Is Prone Positioning Effective in Improving Hypoxemia for Non-ventilated Patients with COVID-19? A Rapid Evidence Assessment

Klair Holmes, SPT; Kathryn Kazmierczak, SPT; Kent Irwin, PT, DHS, GCS; Christian C. Evans, PT, PhD. Midwestern University, Physical Therapy Program, Downers Grove, IL 60515

Background: The COVID-19 pandemic has led to an escalation in hospitalizations and mortality rates due to expanding numbers of patients with Acute Respiratory Distress Syndrome. 29-91% of patients admitted with COVID-19 require mechanical ventilation support. Prone positioning (PP) has the potential to reduce hypoxia and fatality in non-ventilated patients with COVID-19 (see Figure 1).

Purpose: To evaluate the effect of PP on SpO_2 for non-ventilated adults with COVID-19 and hypoxemia and to examine other outcomes related to ventilation/hypoxemia.

Methods: The design was a Rapid Evidence Assessment (REA). The PEDro, Medline Complete, and Cochrane Central Register of Controlled Trials databases were searched with the terms: COVID 19 or Covid-19 or Covid19 or SARS COV2 or coronavirus and prone positioning or proning.

Inclusion criteria: included non-ventilated adults, diagnosed with COVID-19, and treated with PP.

Exclusion criteria: patients on mechanical ventilation, <18 y/o, raw data or indicator of central tendency and variability not available. The primary outcome was SpO_2, and secondary outcome measures included PaO_2/FIO_2 , PaO_2, $PaCO_2$, and respiratory rate (RR). The quality of the studies was appraised using the SIGN Methodology Checklist.

Figure 1. Effect of Prone Positioning on Lungs

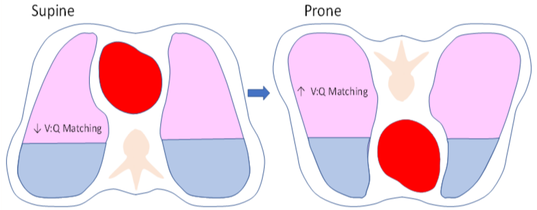
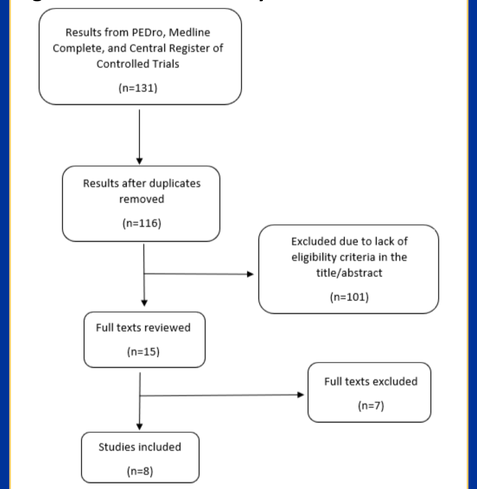


Figure 2. Search and Study Selection



Full Reference for Included Studies:

1. Caputo ND, Strayer RJ, Levitan R. Early self-proning in awake, non-intubated patients in the emergency department: a single ED's experience during the COVID-19 pandemic. *Acad Emerg Med*. 2020;27(5):375-378.
2. Coppo A, Bellani G, Winterton D, et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. *Lancet Respir Med*. 2020;8(8):765-774.
3. Damarla M, Zaeh S, Niedermeyer S, et al. Prone positioning of nonintubated patients with COVID-19. *Am J Respir Crit Care Med*. 2020;202(4):604-606.
4. Elharrar X, Trigui Y, Dols AM, et al. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. *JAMA*. 2020;323(22):2336-2338.
5. Sartini C, Tresoldi M, Scarpellini P, et al. Respiratory parameters in patients with COVID-19 after using noninvasive ventilation in the prone position outside the intensive care unit. *JAMA*. 2020;323(22):2338–2340.
6. Thompson AE, Ranard BL, Wei Y, et al. Prone positioning in awake, nonintubated patients with COVID-19 hypoxemic respiratory failure. *JAMA Intern Med*. 2020;180(11):1537–1539.
7. Tu GW, Liao YX, Li QY, et al. Prone positioning in high-flow nasal cannula for COVID-19 patients with severe hypoxemia: a pilot study. *Ann Transl Med.* 2020;8(9):598.
8. Xu Q, Wang T, Qin X, et al. Early awake prone position combined with high-flow nasal oxygen therapy in severe COVID-19: a case series. *Crit Care*. 2020;24(1):250.

Table 1: Study design, subject selection and characteristics

	Caputo *et al*, 2020[11]	Coppo *et al*, 2020[10]	Damarla *et al*, 2020[12]	Elharrar *et al*, 2020[13]	Sartini *et al*, 2020[14]	Thompson *et al*, 2020[15]	Tu *et al*, 2020[9]	Xu *et al*, 2020[16]
Primary Design Subcategory	Cohort Study Pilot Study	Cohort Study	Cohort Study	Cohort Study	Cohort Study	Cohort Study	Cohort Study Pilot Study	Retrospective Study
Participants	50	56	10	24	15	25	9	10
Setting	ED	ED, Non-ICU (medical wards and respiratory high-dependency unit)	ICU	Non-ICU	Non-ICU (medical ward)	Non-ICU (intermediate care unit/step down unit)	ICU	Non-ICU
Hours prone/day, mean or median	≥5 min (data collected at 5 min)	≥3 hrs	Alternate positions every 2 hrs, slept in prone	>1-3 hrs	3 hrs/ 3x day (as tolerated)	≥1 hr (as tolerated)	1-4 hrs	≥16 hrs
Intervention (include SpO_2, high flow O_2)	Median SpO_2 was 80%, self-proning one episode	A single episode of PP lasting for at most 3 hrs	Alternate between prone and supine every 2 hours and sleep in prone	A single episode of PP for as long as tolerated	Two cycles of PP, follow up taken at 14 days	PP for as long as tolerated for 24 hrs	HFNC remained constant before and during proning, one episode of proning	HFNC, used a SpO_2 >90%, PP for as long as the patient could tolerate up to 16 hrs
Criteria for Enrollment	Awake, COVID-19 (+) with SpO_2 <93%, on supplemental oxygen	18-75 yrs, COVID-19 (+), requiring supplemental oxygen or non-invasive CPAP	(+) PCR testing for SARS-CoV-2 RNA, with increasing oxygen requirements	COVID-19 (+), non-intubated, required supplemental oxygen, chest CT with posterior lesions	Hypoxemic (SpO_2 ≤ 93%)	Covid-19 (+), RR< 30 breaths/min, SpO_2<93%, supplemental O_2 6L/min NC, 15 L/min FM	Covid-19 (+), HFNC >2 days, PaO_2/FiO_2 <150 mmHg	Awake, COVID-19 (+) P/F <300 mmHg, SpO_2 greater than 90%
Exclusion Criteria	Pts requiring NIV	Pregnant patients, uncollaborative, had altered mental state, COPD, New York Heart Association class below II	Pts requiring intubation	Impaired consciousness, and acute respiratory failure requiring intubation	Pts requiring NIV	Unable to prone, pts requiring intubation	None has been given	Pts who are pregnant or are not considered severe

Table 2: Outcomes, Limitations and Quality Assessment

	Caputo *et al*, 2020[11]	Coppo *et al*, 2020[10]	Damarla *et al*, 2020[12]	Elharrar *et al*, 2020[13]	Sartini *et al*, 2020[14]	Thompson *et al*, 2020[15]	Tu *et al*, 2020[9]	Xu *et al*, 2020[16]
Outcomes	SpO_2 and rate of patients intubated	PaO_2/FiO_2 ratio, safety and feasibility of PP, $PaCO_2$ and dyspnea	SpO_2 and RR	PaO_2, $PaCO_2$, dyspnea, and discomfort (VAS)	PaO_2/FiO_2 ratio, RR, comfort, and SpO_2	SpO_2	SaO_2, PaO_2 and, $PaCO_2$	$PaCO_2$ and PaO_2/FiO_2
Key Results	SpO_2 increased from 84% to 94%, 13 out of 50 patients total received intubation	Increase in PaO_2/FiO_2 by more than 50% from supine to prone, the increase was not significant when returning back to supine	Increase in SpO_2 from 94% to 98% and decrease RR from 31 to 22 bpm	63% of patients were able to tolerate PP for ≥3 hours, however, there was only an increase in PaO_2 in 25% of them.	The decrease in RR and comfort, all had improved SpO_2 and PaO_2/FiO_2 ratio during PP	Increase in SpO_2 one hour after PP compared to baseline	Increase in SaO_2 from 90% to 96% and PaO_2 from 69 to 108 mmHg, a decrease in $PaCO_2$ from 47 to 39 mmHg	Median $PaCO_2$ increased and the median PaO_2/FiO_2 elevated
Strengths	Supportive for acute setting, PP was the only invention conducted	No adverse events related to procedure occurred, compared non-responders with the responders	8/10 of patients did not require mechanical ventilation, no adverse events with PP	10-day follow-up, measured response in re-supination. None of the participants received major complications	14 day follow up	SpO_2 of ≥ 95% after 1 hr of PP was associated with a lower rate of intubation	No adverse events occurred, 7 out of 9 patients avoided invasive mechanical ventilation	All patients survived, none of the patients progressed to critical condition or needed intubation
Limitations	13 out of 50 pts failed to improve SpO_2 and required endotracheal intubation, short PP episode	Lack of a control group, single-center, and possible selection bias	Small sample size, selection bias possible, no control group, only one episode of data collection	Small sample size, only a single episode of PP was evaluated, short follow-up, clinical outcomes were not assessed, variable length of intervention	Small sample size, lack of control group, short duration of PP, patients were not included if NIV failed while in PP	No control group, small sample size, the inclusion of both intubated and non-intubated patients	No control group, the small sample size	No control group, the small sample size
SIGN Methodology Checklist[1]	Acceptable	Acceptable	Low Quality	Acceptable	Acceptable	Low Quality	Low Quality	Low Quality

Abbreviations: High-Flow Nasal Cannula = HFNC; Non-Intubated Ventilation = NIV; Prone Position = PP; Respiratory Rate = RR; Nasal cannula = NC; Non-rebreather face mask = FM; Patients = Pts, Sign Methodology Checklist 3: Cohort Studies[8,7]

Results:

- A total of 116 studies were identified and 8 met all inclusion/exclusion criteria (Table 1).
- A total of 199 subjects were included.
- Four studies were of acceptable quality, whereas four studies were of low quality based on the SIGN Methodology Checklist (Table 2).
- Four out of 8 studies found a significant increase in SpO_2 post-PP compared to pre-PP (Table 2).
- Two studies observed that RR was reduced with PP and 3 found PP increased PaO_2/FiO_2 (Table 2).
- The longer the participants remained in PP the more successful the treatment.

Clinical Significance:

- Due to heterogeneity in methods, lower quality study designs and varied results, there is moderate support for PP for improving SpO_2 in non-ventilated patients with COVID-19.
- Not all non-ventilated patients with hypoxemia due to COVID-19 benefit from PP or tolerate it.
- Trend for a more favorable outcome when patients remained prone for longer duration.

Limitations:

- All 8 studies had significant limitations.
- There were varying degrees of bias due to lack of a well-controlled study design (all cohort studies), small sample size, lack of follow-up, and non-standardized PP protocols.

Conclusion: This Rapid Evidence Assessment supports the use of PP with non-ventilated patients with COVID-19, but additional higher-level studies are needed to confirm these results.

Acknowledgements: The authors thank the MWU Library and Colleen Bannon, M.L.I.S. for assistance in this project.