 1 | ((lateral positioning) OR (lateral decubitus positioning)) OR (side lying) | 39,946 |
| 2 | ((("COVID-19" [Supplementary Concept] OR "COVID-19 diagnostic testing" [Supplementary Concept] OR "COVID-19 drug treatment" [Supplementary Concept] OR "COVID-19 serotherapy" [Supplementary Concept] OR "COVID-19 vaccine" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept] OR "2019-nCoV" OR "2019nCoV" OR "cov 2" OR "Covid-19" OR "sars coronavirus 2" OR "sars cov 2" OR "SARS-CoV-2" OR "severe acute respiratory syndrome coronavirus 2" OR "coronavirus 2" OR "COVID 19" OR "COVID-19" OR "2019 ncov" OR "2019nCoV" OR "corona virus disease 2019" OR "cov2" OR "COVID-19" OR "COVID19" OR "nCov 2019" OR "nCoV" OR "new corona virus" OR "new coronaviruses" OR "novel corona virus" OR "novel coronaviruses" OR "SARS Coronavirus 2" OR "SARS2" OR "SARS-COV-2" OR "Severe Acute Respiratory Syndrome Coronavirus 2") OR ((19[tiab] OR 2019[tiab] OR "2019-nCoV" OR "Beijing" OR "China" OR "Covid-19" OR epidem*[tiab] OR epidemic* OR epidemy OR new[tiab] OR "novel"[tiab] OR "outbreak" OR pandem* OR "SARS-CoV-2" OR "Shanghai" OR "Wuhan") AND ("Coronavirus Infections"[Mesh] OR "coronavirus"[MeSH Terms] OR coronavirus*[all] OR corona-virus*[all] OR cov[tiab] OR pneumonia-virus*[tiab]))) AND 2019/12/1:3000/12/31[PDAT]) | 176,657 |
| 3 | randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh]) | 4,520,121 |
| 4 | (((systematic review[ti] OR systematic literature review[ti] OR systematic scoping review[ti] OR systematic narrative review[ti] OR systematic qualitative review[ti] OR systematic evidence review[ti] OR systematic quantitative review[ti] OR systematic meta-review[ti] OR systematic critical review[ti] OR systematic mixed studies review[ti] OR systematic mapping review[ti] OR systematic cochrane review[ti] OR systematic search and review[ti] OR systematic integrative review[ti]) NOT comment[pt] NOT (protocol[ti] OR protocols[ti])) NOT MEDLINE [subset]) OR (Cochrane Database Syst Rev[ta] AND review[pt]) OR systematic review[pt] | 202,510 |
| 5 | #1 AND #2 | 33 |
| 6 | #1 AND #2 AND (#3 OR #4) | 4 |
| | COCHRANE | |
| 1 | ((lateral positioning) OR (lateral decubitus positioning)) OR (side lying) | 1444 |
| 2 | COVID-19 OR SARS-COV2 OR nCOV-2019 OR Coronavirus OR Coronavirus of 2019 | 7401 |
| 3 | (randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR drug therapy OR randomly OR trial OR groups) | 1538615 |
| 4 | (((systematic review OR systematic literature review OR systematic scoping review OR systematic narrative review OR systematic qualitative review OR systematic evidence review OR systematic quantitative review OR systematic meta-review OR | 33327 |

| | | |
|---|---|---|
| | systematic critical review OR systematic mixed studies review OR systematic mapping review OR systematic cochrane review OR systematic search and review OR systematic integrative review) NOT comment NOT (protocol OR protocols)) NOT MEDLINE) OR (Cochrane Database Syst Rev AND review) OR systematic review | |
| 5 | #1 AND #2 | 7 |
| 6 | #5 AND (#3 OR #4) | 7 (2 cochrane reviews, 5 trials) |
| Clinical trials.gov | | |
| 1 | COVID 19 AND lateral positioning AND trials | 3 |
| Google Scholar | | |
| 1 | Allintitle: positioning AND COVID | 115 |

Table 3. Detailed search strategy for proning

| # | Query | Results |
|---|---|---|
| Pubmed | | |
| 1 | ((prone positioning) OR (proning)) OR (proning position) OR (prone) | 85,169 |
| 2 | ((("COVID-19" [Supplementary Concept] OR "COVID-19 diagnostic testing" [Supplementary Concept] OR "COVID-19 drug treatment" [Supplementary Concept] OR "COVID-19 serotherapy" [Supplementary Concept] OR "COVID-19 vaccine" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept] OR "2019-nCoV" OR "2019nCoV" OR "cov 2" OR "Covid-19" OR "sars coronavirus 2" OR "sars cov 2" OR "SARS-CoV-2" OR "severe acute respiratory syndrome coronavirus 2" OR "coronavirus 2" OR "COVID 19" OR "COVID-19" OR "2019 ncov" OR "2019nCoV" OR "corona virus disease 2019" OR "cov2" OR "COVID-19" OR "COVID19" OR "nCov 2019" OR "nCoV" OR "new corona virus" OR "new coronaviruses" OR "novel corona virus" OR "novel coronaviruses" OR "SARS Coronavirus 2" OR "SARS2" OR "SARS-COV-2" OR "Severe Acute Respiratory Syndrome Coronavirus 2") OR ((19[tiab] OR 2019[tiab] OR "2019-nCoV" OR "Beijing" OR "China" OR "Covid-19" OR epidem*[tiab] OR epidemic* OR epidemy OR new[tiab] OR "novel"[tiab] OR "outbreak" OR pandem* OR "SARS-CoV-2" OR "Shanghai" OR "Wuhan") AND ("Coronavirus Infections"[Mesh] OR "coronavirus"[MeSH Terms] OR coronavirus*[all] OR corona-virus*[all] OR cov[tiab] OR pneumonia-virus*[tiab]))) AND 2019/12/1:3000/12/31[PDAT]) | 176,657 |
| 3 | randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh]) | 4,520,121 |
| 4 | (((systematic review[ti] OR systematic literature review[ti] OR systematic scoping review[ti] OR systematic narrative review[ti] OR systematic qualitative review[ti] OR systematic evidence review[ti] OR systematic quantitative review[ti] OR systematic meta-review[ti] OR systematic critical review[ti] OR systematic mixed studies review[ti] OR systematic mapping review[ti] OR systematic cochrane review[ti] OR systematic search and review[ti] OR systematic integrative review[ti]) NOT comment[pt] NOT (protocol[ti] OR protocols[ti])) NOT MEDLINE [subset]) OR (Cochrane Database Syst Rev[ta] AND review[pt]) OR systematic | 202,510 |

| | | |
|---|---|---|
| | review[pt] | |
| 5 | #1 AND #2 | 1,332 |
| 6 | #1 AND #2 WITH filter (Clinical Trial, Randomized Controlled Trial) | 11 |
| COCHRANE | | |
| 1 | ((prone positioning) OR (proning)) OR (proning position) OR (prone) | 1,974 |
| 2 | COVID-19 OR SARS-COV2 OR nCOV-2019 OR Coronavirus OR Coronavirus of 2019 | 7401 |
| 3 | #1 AND #2 | 74 (5 Cochrane Reviews, 69 Trials) Cross Referenced with Clinicaltrials.gov* |
| Google Scholar | | |
| 1 | allintitle: prone OR proning OR prone positioning OR prone position AND COVID | 48 |

# Appendix 3. Characteristics of Included Studies

Table 4. Study Characteristics of Included Studies for Side Lying (n=1)

| Study ID Title Author | Study Design | Setting/Country | Total number of Patients Included | Population | Intervention | Comparator/Control | Outcomes |
|---|---|---|---|---|---|---|---|
| Targeted lateral positioning decreases lung collapse and overdistension in COVID-19-associated ARDS<br><br>Micek 2021 | Prospective observational study | Brazil | 5 | Patients with COVID-19 associated ARDS in the first days of mechanical ventilation<br><br>ARDS by Berlin Criteria | Targeted lateral position<br><br>defined by selecting the less aerated lung to be positioned up and the more aerated lung to be positioned down. During all the procedures, the patients were deeply sedated and under muscle paralysis | | Regional overdistension and collapse |

Table 5. Study Characteristics of Included Studies for Proning (n=4)

| Study ID Title Author | Study Design | Setting/Country | Total number of Patients Included | Population | Intervention | Comparator/Control | Outcomes |
|---|---|---|---|---|---|---|---|

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Awake prone positioning in patients with hypoxemic respiratory failure due to COVID-19: the PROFLO multicenter randomized clinical trial<br><br>Rosen et.al 2021 | prospective multicenter, open-label, parallel arm, randomized clinical superiority trial | Sweden | 75 | Adults ≥ 18 years old<br>- SARS-CoV-2 reverse transcription polymerase chain reaction tests on naso- or oropharyngeal swabs<br>- hypoxemic respiratory failure,<br>-HFNO or NIV for respiratory support<br>- PaO2/FiO2-ratio ≤ 20 kPa or corresponding values of SpO2 and FiO2 | at least 16h Awake Prone Positioning (APP) per day Prone and semi-prone posi- tioning was allowed During in-hospital transportation, oxygenation by face mask and positioning appropriate for adequate monitoring and safety was allowed | APP was not encouraged but could be prescribed by the attending clinician at his/her discretion. | Primary outcome<br>- intubation within 30 days after enrollment<br><br>secondary outcome<br>- duration of APP use of NIV<br>- time of NIV for patients included with HFNO<br><br>- use of vasopressors/inotropes<br><br>- CRRT,ECMO<br>- Ventrilator-free days<br>- Days free of NIV/HFNO for patients not intubation<br>- Hospital and ICU length of stay<br>- 30 day mortality<br>- WHO ordinal scale for clinical improvement at day 7, 30<br>- Adverse events |
| Self-proning in COVID-19 patients on low-flow oxygen therapy: a cluster randomized controlled trial | Single-centre cluster randomized controlled trial | Geneva, Switzerland | 27 | patients aged ⩾18 years<br><br>on low-flow oxygen therapy (defined as 1–6 L·min−1) through nasal cannulas to obtain a SpO2 | self-proning for 12 h per day as an addition to usual care for 24 h | Usual care consisted of<br>1) oxygen titration with nasal cannula according to our institutional recommendations to target SpO2 values between 90% and 94%. | The pre-specified **primary outcome** was oxygen needs assessed by nasal cannula oxygen flow at 24 h.<br><br>**Secondary outcomes** were the SpO2/FiO2 ratio (defined as SpO2 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Kharat et. Al 2021 | | | | level of 90–92%. | | | percentage divided by the FiO2) at 24 h<br><br>respiratory and heart rate at 24 h,<br><br>patient trajectory (transfer to critical care unit)<br><br>potential intervention-related adverse effects as defined by neck pain,<br><br>position-related discomfort and gastroesophageal reflux |
| Standard Care Versus Awake Prone Position in Adult Nonintubated Patients with Acute Hypoxemic Respiratory Failure Secondary to COVID-19 Infection—A Multicenter Feasibility Randomized Controlled Trial<br><br>Jayakumar et.al, 2021 | Multicenter feasibility randomized controlled trial | India | 60 | 18 years of age and requiring 4 or more liters per minute (LPM) of supplemental oxygen to maintainSpO2 92%<br><br>PaO2/FiO2 ratio between 100 and 300 mmHg (mild to moderate ARDS) with PaCO2 <45mmHg<br><br>Patients with AHRF and | lie prone for a minimum of 6 hours in a day (cumulative) | Patients randomized to standard care were allowed to change their position as per their comfort (supine, semi sitting, sitting or lateral).<br><br>If patients in the standard arm wished to lie prone for comfort, this was allowed. | primary outcome measure<br>proportion of patients adhering to the protocol in each group<br><br>Secondary outcomes<br>proportion of patients requiring escalation of respiratory support in either group<br><br>number of hours prone and maximum hours of continuous prone positioning in a day<br><br>length of stay in the ICU<br><br>ICU mortality |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Hemodynamic hemodynamic shock requiring <0.1mcg/kg/min of norepinephrine were also considered for inclusion. | | | adverse events<br><br>reasons for not lying prone |
| Awake prone positioning strategy for non-intubated Hypoxic Patients with COVID-19: A pilot trial with embedded implementation evaluation<br><br>Taylor, et. al 2021 | Pragmatic, two-arm parallel cluster RCT and a qualitative study | North Carolina, USA | 40 | positive for SARS-CoV-2 within 7 days or were suspected to have COVID-19 pneumonia,<br><br>room air oxygen saturation,93% or<br><br>oxygen requirement of 3 liters per minute or greater without the need for mechanical ventilation. | Awake Prone Positioning Strategy (APPS)<br><br>Patients were encouraged to sustain the prone position as long as possible but were allowed to return to the supine position as necessary | Usual Care | the primary outcome<br><br>establish outcomes relative to successful implementation of a future definitive RCT.<br><br>Specific research outcomes<br>nadir oxygen saturation to fraction of inspired oxygen (S/F) ratio<br><br>time spent with S/F ratio less than 315<br><br>receipt of intensive care, greater than 6 L/min<br><br>oxygen support<br><br>intubation<br><br>hospital length of stay<br><br>hospital mortality |

# Appendix 4. Study Appraisal

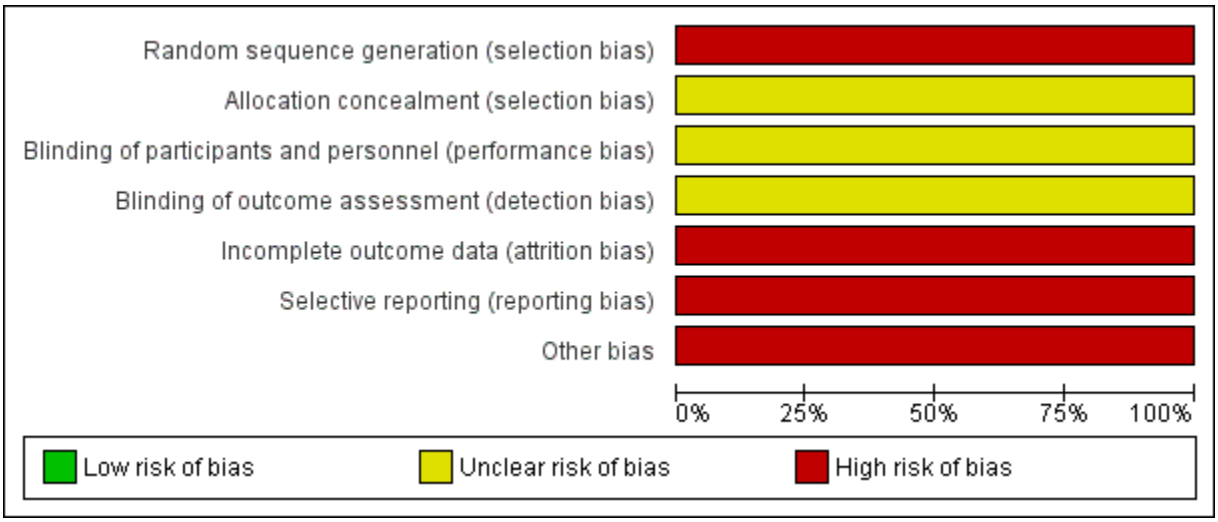


Figure 3. Risk of Bias (Micek et. al 2021) in side lying in patients with severe to critical COVID 19

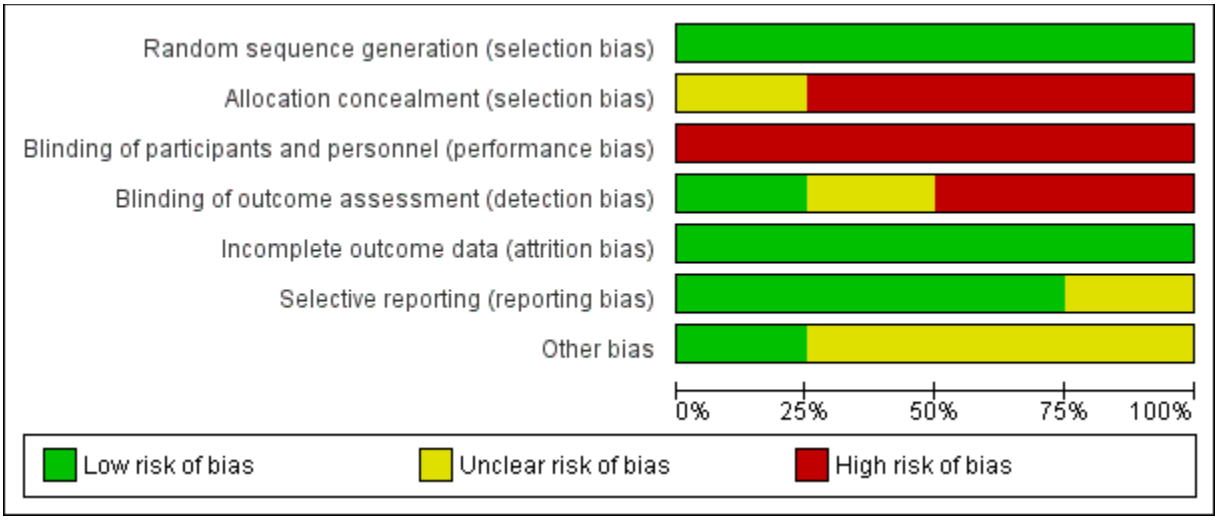


Figure 4. Risk of Bias (Rosen et. al, Taylor et. al, Kharat et. al, Jayakunar et. al 2021) in proning in non inubated severe patients with COVID -19

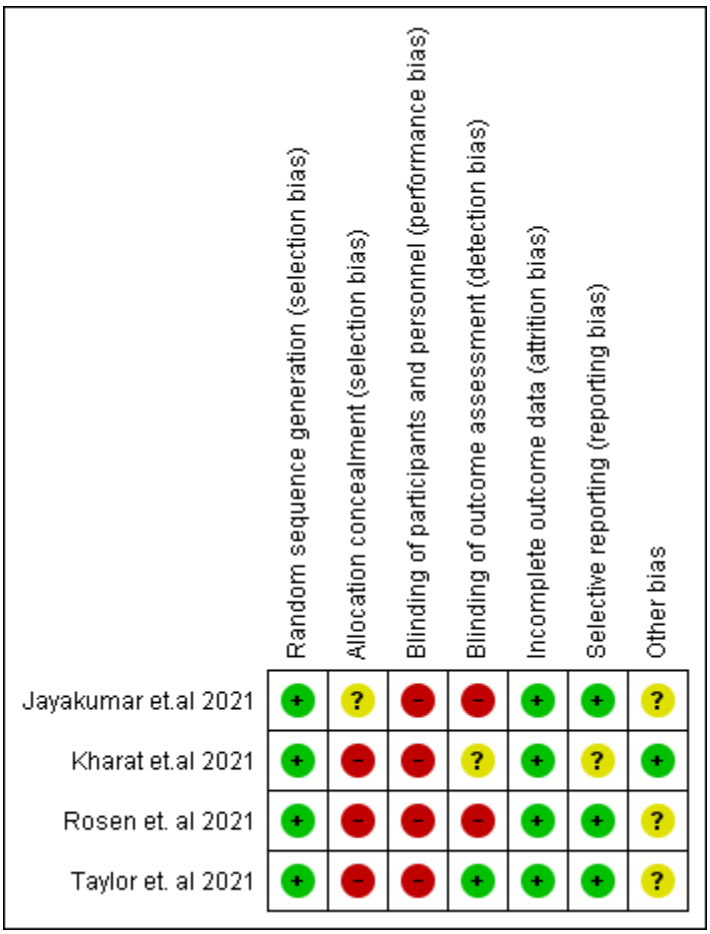


Figure 5. Risk of Bias Summary of included studies for proning

# Appendix 5. GRADE Evidence Profile

Table 6. GRADE Evidence Profile for side lying

| Certainty assessment | | | | | | | Impact | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | | | |
| **Regional overdistension** | | | | | | | | | |
| 1 | observational studies | serious [a] | very serious [b] | not serious | very serious [c] | none | There was a marginal two-way interaction between position and PEEP (p= 0.073). The main effect of position showed a statistically significant difference in the % of overdistension within the right lung: less overdistension along the PEEP titration in targeted lateral (right down) than supine position (p=0.005) there was no statistically significant differences for position and overdistension of the left lung | ⨁◯◯◯ VERY LOW | CRITICAL |
| **Lung Collapse** | | | | | | | | | |
| 1 | observational studies | serious [a] | very serious [b] | not serious | very serious [c] | none | There was a statistically significant two-way interaction between position and PEEP (p=0.014) in the percent of collapse within the left lung: less collapse along the PEEP titration was found within the left lung in targeted lateral (right down) than supine position there was no statistically significant differences for right lung collapse on lateral position | ⨁◯◯◯ VERY LOW | CRITICAL |

**Explanations**

a. inadequate control of confounding factors
b. effect size was not available
c. total population was only at 5

Table 7. GRADE Evidence Profile for proning

| Certainty assessment | | | | | | | № of patients | | Effect | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Prone positioning | supine positioning | Relative (95% CI) | Absolute (95% CI) | Certainty | Importance |
| **Mortality** | | | | | | | | | | | | |
| 3 | randomized trials | serious [a] | serious [b] | serious [c] | serious [d] | none | 9/93 (9.7%) | 41/82 (50.0%) | **RR 1.89** (0.67 to 5.36) | **445 more per 1,000** (from 165 fewer to 1,000 more) | ⨁◯◯◯ VERY LOW | |
| **Need for Intensive Care** | | | | | | | | | | | | |
| 4 | randomized trials | serious [a] | serious [b] | serious [c] | serious [d] | none | 56/103 (54.4%) | 46/99 (46.5%) | **RR 1.14** (0.81 to 1.62) | **65 more per 1,000** (from 88 fewer to 288 more) | ⨁◯◯◯ VERY LOW | |
| **Need for intubation** | | | | | | | | | | | | |
| 3 | randomized trials | serious [a] | serious [b] | serious [c] | serious [d] | none | 16/93 (17.2%) | 17/82 (20.7%) | **RR 1.00** (0.56 to 1.77) | **0 fewer per 1,000** (from 91 fewer to 160 more) | ⨁◯◯◯ VERY LOW | |

**Explanations**

a. personnel and outcome assessors were not blinded
b. downgrade by 1 due to substantial heterogeneity
c. no reported outcomes on Change in PF RATIO, PaO2, SpO2 and ROX index
d. downgraded due to a wide confidence interval

## Appendix 6. Forest Plots

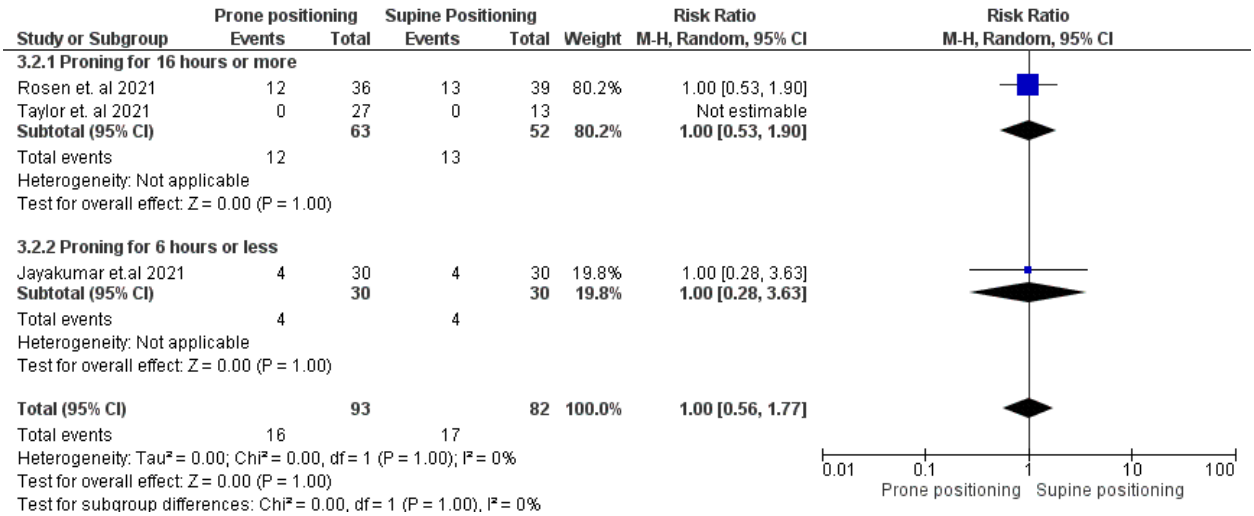


Figure 6. Forest Plot on the outcome of proning and need for intubation

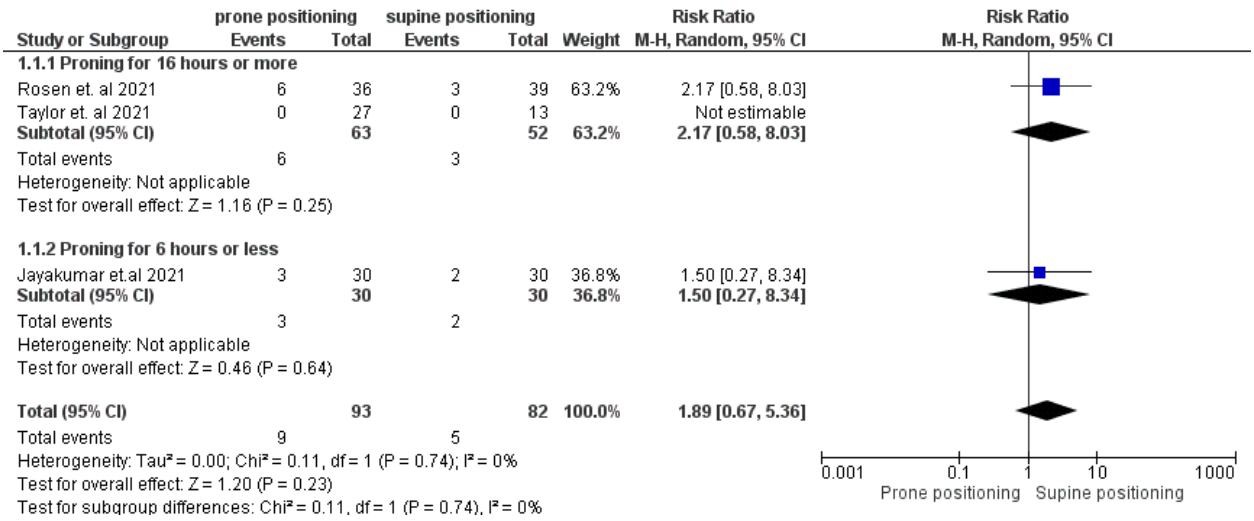


Figure 7. Forest plot on the outcome of proning and mortality

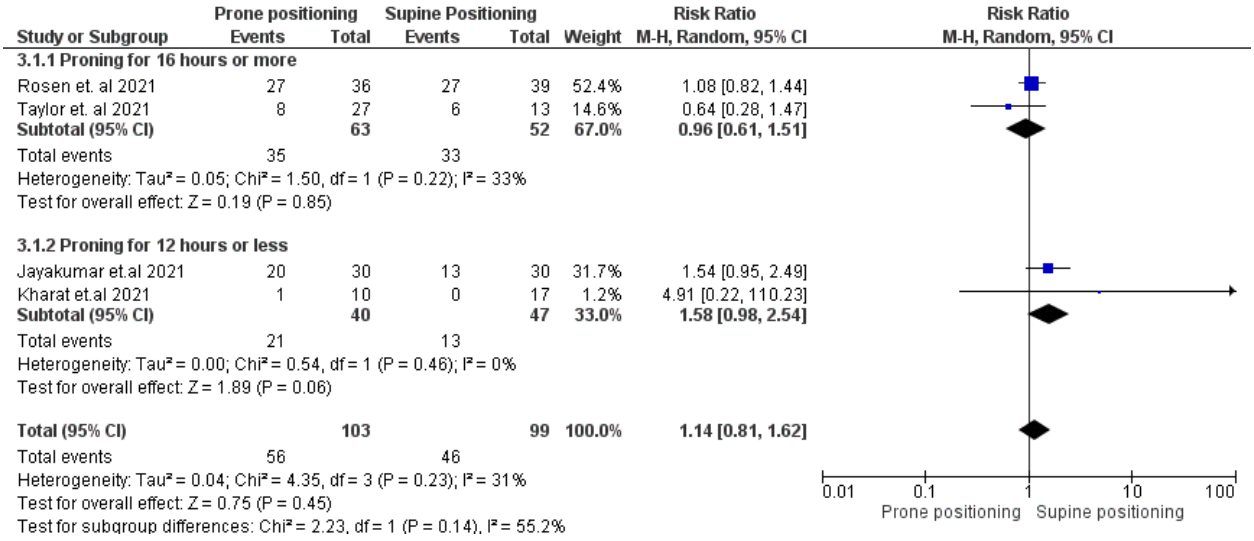


Figure 8. Forest Plot on the outcome of proning and need for intensive care

# Appendix 7. Characteristics of Ongoing Studies

Table 8: Study Characteristics of Ongoing studies for side lying (n=3)

| Title<br>Identifier<br>Expected Completion Date | Intervention | Comparator/Control | Patients/Population Recruited | Outcomes |
|---|---|---|---|---|
| Immediate effect of prone and side lying position on oxygen saturation in patients with COVID 19- A Randomised Controlled Trial<br><br>Main ID:<br>CTRI/2021/03/031939 | Prone position after doing Diaphragmatic breathing exercises, thoracic expansion exercise<br><br>Lateral Position after doing Diaphragmatic breathing exercises, thoracic expansion exercise patients will adopt the position (supine) after breathing exercises for 1 hour.<br>Frequency - 1 session per day<br>The patient's face could be placed on either side and patients were allowed to adjust their position for comfort. | Supine Position after doing Diaphragmatic breathing exercises, thoracic expansion exercise and patients will adopt the position (supine) after breathing exercises for 1 hour.<br><br>Frequency - 1 session per day | NOT YET RECRUITING<br><br>Patients who required additional oxygen supplementation (HFNC)<br><br>Age group of >30 years both male and female | Spo2Timepoint: 1 hour |
| Awake Prone Position Versus Repeated Position Change in Moderate to Severe COVID-19 patients: A Pilot Randomized Controlled Trial<br><br>Main ID:<br>CTRI/2020/07/026532 | Repeated Position Change: One hour right lateral, two hours prone and one hour left lateral | Awake Prone Positioning: Awake Prone Positioning for 4h in patients presented with shortness of breath | NOT YET RECRUITING<br><br>Adult patients (aged between 18 and 75y) with laboratory confirmed diagnosis of COVID-19 pneumonia,<br><br>self-reported symptom of shortness of breath patients, | Primary Outcome<br>compare repeated positioning with 4h continuous prone positioning in terms of self-reported dyspnea in a 10-point visual analogue scale<br>Time point: 4hour since randomization<br><br>Secondary Outcome<br>oxygenation status (room air oxyhemoglobin |

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| | | | | saturation or PaO2/FiO2 ratio in arterial blood gas)<br><br>requirement of rescue therapy (high flow nasal oxygen) in both the groups.<br><br>hemodynamic variables in both the groups.<br><br>requirement of mechanical ventilation within 24h in both the groups.<br><br>the change in respiratory rate in both the groups.<br><br>Timepoint: 4 hour since randomization<br>Secondary ID(s) |
| NCT04475068<br><br>Feasibility and Physiological Effects of a Postural Recruitment Maneuver in Patients With Acute Respiratory Distress Syndrome Due to COVID-19 Infection | Lateral Position (left and right lateral decubitus)<br><br>patients will be sedated deeply with sedatives and opioids and paralyzed.<br><br>Patients will be evaluated in 5 positions sequentially: 1) Supine 2) Left lateral 3) Supine 4) Right lateral 5) Supine.<br><br>Each step will last 30 minutes.<br><br>Aeration measured by Electric Impedance Tomography (EIT) and lung ultrasound, distribution of the lung ventilation and perfusion measured by EIT, ventilator and hemodynamic parameters, esophageal pressure, and | | Patients > 18 years of age<br><br>Patients with moderate-to-severe ARDS as per the Berlin definition<br><br>Infection due to COVID-19<br><br>Body mass index (BMI) ≤ 35 kg /m^2.<br>Exclusion Criteria: | Effects of a postural recruitment maneuver in lung aeration<br><br>Lung aeration measured by ultrasound reaeration score, ranges from 0 (all regions are well aerated) to 36 (all regions are consolidated).<br><br>Effects of a postural recruitment maneuver in distribution of ventilation<br><br>Distribution of ventilation measured by EIT (distribution and changes in the impedance in AU, arbitray units)<br><br>Effects of a postural recruitment maneuver in gas exchange |

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| | blood gas analysis will be recorded at the end of each step. Continuous monitoring of blood pressure, heart rate and saturation of arterial blood (SpO2) will be carried out during all steps of the protocol to assess the tolerance to the procedure. | | | Gas exchange measured by blood gas analysis (PaO2, PaCO2, in mmHg) and capnography (end-tidal CO2, in mmHg)<br><br>Effects of a postural recruitment maneuver in respiratory mechanics<br><br>Respiratory mechanics measured by esophageal balloon (esophageal pressure, transpulmonary pressure, in cmH2O)<br><br>Effects of a postural recruitment maneuver in hemodynamic<br><br>Hemodynamic data measured by invasive arterial monitoring (mean arterial pressure, in mmHg)<br><br>Secondary outcome<br>Feasibility of a postural recruitment maneuver<br><br>Oxygenatory tolerance evaluated with pulse oximeter (arterial oxygen saturation, in percentage) |

Table 9. Study characteristics of ongoing studies for proning (n=30)

| Title<br>Identifier<br>Expected Completion Date | Intervention | Comparator/Control | Patients/Population Recruited | Outcomes |
|---|---|---|---|---|
| NCT04424797<br><br>Prone Positioning on Admission for Hospitalized COVID-19 Pneumonia Protocol | The Prone Experimental Group will position patient in approximately 15-degree reverse trendelenburg and | The Standard Supine Control Group will utilize standard oxygen (O2) device in supine position at approximately 30-60 degrees to target | Patients >18 years old and above<br><br>Patients admitted to the hospital floor with primary diagnosis of confirmed COVID-19 pneumonia and respiratory failure requiring | Primary Outcome<br>Incidence of intubation<br><br>Secondary Outcome<br>Maximum oxygen |

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| Estimated completion date<br>July 31, 2022 | prone using pillows for comfort. The participant will be asked to rotate to prone positioning every 2 hours while awake and encourage to sleep prone overnight as possible with a goal of 10-12 hours daily. | peripheral capillary oxygen saturation (SpO2) >90% and the participant or nurse will document time in non-supine position. | greater than or equal to 2 Liters(L) Nasal Cannula (NC) to maintain SpO2>90%<br><br>Ability to independently change positions in bed<br><br>Able to tolerate prone positioning | Measure of maximum oxygen requirements<br><br>Length of Stay<br>Measured in days of hospitalization<br><br>Ventilator-free days<br>Measured in days not on a ventilator<br><br>Treatment failure of prone positioning due to worsening SpO2 status while prone<br><br>Whether or not the participant met treatment failure descriptions<br><br>Mortality Whether or not the participant died while hospitalized |
| ACTRN12620000740998<br><br>A Randomised Controlled Trial of Early Prone Positioning to Improve Oxygenation in Non-Intubated Adults Admitted to Intensive Care with COVID-19<br><br>Estimated completion date: no data<br><br>Not yet recruiting | lying prone for up to 12 hours a day in a prone position<br><br>no minimum time been period of proning and no restriction on participants positioning outside of the 'intervention' periods.<br><br>If this duration is not tolerated for an individual patient, staff will trial a variety of comfort measures<br><br>The intervention will continue for 72 hours (a maximum of 36 hours prone). | | Adults, over the age of 18<br><br>COVID-19 Diagnosis Confirmed – either by PCR or as per any unit policy changes that may be applied during the enrolment period<br><br>Admitted to Intensive Care<br><br>Any severity of disease (As defined by National COVID 19 Clinical Evidence Taskforce "Australian Guidelines for the clinical care of people with COVID-19" assessable at https://covid19evidence.net.au ).<br><br>For patients with severe disease, the treating intensivist must be consulted prior to randomisation (see exclusion criterion #2) | Primary Outcome<br>Oxygen Saturations in the blood<br><br>difference in average gradient of the PaO2:FiO2 (PF ratio) in the prone and control groups over the trial period (72 hours).<br><br>Calculate by pulse oximetry recordings and oxygen delivery method<br><br>Secondary Outcome(s)<br>Median number of hours spent prone per day during trial period in the intervention group<br><br>Number of adverse events in the prone group compared to |

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| | If a participant is unable to tolerate a 12h/day prone position as above<br><br>Step 1 - Trial 3 x 3hr sessions/9 hours a day<br>Step 2 - If needing longer breaks not prone - Trial 2 x 4hr sessions/8 hours a day<br>Step 3 - Trial 2 x 3hr sessions/6 hours a day<br>Step 4 - 3 x 2 hour sessions/6 hours a day<br>Step 5 - 2 x 2 hours sessions/4 hours a day<br>Step 6 - Abandon proning, document in EMR why proning was abandoned | | Willing and able to tolerate prone positioning (A pre-enrollment screening test to ensure they can tolerate the position and can maneuver into & out of the prone position with minimal assistance from their usual care staff only. )<br><br>Prior informed consent has been obtained from the patient | control, as collected by staff survey, and any other incidence of adverse events brought to the attention of investigators. |
| CTRI/2020/06/025804<br><br>Effectiveness of awake self proning strategy in COVID-19: An open-labelled randomized controlled trial<br><br>Not yet recruiting | :The COVID-19 patient will be asked to be in prone position and its effect on improvement of their blood oxygenation will be seen using a finger saturation probe. | The COVID-19 patient will be lying supine or sitting and its effect on improvement of blood oxygenation will be seen using a finger saturation probe | >18 years of age<br><br>Diagnosed as COVID-19 positive by RT- PCR<br><br>Oxygen saturation < 94% as assessed by pulse oximeter or requiring oxygen support<br><br>Can communicate and self-prone | Primary outcomes (Phase 1 study):<br><br>Oxygen saturation measured using by pulse oximeter at 0, 10, 20, 30, 40 minutes<br><br>Primary Outcomes (Phase 2 study):<br><br>Need for endotracheal intubation and mechanical ventilation measured at discharge or death<br><br>Mortality up to 30 days after enrolment<br><br>Oxygen saturation measured using by pulse oximeter at 0, 10, 20, 30, 40 minutes<br><br>Primary Outcomes (Phase 2 study): |

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| | | | | Need for endotracheal intubation and mechanical ventilation measured at discharge or death<br><br>Mortality up to 30 days after enrolment<br><br>Secondary Outcome<br>For phase 2 study:<br><br>Phase 2 study:<br><br>Time to endotracheal intubation/ventilation measured using hospital record at discharge.<br><br>Duration of requirement of oxygen support measured using clinical proforma at patient discharge<br><br>Duration of hospital stay measured using using hospital record at discharge |
| CTRI/2020/12/029587<br><br>Efficacy of awake prone positioning with high flow nasal cannula versus prone positioning with non-rebreathing mask in COVID-19 patients. A prospective comparative study.<br><br>Not yet recruiting | Awake prone position with high flow nasal cannula: Oxygen will be given through high flow nasal oxygen at flows of 60 L/min and FiO2 adjusted to obtain oxygenation (SpO2 â?¥92%).<br><br>A minimum of 8 hours of prone positioning per day shall be encouraged. | Awake prone positioning with non-rebreathing mask: Patient will receive high flow oxygen@10 to 15 liter/min with non-rebreathing mask to maintain adequate oxygenation ((SpO2 â?¥92%).<br><br>All patients shall be encouraged prone positioning in this group also | Adult Confirmed COIVD19 positive patients admitted to ICU for acute hypoxemic respiratory failure.<br><br>Acute hypoxemic respiratory failure defined by respiratory rate â?¥25 breaths/min, and PaO2/FiO2 â?¤300 mm Hg while spontaneously breathing under standard oxygen therapy. | Primary Outcome<br>rates of intubation between the two groups at 28 days<br><br>Secondary Outcome<br>arterial oxygen partial pressures after 1 hour, 6 hours, 12 hours and then every 24 hours after enrolment.<br><br>intubation free ICU stay of patients.<br><br>percentage of patients who required non-invasive ventilation at 28 days |

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| NCT04547283<br><br>Awake-Prone Positioning Strategy for Hypoxic Patients With COVID-19: A Pilot Randomized Controlled Trial<br><br>COMPLETED<br>Not yet published<br>No results | Clinical team guidance on prone positioning of patients | No clinical team recommendation, patients will remain in their natural choice of position | 18 Years old and above<br><br>hospitalized patients with positive COVID testing during hospitalization or 7 days prior OR Hospitalized with suspected COVID pneumonia<br>room air oxygen saturation <93% or oxygen requirement > or equal to 3 Liters per minute | Primary Outcome Measures:<br>Average S/F ratio<br><br>Average oxygen saturation to fraction of inspired oxygen ratio<br><br>Time spent with S/F ratio < 315<br><br>Time spent with oxygenation saturation to fraction of inspired oxygen ratio less than 315<br><br>Secondary Outcome Measures<br>Highest oxygen support<br><br>Highest level of supplemental oxygen required<br><br>Number of patients requiring ICU admission during study<br><br>Number of patients requiring ICU admission during study period<br><br>Number of patients requiring ICU admission during hospitalization<br><br>Number of patients requiring ICU admission during hospitalization<br><br>Number of patients experiencing who die prior to discharge<br><br>Number of patients who die prior to hospital discharge |

| | | | | |
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| | | | | Number of patients requiring intubation<br><br>Number of patients requiring intubation<br><br>Hospital length of stay<br><br>Number of days from hospital admission to discharge |
| NCT04359797<br><br>Pragmatic Trial Exploring Impact of Patient Positioning in the Management of Patients Infected With COVID-19: Supine vs. Prone<br><br>COMPLETED<br>Not yet published<br>No results | prone position for as much time as is tolerable during hospitalization. | remain in their natural choice of position, which is anticipated to favor a supine, semi-recumbent position. | 18 years old and above<br><br>patients admitted to VUMC who test positive for COVID-19 and require supplemental oxygen, but are not yet mechanically ventilated. | Primary Outcome Measures: Modified WHO Ordinal Scale<br><br>The highest level of support on the 5th day after enrollment according to the following scale adjusted for patient status at enrollment according to the same scale and ranked by mean FIO2 within each category, as appropriate.<br><br>Death<br><br>ECMO<br><br>Mechanical ventilation (ranked by mean FIO2)<br><br>Non-invasive ventilation such as BiPAP (ranked by mean FIO2)<br><br>High flow nasal cannula,<br><br>Standard nasal cannula (titrated by L/min up to 15 L/min) or face mask (ranked by mean FIO2)<br>Room air |

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| | | | | Secondary Outcome Measures<br>FIO2 |
| NCT04350723<br><br>Awake Prone Position in Hypoxemic Patients With Coronavirus Disease 19 (COVI-PRONE): A Randomized Clinical Trial (COVI-PRONE)<br><br>Recruiting | The oxygen mask or NIPPV or HFNC will be initiated at the treating team's discretion. The patient will be observed for 15 minutes to ensure that: SPO2 > 90% and the patient is tolerating oxygen mask or NIPPV or HFNC treatment.<br><br>Proning once SPO2 >90%<br><br>Procedure: Awake Proning<br>The duration of proning will be a total of 8-10 hours with 1-2 hours break in supine position. | The patient will receive usual care without proning at the discretion of the treating team.<br><br>The oxygen mask or NIPPV or HFNC will be initiated, the choice of starting oxygen mask versus NIPPV versus HFNC will be up to the treating team | Adults ≥ 18 years of age.<br><br>Suspected or confirmed COVID-19.<br><br>Hypoxemia on room air (SPO2<90%), and oxygen requirement ≥ 0.4 FiO2 (i.e. ≥ 40% oxygen).<br><br>Bilateral or unilateral chest infiltrates on x-ray as interpreted by the treating team.<br><br>Admitted to the ICU or an acute care bed where hemodynamic and respiratory monitoring is feasible. | Primary Outcome Measures:<br>Endotracheal intubation<br><br>Secondary Outcome Measures:<br>Mortality<br><br>Invasive mechanical ventilation free days<br><br>Non-invasive ventilation free days<br><br>ICU length of stay<br><br>Hospital length of stay<br><br>Change in oxygenation<br><br>Complications from proning, |
| NCT04395144<br><br>Randomized-controlled Trial of HFNC Alone vs HFNC and Awake Self-proning for Treatment of Severe COVID-19<br><br>Completed<br>Not yet published<br>No results | Prone positioning of patients on nasal high-flow oxygen therapy<br><br>Procedure: Awake Prone Positioning<br>Patients will receive instruction to remain in prone position as long and as often as possible, up to 16h/24h | Standard decubitus positioning of patients on nasal high-flow oxygen therapy<br><br>Patients will not receive any special instructions with regards to proning. | COVID-19, either confirmed by SARS-CoV-2 assay, or clinically suspected, with results of the assay pending;<br><br>Lung infiltrates documented on chest X-ray or chest CT-scan;<br>Significant respiratory distress that requires treatment with HFNO. | Primary Outcome Measures:<br>Rate of Therapeutic failure, defined as a combined outcome of rate of intubation or death<br><br>Secondary Outcome Measures:<br>Intubation rate<br><br>Mortality<br><br>Days spent on mechanical ventilation<br><br>Days spent in the ICU<br><br>Hospital stay (in days) |

| | | | | |
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| | | | | Other Outcome Measures: Time in prone position<br><br>Total time spent in prone position, as recorded by nursing or respiratory therapists<br><br>Oxygenation (SpO2/FiO2 ratio)<br><br>Daily evolution of oxygenation |
| CTRI/2020/12/029898<br><br>Self-prone positioning to reduce the need for ventilatory support in COVID-19 patients- a randomized controlled trial<br><br>Not yet recruiting | The intervention group (group P) will be instructed to lie prone for a session of at least two hours and a total duration of 12 hours in a day. | The control group participants will receive the conventional treatment for COVID-19 | Suspected (presenting with dyspnea, fever, cough) or confirmed COVID-19 positive having SpO2 â?¥90% with FiO2 â?¤0.6. | Primary Outcome Requirement of ventilatory support<br><br>Secondary Outcome oxygen requirement, oxygen saturation, requirement of ICU admission, duration of hospital stay and adverse effects of prone position. |
| CTRI/2021/03/031939<br><br>Immediate effect of prone and side lying position on oxygen saturation in patients with COVID 19- A Randomised Controlled Trial<br><br>Not yet recruiting | Prone position after doing Diaphragmatic breathing exercises, thoracic expansion exercise<br><br>Lateral Position after doing Diaphragmatic breathing exercises, thoracic expansion exercise:<br><br>Frequency - 1 session per day | Supine Position after doing Diaphragmatic breathing exercises, thoracic expansion exercise:<br><br>Frequency - 1 session per day | Both male& female patients with covid 19.<br><br>Patients who are willing to participate in the study.<br><br>Patients with definite diagnosis of COVID-19<br><br>Patients who required additional oxygen supplementation (HFNC)<br><br>Age group of >30 years both male and female | Primary Outcome Spo2Timepoint: 1 hour |
| CTRI/2020/07/026532<br><br>Awake Prone Position Versus Repeated Position Change in Moderate to Severe COVID-19 | Repeated Position Change: One hour right lateral, two hours prone and one hour left lateral | Awake Prone Positioning for 4h in patients presented with shortness of breath | Adult patients (aged between 18 and 75y) with laboratory confirmed diagnosis of COVID-19 pneumonia, | Primary Outcome repeated positioning with 4h continuous prone positioning in terms of self-reported |

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| patients: A Pilot Randomized Controlled Trial<br><br>Not yet recruiting | | | | dyspnea in a 10- point visual analogue scale<br><br>Secondary Outcome oxygenation status (room air oxyhemoglobin saturation or PaO2/FiO2 ratio in arterial blood gas)<br><br>requirement of rescue therapy (high flow nasal oxygen) in both the groups.<br><br>hemodynamic variables in both the groups.<br><br>requirement of mechanical ventilation within 24h in both the groups.<br><br>change in respiratory rate in both the groups. |
| NCT04760561<br><br>Effects of Self-prone Positioning on Oxygenation and Physiological Outcomes Among Awake Non-intubated Patients With COVID-19<br><br>Not yet recruiting | Each patient in the intervention group will be helped into the prone position and encouraged to stay in the prone position as long as tolerated (at least 1 hour).<br><br>Self-prone position will be performed 45 minutes up to 1 hour after meals to avoid gastrointestinal side effects.<br><br>The patient will be maintained in prone position until the patient becomes too tired and | conventional positioning interventions provided by the critical care nurses, which will not include self-prone positioning. | Aged 18-75 years old<br><br>Awake non-intubated spontaneously breathing patients<br><br>Confirmed diagnosis of severe COVID-19; manifesting as dyspnea with respiratory rate ≥ 30 breaths/min, pulse rate ≥ 100 beats/min, oxygen saturation ≤93%, or partial pressure of arterial oxygen (PaO2) to fraction of inspired oxygen (FiO2) ratio ≤ 150 mmHg.<br><br>Positive RT-PCR for SARS-CoV-2 from analysis of nasopharyngeal, oropharyngeal swab, or tracheal secretion specimens and with chest X-ray showing bilateral infiltrations or chest computerized tomographic (CT) images showing exudation or consolidation. | Primary Outcome Measures: Oxygenation<br><br>arterial oxygen pressure/fractional inspired oxygen PaO2/FiO2 ratio mmHg.<br><br>SpO2<br><br>Peripheral oxygen saturation<br><br>ROX<br><br>combination of the ratio of oxygen saturation measured by pulse oximetry to fraction of inspired oxygen and respiratory rate ([SpO2/FiO2]/respiratory rate)<br><br>PaO2mmHg |

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| | uncomfortable to keep that position. | | Requiring supplemental oxygen (nasal cannula, non-invasive CPAP, non-rebreathing face mask)<br><br>Capable of adopting a prone posture independently. | Partial pressure of oxygen within arterial blood<br><br>PCO2mmHg<br><br>The partial pressure of carbon dioxide within arterial blood<br><br>SaO2<br>pH<br>Respiratory Rate (RR) (bpm)<br>Heart Rate (HR) (bpm)<br>Blood Pressure (BP) mmHg<br><br>Positive response to prone<br><br>Secondary Outcome Measures:<br>Prone position adverse events<br><br>respiratory distress, dyspnea, use of accessory respiratory muscles, oxygen desaturation SpO2≤70%, hypotension SBP≤90 mmHg, vomiting, aspiration, musculoskeletal pain, discomfort, facial edema, pressure ulcers and accidental withdrawal of catheters, tubes and/or drainages. |
| NCT04391140<br><br>Effectiveness of Prone Positioning Combined With High-flow Nasal Cannula for Patients With COVID-19 Induced ARDS<br><br>Recruiting | Combination of prone position and HFNC<br><br>HFNC set to a SpO2 of 90-95% combined with prone position. At least 2 sessions of 30 minutes or more will be performed daily. | HFNC set for a SpO2 90-95% if unless indication for intubation is present. | COVID-19 pneumonia according to the diagnostic criteria in effect at the time of inclusion or very strongly suspected.<br><br>Patient treated by nasal high flow. Moderate or severe ARDS:<br><br>Informed consent. | Primary Outcome Measures :<br>Therapeutic failure death or intubation<br><br>Secondary Outcome Measures:<br>Feasibility and safety of prone position in HFNC patients |

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| | | | | Comfort measurement using a visual-analog scale.<br><br>Presence of complications related with prone position and the use of high-flow nasal cannula:<br><br>Skin ulcers.<br>Intravascular lines displacement<br>HFNC related events (hot air feeling, nasal lesions)<br><br>Efficacy of prone position in HFNC patients<br><br>Evolution of the oxygenation (SpO2/FiO2) in prone position.<br>Efficacy<br><br>Length of HFNC therapy<br>Length of ICU stay<br>Length of mechanical ventilation (in those who require intubation)<br>ICU and hospital mortality |
| IRCT20160126026217N4<br><br>Investigation of the effects of prone position on respiratory status, hemodynamics, hospital stay and transfer to intensive care unit in patients with Covid-19: A randomized controlled clinical trial<br><br>Pending Recruiting Status | In this group, participants will be in the prone position for 90 minutes for the first time. After evaluating the initial outcomes, the participant will be asked to be in the prone position for 6 to 8 hours until the clearance time, and then the secondary outcomes will be evaluated. | In this group, participants will be in their usual position for 90 minutes for the first time, after evaluating the initial outcomes, the participant will be asked to be in his usual positions until the time of discharge, and then the secondary outcomes will be evaluated. | All patients with COVID-19 based on standard diagnosed test and had at least one respiratory symptom<br>Age between 18 and 65 years<br>Willing to participate in the study | Primary Outcomes<br>Breath shortness.<br><br>Heart rate<br>Mean blood pressure.<br>Oxygen saturation.<br>Respiratory rate.<br><br>Secondary Outcomes<br>Hospital stay<br>Mortality rate of patients.<br>Percentage of patients transferred to the intensive care unit. |
| NCT04363463 | Two sessions minimum of prone position over | semi-seated in bed or seated in a chair during | | Primary Outcome Measures: |

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| Impact of Prone Position in Patients Under Spontaneous Breathing on Intubation or Non-invasive Ventilation or Death Incidence During COVID-19 Acute Respiratory Distress<br><br>Recruiting<br><br>Estimated Completion Date: August 2022 | the day. With a total objective of at least 2h30 of cumulated duration over the day. The objective is to spend as much time as possible in prone position if the patient tolerates it well. | the day. The prone position is not allowed during the day (it is allowed at night if it is the natural sleeping position). | Patients aged from 18 to 85 years old with COVID-19 documentation Undergoing oxygen therapy (nasal cannula, medium or high concentration mask or high flow nasal oxygen therapy)<br><br>Able to move to PP by him/herself or with minimal assistance Written consent<br><br>Hospitalized in COVID medical department for less than 72 hours | Percent age of patients who will have endotracheal intubation or non-invasive ventilation at two pressure levels and/or die, in each of the 2 randomization groups.<br><br>Endotracheal intubation Or non-invasive ventilation (NIV) with two pressure levels And/or death<br><br>Secondary Outcome Measures:<br>Duration in days for the change of 2 points on the WHO ordinal scale<br><br>Rate (%) of intubation and invasive ventilation in the 2 randomization groups.<br><br>Rate (%) of non-invasive ventilation at two pressure levels in the 2 randomization groups<br><br>Duration of oxygen therapy in the 2 randomization groups.<br><br>Duration of hospitalization in the 2 randomization groups.<br><br>Hospital mortality and mortality at D28 in the 2 randomization groups<br><br>Rate (%) of need for transfer to intensive care unit<br><br>Rate (%) of use of non-invasive ventilation at two pressure levels, intubation |

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| | | | | throughout the entire stay when the stay is longer than 28 days.<br><br>Compare the impact of the use of non-invasive ventilation and intubation on the entire hospital stay when the hospital stay is longer than 28 days between the two groups. |
| ISRCTN54917435<br><br>Awake prone positioning with high flow nasal cannula in critically ill COVID-19 patients<br><br>COMPLETED<br>Not yet published<br>No results | prone position or semi-recumbent position with the head of the bed elevated to 30 degrees with the target of 16 hours per day and night.<br><br>Follow-up is at 2 months after the end of inclusion. | Patients are neither prohibited nor encouraged and may be prescribed by the treating physician at their discretion. All other treatment or interventions for all included patients will follow ordinary local guidelines at the present hospital and are not affected by the study protocol. | Age 18 year or older<br><br>Admission to a hospital with confirmed or strongly suspected COVID-19 infection<br><br>Hypoxic respiratory failure defined as a PaO2/FiO2 ratio = 20 kPa (150 mmHg) and/or a FiO2 of = 0.5 to reach a SpO2 of 94% for more than 1 hour<br><br>Oxygen supplementation (ongoing or planned) with high flow nasal cannuale or noninvasive ventilating support | Primary Outcome<br>Rate of intubation for mechanical ventilation support, recorded in EHR at inclusion and once if applied.<br><br>Secondary Outcome(s)<br><br>Time in prone position (pp); every time the patient changes position the timepoint will be recorded in a preprinted protocol (CRF) or the PDMS if available, total time measured once per day and night in hospital<br><br>Need for vasoactive drugs, day and time for start, change of infusion rate or stop of vasopressor infusion, recorded in PDMS or EHR, evaluated once per day and night in hospital<br><br>Days on ventilator support, day and time of intubation and start of ventilator support, day and time of extubation and end of ventilator support, recorded in PDMS or EHR, checked once a day in hospital |

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| | | | | In-hospital and ICU length of stay: timepoint recorded in the EHR when enrolled and discharge at hospital/ICU<br><br>Rate of complications reported in a preprinted protocol (CRF) every 24th hour after inclusion<br><br>7- and 30-day mortality: day and time of death recorded in the EHR, checked once within a month after discharge from the hospital<br><br>Clinical improvement measured using WHO ordinal scale at baseline, day 7 and day 30 |
| IRCT20151020024625N12<br><br>Comparison of prone and supine position on oxygenation of patients with COVID-19 with acute hypoxemia treated using reservoir mask<br><br>COMPLETED<br>Not yet published<br>No results | Patients who need to continuous oxygen therapy by reserve bag will be placed in a prone position for one hour, every three hours up to three days. | Patients who need to continuous oxygen therapy by reserve bag will be placed in a supine position | Confirmed COVID-19 based on PCR test PaO2/FiO2 ratio between 150-300 | Arterial blood oxygen saturation level |
| IRCT20210316050722N1<br><br>Evaluation of pulmonary rehabilitation and prone position on respiratory parameters in patients with COVID-19 admitted to non- specialized ward of Hajar hospital of Shahrekord; a double blind randomized clinical trial<br><br>Recruiting | The second group of standard treatment measures of the state oxygen protocol with a normal mask + 2 hours of prone position + 15 minutes of lung rehabilitation.<br><br>Intervention group: Group 3 standard treatment measures of | Control group: Group 1 will only receive the standard treatments recommended in the national protocol. | Covid-positive patients admitted to non-specialized wards<br><br>From 18 to 75 years old<br><br>Non-intubated and supported by oxygen therapy,<br>No bed sores on shoulders, knees, and face,<br><br>Estimated weight less than 100 kg | Spo2. Timepoint: 30 and 60 minutes after being in the prone position and also 60 minutes after the patient is in the supine position |

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| | the state oxygen protocol with reservoir mask + 2 hours of prone position + 15 minutes of lung rehabilitation. | | | |
| NCT04358939<br><br>Evaluation of Prone Position in Conscious Patients on Nasal High-flow Oxygen Therapy for COVID-19 Disease Induced Acute Respiratory Distress Syndrome<br><br>COMPLETED<br>not yet published<br>No results | Prone positioning of patients on nasal high-flow oxygen therapy with usual care<br><br>the objective is to spend as much time as possible, up to 16 hours and beyond in prone position every 24 hours. At least two sessions of at least 30 minutes each must be performed daily. | Patients on nasal high-flow oxygen therapy with usual care and positioned in supine | Adult patient with COVID-19 pneumonia according to the diagnostic criteria in effect at the time of inclusion or very highly suspected.<br><br>Patient treated with nasal high-flow<br><br>Mild, moderate or severe ARDS: bilateral radiological opacities not fully explained by effusions, atelectasis or nodules; acute hypoxemia with worsening within the previous 7 days, not fully explained by left ventricular failure; PaO2/FiO2 ratio < 300 mmHg (or equivalent SpO2/FiO2).<br><br>Covered by or having the rights to French social security<br><br>Informed Consent | Primary Outcome Measures:<br>Therapeutic failure within 14 days of randomization<br><br>Secondary Outcome Measures:<br>Therapeutic failure within 28 days of randomization<br><br>Timeframe of intubation or death<br><br>Evolution of oxygenation (PaO2/FiO2 ratio or SpO2/FiO2 surrogate) over the 14 days following randomization<br><br>Evolution of the SpO2/FiO2 ratio during the first prone session<br><br>Evolution of the ROX index during the first prone session<br><br>Evolution of the World Health Organization disease severity score of COVID<br><br>Patient comfort before, during and after the first prone position session<br><br>Occurrence of skin lesions on the anterior surface of the body<br><br>Displacement of invasive devices during reversals |

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| | | | | Days of nasal High-Flow therapy use in the general population, in non-intubated patients and in intubated patients<br><br>Days spent in the intensive care unit and in the hospital<br><br>Mortality in the intensive care unit and in the hospital<br><br>Ventilator-free-days within 28 days of randomization |
| NCT04477655<br><br>Prone Positioning in Non-intubated Patients With Severe COVID-19: a Randomized Controlled Trial<br><br>COMPLETED<br>Not yet published<br>No results | Patients will be asked to remain in prone position throughout the day as long as possible, with breaks according to tolerance.<br><br>Patients will be asked to remain in prone position or lateral decubitus throughout the day as long as possible. | Prone positioning will be allowed as a rescue therapy.<br><br>Oxygen therapy through high flow nasal cannula (HFNC). Inspired fraction of oxygen will be titrated to maintain a capillary saturation of ≥92% | Adult patients with confirmed COVID-19, and requirement of a fraction of inspired oxygen (FiO2) ≥30% through high-flow nasal cannula (HFNC) to maintain a capillary saturation of ≥90% | Primary Outcome Measure:<br>Intubation rate<br><br>Secondary Outcome Measures :<br>Total hours of prone position at day<br><br>Total number of prone sessions at day<br><br>Hours of the longest prone session each day<br><br>Change in oxygenation 1-hour after first prone session<br><br>Change in the ROX-index 1-hour after first prone session<br><br>Total days of prone positioning<br>Adverse effects of prone positioning therapy<br><br>Mechanical ventilation days<br><br>Intensive care unit length of stay |

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| | | | | Hospital length of stay<br><br>Hospital mortality |
| NCT04366856<br><br>PROne Positioning in coVID-19 Oxygeno-dependent Patients in Spontaneous Ventilation (PROVID Study)<br><br>Recruiting | the interventional group will be suggested to spend at least 6 hours a day in prone position | the control group will get no instruction regarding positioning | Laboratory-confirmed SARS-CoV-2 infection as determined by PCR and/or CT scan showing typical radiological findings (ground glass abnormalities)<br><br>Need for O2 3L/min to get an SpO2 higher or equal to 95%.<br>Patient able to understand and to get in prone position themself<br>No therapeutic limitation | Primary Outcome Measures:<br>Proportion of patients who meet one or both following criteria: need for intubation (for mechanical ventilation), occurrence of death during hospital stay.<br><br>Secondary Outcome Measures:<br>Proportion of patients admitted to ICU (for patients included out of ICU)<br><br>Days alive and free from non invasive ventilation (NIV) or high flow nasal canula oxygen delivery (HFNC) (for those neither under NIV or HFNC at the time of study inclusion)<br><br>Days alive and out of ICU<br><br>Maximum oxygenotherapy rate during hospital stay |
| NCT04347941<br><br>Awake Prone Positioning to Reduce Invasive VEntilation in COVID-19 Induced Acute Respiratory failurE (APPROVE-CARE)<br><br>Recruiting | 16 hours per day in Prone Positioning with 45 minutes breaks for meals | Standard of care. Prone positioning may be administered as a rescue therapy | Suspected or confirmed COVID19 infection<br><br>Bilateral Infiltrates on CXR<br><br>SpO2 <94% on FiO2 40% by either venturi facemask or high flow nasal cannula<br>RR <40<br><br>Written informed consent | Primary Outcome Measures:<br>The effect of prone positioning on requirement for invasive mechanical ventilation in patients with COVID 19 induced respiratory failure<br><br>Secondary Outcome Measures:<br>Length of time tolerating prone positioning |

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| | | | | PaO2/FiO2 measured before prone positioning<br><br>PaO2/FiO2 ratio after 1 hours of prone positioning<br><br>SpO2/FiO2 ratio measured before prone positioning<br><br>SpO2/FiO2 ratio after 1 hours of prone positioning<br><br>Number requiring increase in ventilatory assistance (CPAP+BIPAP+IMV etc)<br><br>Work of breathing assessment (Respiratory distress scale)<br><br>Changes in bioimpedance measures of lung edema in patients in PP<br><br>Use of awake prone positioning as a rescue intervention in control patients |
| NCT04667286<br><br>Awake Pronation for Covid-19 Treatment<br><br>Recruiting | Oxygen via a Venturi mask in order to keep an oxygen saturation between 92 and 96% plus PP for a minimum of 10 hrs a day | Oxygen via a Venturi mask in order to keep an oxygen saturation between 92 and 96% | confirmed COVID-19 infection using PCR<br>Acute Respiratory Failure ( 200 <PaO2/FiO2 <300) and respiratory rate < 30 atti/min<br>O2 therapy initiated <72 hrs<br>informed consent | Primary Outcome Measures:<br>number of day free of ventilatory support<br><br>Secondary Outcome Measures:<br>changes in respiratory pattern<br>daily changes in the ratio SaO2/FiO2<br><br>dyspnea<br><br>comfort during PP<br><br>Other Outcome Measures:<br>number of hours on PP |

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| NCT04477655<br><br>Prone positioning in non-intubated patients with COVID-19 associated acute respiratory failure, the PRO-CARF trial | remain in a prone position throughout the day as long as possible, with breaks according to tolerance | prone positioning will be allowed as a rescue therapy. Staff intensivists will monitor the patient's status in both groups on a 24/7 basis. All other treatment will be unchanged and left to the attending physicians | all adult patients admitted to the COVID-19 unit who test positive for COVID-19 by PCR-test and in need for oxygen are eligible for inclusion.<br><br>fraction of inspired oxygen ≥30% for an oxygen capillary saturation of ≥90%. | Endotracheal intubation rate for mechanical ventilation at 28 days. |
| NCT04589936<br><br>Prone Position to Improve Oxygenation in COVID-19 Patients Outside Critical Care (PRONE-COVID) | Patient will first lay supine for a given time period, followed by lateral position on either side, then prone position, lastly return to supine position. Participants are anticipated to stay in prone position for a minimum of 30min to a maximum of 2 hours depending on tolerability. | Patient will first lay supine for a given time period, followed by lateral position on either side, then prone position, lastly return to supine position. Participants are anticipated to stay in prone position for a minimum of 30min to a maximum of 2 hours depending on tolerability. Participants will be guided in how to independently position themselves and rotate through the cycle of positions. | Have confirmed or suspected COVID-19 or non-COVID pneumonia (confirmed with radiological changes)<br><br>FiO2 ≥24% or requiring basic respiratory support (supplementary oxygen via face mask, nasal cannula, venturi, non-rebreathe bag) to achieve clinical target SpO2 (e.g. SpO2 92-96%), ensuring patient is on appropriately titrated oxygen to be within this range.<br><br>Be able to provide informed consent<br><br>Communicate and cooperate with the procedure<br><br>Rotate and adjust position independently<br><br>No anticipated airway issues | Primary Outcome Measures<br>Peripheral Oxygen saturation (FiO2)<br><br>Secondary Outcome Measures:<br>PaO2 :FiO2 ratio calculated from formulae<br><br>Respiratory rate measured with Masimo device<br><br>Heart rate measured with Masimo device<br><br>Blood pressure measured with Masimo device<br><br>Patient reported severity of breathlessness on a continuous linear scale of 0 to 10cm (10cm being the most severe)<br><br>Patient tolerability of prone position on a continuous linear scale of 0 to 10cm (10cm being the most unacceptable)<br><br>Investigator experience of delivering prone positioning<br><br>To assess patient's peripheral oxygen saturation |

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| NCT04427969<br><br>Early Prone Position on Coronavirus Disease 2019 Pneumonia (Prone Position) | Behavioral: prone position<br>to lay in prone position at least 12 hour in a day at ICU | patient who only get conventional oxygen therapy as respiratory supply | Patients who developed acute respiratory failure due to coronavirus disease 2019 pneumonia<br>received conventional oxygen therapy with reservoir mask oxygen at the stage of admission to the intensive care unit<br>older than 18 years old | Primary Outcome Measure:<br>intensive care unit stay<br><br>short term mortality<br><br>Secondary Outcome Measure<br>blood gases |
| NCT04325906<br><br>Early PP With HFNC Versus HFNC in COVID-19 Induced Moderate to Severe ARDS | Proning + HFNC | HFNC only no proning | COVID-19 induced adult ARDS patients admitted to the medical ICU<br>PaO2/FiO2 is less than 200mmHg or FIO2 ≥ 0.4 is required to maintain SpO2 at 88-93% on HFNC treatment | Primary Outcome Measure:<br>Treatment failure<br>Intubation rate<br><br>Secondary Outcome Measures:<br>Efficacy of PP |
| NCT04344587<br><br>Awake Prone Position for Early Hypoxemia in COVID-19 (APPEX-19) | Self-proning<br><br>A recommendation to "prone" while lying in bed (4 times for 1-2 hours each during the day and at night every 24 hours).<br>A reminder to keep track of the time spent in 1) prone position, 2) lying flat on back, 3) lying on side, 4) sitting up, and 5) standing or walking | Usual Care | Assigned to or admitted to a COVID-19 ward team at a participating site (these teams only admit patients who are under investigation for COVID-19 or who have confirmed COVID-19 infection) via the emergency department (ED) within the last 24 hours<br><br>Have access to their own functioning smartphone in the hospital room<br><br>English or Spanish-speaking<br>Ability to read simple instructions and answer simple written questions | Change in respiratory status<br>Length of time in each position<br><br>Reports of dyspnea, discomfort<br><br>Length of hospital stay<br><br>Invasive mechanical ventilation<br><br>ARDS diagnosis<br><br>Loss of IV access as a consequence of turning<br>Hospital mortality |
| NCT04383613 | The intervention is prone positioning (i.e., | Standard of care | Patients ≥ 18 years of age | All-cause mortality (4 weeks) |

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| Prone Positioning for Patients on General Medical Wards With COVID19 (COVID-PRONE) | instructing a patient to lie on their stomach while they are in bed) for 7 days or until the first of study hospital discharge or not requiring supplemental oxygen for >24 hours or study outcome. | Not specifically instructed to lie on their stomach | COVID-19 infection is suspected by the treating clinician or confirmed by diagnostic test<br><br>Able to lie on their stomach with verbal instruction<br><br>Requiring supplemental oxygen less than or equal to 50% FiO2<br><br>Capable to make treatment related decisions<br><br>Hospitalized in the last 48 hours with suspected or confirmed COVID-19 infection or diagnosed for nosocomial infection in the last 48 hours during their hospital stay | Invasive or non-invasive mechanical ventilation need for FiO2 of 60% or more |
| KCT0005258<br><br>The effect of prone positioning on non-intubated patients with postoperative acute respiratory failure | Prone positioning at least 12 hours in prone positioning group position change q 2hr(within 45 degree of Lt or Rt decubitus position change). dexmedetomidine continuous infusion if RASS > +1, target : light sedation | supine positioning and keep going management of respiratory failure | adult patients (18 years and older) with acute respiratory failure <br />- 30 minutes after applying High flow nasal cannula(FiO2 0.5, flow 50L) -> $PaO_2$< 150 ㎜ Hg, $PaCO_2$< 50 ㎜ Hg | Intubation rate within 7 days<br><br>Lung ultrasound reaeration score<br><br>$PaO_2/FiO_2$ ratio \<br><br>Mechanical ventilation (MV) duration<br><br>ventilator-free days<br><br>tracheostomy rate<br>ICU, 30 days, 90 days mortality<br><br>Complication related to prone positioning<br>sedative |