



# Prone positioning in high-flow nasal cannula for COVID-19 patients with severe hypoxemia: a pilot study

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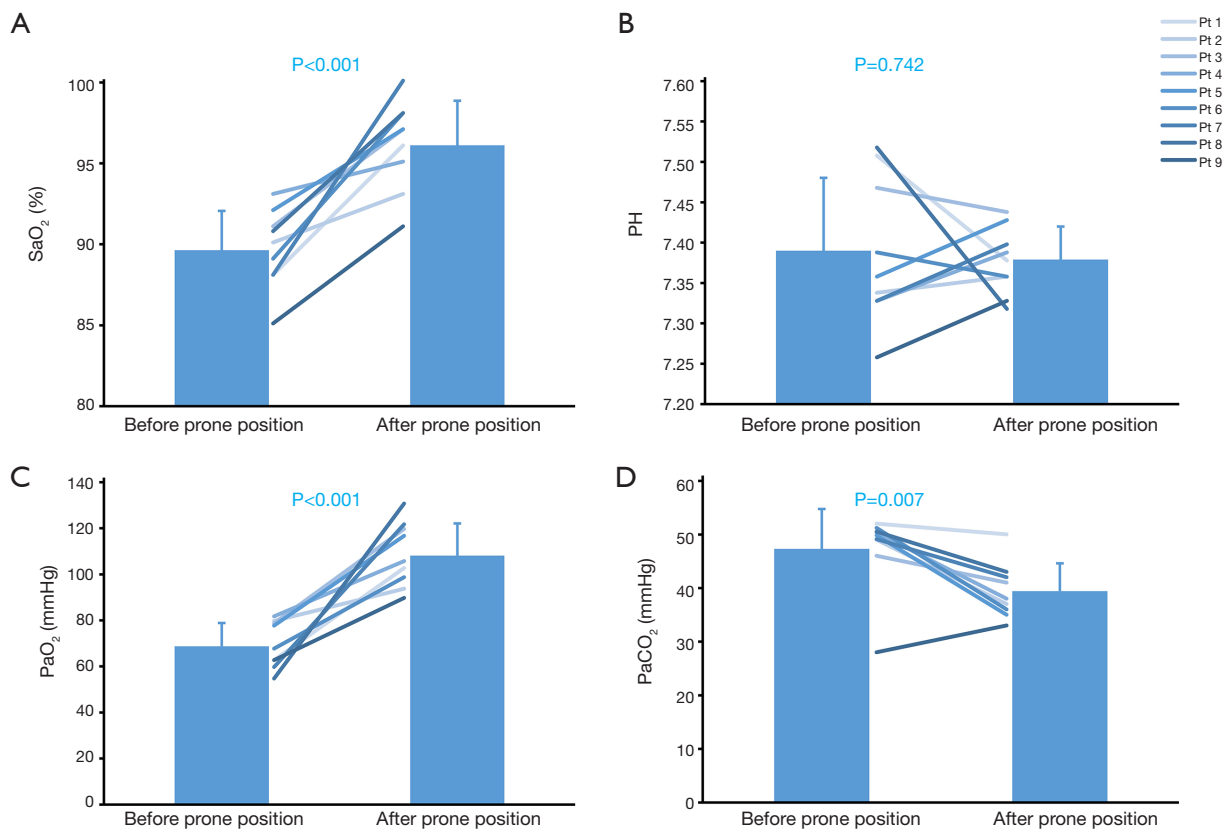
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The COVID-19 outbreak has become a global pandemic within only a few months. COVID-19 patients complicated with severe hypoxemia usually required high-flow nasal cannula (HFNC) and mechanical ventilation. Prone positioning is a salvage therapy for refractory hypoxemia and has proven to be effective in increasing tidal volume and improving oxygenation and diaphragmatic function in patients with acute respiratory distress syndrome (ARDS) (1-3). However, all these studies were conducted in intubated patients. A recent study revealed that early application of prone positioning with the HFNC might avoid the need for intubation in moderate to severe ARDS patients (4), suggesting that the benefits of prone positioning also exists in the non-intubated patients (5). Also, endotracheal intubation may carry high nosocomial infection risk for the physicians who perform this procedure. Avoiding intubation could also be protective of them. Based on these potential beneficial effects, we conducted a pilot study and reviewed our preliminary experience of prone positioning in HFNC to treat COVID-19 who were complicated with severe hypoxemia.

Patients diagnosed with COVID-19 were enrolled if HFNC was delivered more than 2 days, and PaO<sub>2</sub>/FiO<sub>2</sub> was less than 150 mmHg. The flow rate was initially set at 50–

60 L/min, and the fraction of inspired oxygen concentration (FiO<sub>2</sub>) was titrated to maintain the SpO<sub>2</sub> more than 90%. Between 1 February and 10 March 2020, 9 patients were included in this pilot study, and informed consents were obtained from participants or their family members. The clinical characteristics of these 9 COVID-19 patients were summarized in *Table 1*.

Prone positioning was applied with a median of 5 (IQR: 3–8) procedures per subject (twice daily). The median duration was 2 (IQR: 1–4) hours. HFNC settings were kept constant before and during the prone positioning. Physicians and nurses monitored the respiratory and hemodynamic parameters closely. Patients who could not tolerate prone positioning were allowed to interrupt and back to the supine position. No sedation was used in this study for safety concerns. The arterial blood before and after prone positioning were collected at the first time (*Figure 1*). The mean blood oxygen saturation was increased from 90%±2% to 96%±3% (P<0.001), and the mean blood oxygen partial pressure was increased from 69±10 to 108±14 mmHg (P<0.001). The mean partial pressure of carbon dioxide was decreased from 47±7 to 39±5 mmHg (P=0.007). Two patients ultimately required invasive mechanical ventilation: One was successfully extubated after 8 days, and the other received venovenous extracorporeal membrane



**Figure 1** Comparison of SaO<sub>2</sub>, PaO<sub>2</sub>, PaCO<sub>2</sub> and PH before and after prone positioning.

oxygenation.

This is the first study to evaluate the effect of prone positioning during HFNC in COVID-19 patients. Our study revealed that prone positioning was safe and associated with improved oxygenation in HFNC patients with severe hypoxemia. We did not observe any major adverse events, such as hemodynamic instability or aspiration.

Although the results are encouraging, they should be interpreted with great caution. Although prone positioning has been reported to have physiological effects of “lung recruitment”, which could improve ventilation-perfusion matching, further investigation of the mechanism is still warranted in HFNC patients. In the current study, 7 out of 9 patients successfully avoided invasive mechanical ventilation, which indicated that prone positioning might help avoid intubation in HFNC patients. However, the small sample size of the study and lack of controlled group precluded the establishment of definitive conclusions.

Besides, the optimal timing of prone positioning initiation in severe hypoxemia patients with HFNC remains

unknown. In the PROSEVA trial, Guérin *et al.* included ARDS patients with PaO<sub>2</sub>/FiO<sub>2</sub> less than 150 mmHg and FiO<sub>2</sub> at least 60% (2). However, this enrollment criteria were based on intubated patients rather than HFNC. In this study, prone positioning was used as a “salvage therapy”. It should be noted that if the invasive mechanical ventilation is inevitable and the situation is emergent, delayed intubation of patients will increase, rather than decrease, the mortality (6,7). When combined with HFNC, whether prone positioning should be used as “preemptive strategy” or “salvage therapy” need to be further evaluated.

In conclusion, our pilot study revealed that prone positioning combined with HFNC could improve oxygenation and potentially avoided invasive mechanical ventilation. Further large-scale studies are needed to confirm our results.

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**Table 1** Clinical characteristic of 9 HFNC patients with COVID-19

Variables	Outcome
Age (yrs)	51±11
Male sex, n (%)	4 (44.44%)
Symptoms on admission, n (%)	
Fever	9 (100%)
Cough	6 (66.67%)
Dyspnea	2 (22.22%)
Comorbidities, n (%)	
Hypertension	3 (33.33%)
Diabetes mellitus	1 (11.11%)
WBC ( $\times 10^9/L$ )	5.08±1.64
ALC ( $\times 10^9/L$ )	0.67±0.10
Lymphocyte %	14.11±3.50
Neutrophils %	80.47±4.97
Creatinine ( $\mu\text{mol/L}$ )	68.93±17.22
D-dimer (mg/L)	0.90 (0.41–2.57)
BNP (pg/mL)	52.53±61.22
Troponin T ( $\mu\text{g/L}$ )	0.01 (0.00–0.02)
FiO <sub>2</sub> (%)	80±5
Flow rate (L/min)	60
Intubation required, n (%)	2 (22.22%)
Duration of HFNC before PP (days)	4±1
Duration from disease onset to inclusion (days)	11±3
Length of stay in ICU (days)	15±7
Length of stay in hospital (days)	28±10

Values are given as mean  $\pm$  standard deviation, median (25–75% interquartile range), n (%). HFNC, high-flow nasal cannula; WBC, white blood count; ALC, absolute lymphocyte count; BNP, pro-brain natriuretic peptide; FiO<sub>2</sub>, fraction of inspiration oxygen; PP, prone positioning; ICU, intensive care unit.

epidemic in Wuhan.

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