

Letters

RESEARCH LETTER

Respiratory Parameters in Patients With COVID-19 After Using Noninvasive Ventilation in the Prone Position Outside the Intensive Care Unit

The pandemic of coronavirus disease 2019 (COVID-19), with a large number of patients requiring respiratory support, threatens to overload intensive care units (ICUs). Noninvasive ventilation (NIV) use in general wards may be an alternative for some patients but has seldom been described and is not used worldwide.¹ One study described the feasibility of NIV in the prone position²; pronation can recruit dorsal lung regions and drain airway secretions, improving gas exchange and survival in acute respiratory distress syndrome (ARDS).³ We report respiratory parameters after using this intervention in a case series of patients with COVID-19.

Methods | On April 2, 2020, in San Raffaele Scientific Institute, Milan, Italy, COVID-19 patients with ARDS were treated either in the ICUs (n = 48) or medical wards (n = 202). Noninvasive ventilation was used for 62 patients with mild to moderate ARDS who had saturation less than 94% on face mask with high-oxygen concentration, applying 10 cm H₂O continuous positive airway pressure and 0.6 fraction of inspired oxygen (FIO₂). In case of poor response to NIV, the intensive care surgeon suggested a trial of NIV in the prone position, which was continued if there was improvement in the first hour of treatment. Noninvasive ventilation cycles were individualized based on a patient's severity of illness, adherence to the treatment, and dyspnea in the periods without NIV.

On April 2, 2020, we performed a cross-sectional survey to identify all patients undergoing the prone position NIV outside the ICU, irrespective of the day they started using this technique. Respiratory parameters were measured at 3 time points: before NIV, during NIV in pronation (60 minutes after start), and 60 minutes after NIV end. We investigated oxygen saturation as measured by pulse oximetry (SpO₂), derived Pao₂:FIO₂,⁴ respiratory rate, and patient's comfort using a numerical rating scale (0, totally uncomfortable, to 10, fully comfortable). Follow-up was conducted at 14 days to determine how many patients were discharged, were still treated in the prone position, or were intubated. Continuous measures were compared using Wilcoxon matched pairs signed rank test or *t* test if paired data were normally distributed. Two-sided *P* < .05 defined statistical significance. All analyses were performed with STATA version 16 (STATA Corp). The study was approved by the Ethics Committee of IRCCS San Raffaele Scientific Institute. Written informed consent was obtained.

Table. Baseline Characteristics of 15 Patients With COVID-19 Who Received Noninvasive Ventilation in the Prone Position Outside the ICU

Characteristics	Value
Age, mean (SD), y	59 (6.5)
BMI, mean (SD)	24 (3.4)
Sex, No. (%)	
Women	2 (13.3)
Men	13 (86.6)
Time, median (IQR), d	
From first symptom appearance	15 (12-21)
From hospitalization	9 (7.5-14)
From NIV start	7 (4-10)
From NIV in the prone position start	5 (3-10)
Pao ₂ :FIO ₂ on first MET call ^a	157 (43.0)

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; COVID-19, coronavirus disease 2019; FIO₂, fraction of inspired oxygen; ICU, intensive care unit; IQR, interquartile range; MET, medical emergency team; NIV, noninvasive ventilation; Pao₂, arterial partial pressure of oxygen.

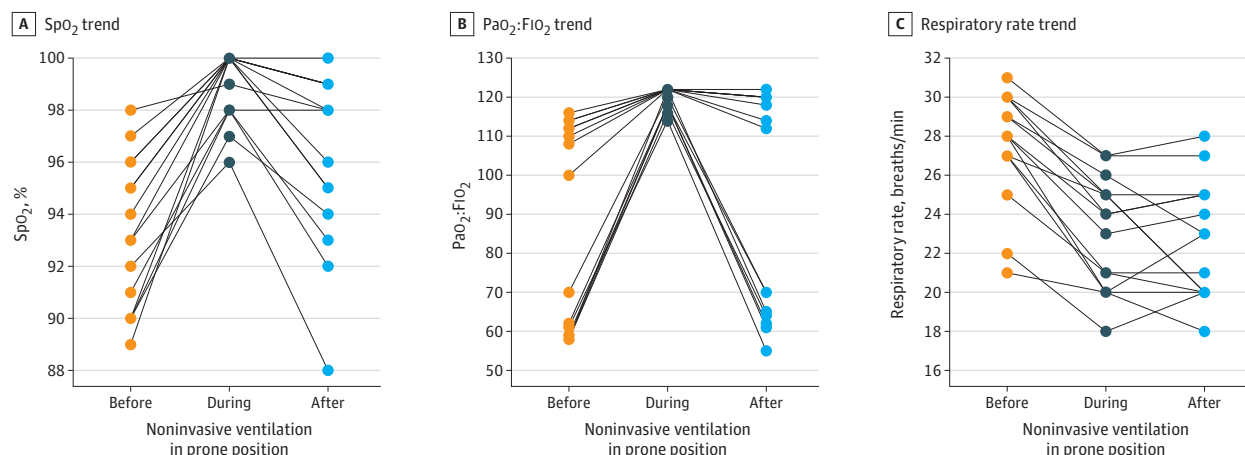
^a The normal Pao₂:FIO₂ ratio is more than 400 mm Hg; a Pao₂:FIO₂ of less than 300 mm Hg indicates acute respiratory distress syndrome.

Results | Fifteen patients receiving NIV in the prone position outside the ICU on April 2 were identified. Mean (SD) age was 59 years (6 years); 13 were men. Noninvasive ventilation in the prone position started a median of 5 days (interquartile range [IQR], 3-10 days) before April 2 (Table) and no patient started NIV in the prone position on April 2. The median number of NIV cycles in the prone position on April 2 was 2 (IQR, 1-3 cycles) for a total duration of 3 hours (IQR, 1-6 hours). Compared with baseline, all patients had a reduction in respiratory rate during and after pronation (*P* < .001 for both) (Figure); all patients had an improvement in SpO₂ and Pao₂:FIO₂ during pronation (*P* < .001 for both); 12 patients (80%) had an improvement in SpO₂ and Pao₂:FIO₂ after pronation; 2 (13.3%) had the same value; and 1 (6.7%) had worsened. Compared with baseline, 11 patients (73.3%) had an improvement in comfort during pronation and 4 (26.7%) had the same value; 13 patients (86.7%) had an improvement in comfort after pronation and 2 (13.3%) had the same value. At the 14-day follow-up, 9 patients were discharged home, 1 improved and stopped pronation, 3 continued pronation, 1 patient was intubated and admitted to ICU, and 1 patient died.

Discussion | Providing NIV in the prone position to patients with COVID-19 and ARDS on the general wards in 1 hospital in Italy was feasible. The respiratory rate was lower and the oxygenation was higher during and after pronation than they were at baseline. Whether intubation was avoided or delayed remains to be determined.

Limitations include the small number of patients, short duration of NIV in the prone position, and lack of a control group. Comparisons of NIV in the prone position with oxygen by face

Figure. Respiratory Parameters in the Individual Patients Before, During, and After Noninvasive Ventilation in the Prone Position



The graphs represent trends of respiratory parameters in the individual patient at the 3 time points. Before pronation: immediately before initiating noninvasive ventilation (NIV) while the patient was still in the supine position. During pronation: after 1 hour of receiving NIV treatment while the patient was in the prone position. After pronation: 1 hour after NIV treatment stopped when the patient was in the supine position. A, Peripheral oxygen saturation (SpO₂),

$P < .001$ between before and during pronation, $P < .004$ between before and after pronation. B, Arterial partial pressure of oxygen (PaO₂) to inspired oxygen fraction (FIO₂), $P < .001$ between before and during pronation, $P < .004$ between before and after pronation. C, Respiratory rate $P < .001$ between before and during pronation, $P < .001$ between before and after pronation.

mask or NIV in the standard position are needed. Importantly, selection bias is possible. Patients were not included if NIV failed while in the prone position or were treated and either died or recovered before April 2. Therefore, patients in the study may not be representative of all patients treated with NIV in the prone position.

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1. Cabrini L, Landoni G, Bocchino S, et al. Long-term survival rate in patients with acute respiratory failure treated with noninvasive ventilation in ordinary wards. *Crit Care Med*. 2016;44(12):2139-2144. doi:[10.1097/CCM.0000000000001866](https://doi.org/10.1097/CCM.0000000000001866)

2. Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. *Crit Care*. 2020;24(1):28. doi:[10.1186/s13054-020-2738-5](https://doi.org/10.1186/s13054-020-2738-5)

3. Guérin C, Reignier J, Richard JC, et al; PROSEVA Study Group. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med*. 2013;368(23):2159-2168. doi:[10.1056/NEJMoa1214103](https://doi.org/10.1056/NEJMoa1214103)

4. Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB; National Institutes of Health, National Heart, Lung, and Blood Institute ARDS Network. Comparison of the SpO₂/FIO₂ ratio and the PaO₂/FIO₂ ratio in patients with acute lung injury or ARDS. *Chest*. 2007;132(2):410-417. doi:[10.1378/chest.07-0617](https://doi.org/10.1378/chest.07-0617)