Editorial Commentary

Prone position versus usual care in hypoxemic COVID-19 patients in medical wards: a randomised controlled trial

Tomoo Kishaba^

Department of Respiratory Medicine, Okinawa Chubu Hospital, Uruma, Japan

Correspondence to: Tomoo Kishaba, MD. Department of Respiratory Medicine, Okinawa Chubu Hospital, 281 Miyazato, Uruma, Okinawa 904-2293, Japan. Email: kishabatomoo@gmail.com.

Comment on: Nay MA, Hindre R, Perrin C, *et al.* Prone position versus usual care in hypoxemic COVID-19 patients in medical wards: a randomised controlled trial. Crit Care 2023;27:240.

Keywords: Comorbidity; consolidation; coronavirus disease 2019 (COVID-19); non-pharmacological; prone position (PP)

Submitted Aug 27, 2023. Accepted for publication Oct 20, 2023. Published online Nov 17, 2023.
doi: 10.21037/jtd-23-1342
View this article at: https://dx.doi.org/10.21037/jtd-23-1342

Coronavirus disease 2019 (COVID-19) can cause pneumonia ranging from mild to severe grades (1,2). The mainstay of treatment for COVID-19 pneumonia includes antiviral drugs such as remdesivir (3,4) and anti-inflammatory drugs such as dexamethasone (5,6). Regarding non-pharmacological treatment of COVID-19 pneumonia, especially in critically ill patients, prone position ventilation (PPV) has shown positive results for most critical COVID-19 pneumonia patients using high-flow nasal cannula (HFNC) or invasive mechanical ventilation (7-10). PPV was originally introduced for severe acute respiratory distress syndrome (ARDS) (11). Prone position (PP) improves ventilation-perfusion mismatch by reversing consolidated lung portions, making it a reasonable strategy for recruiting collapsed lung areas in dependent lungs. However, clinical studies of PPV for mild to moderate COVID-19 pneumonia patients are limited. Ehrmann *et al.* suggested that awake-prone positioning appears more beneficial when done for more than 8 hours per day (12).

In a recent issue of *Critical Care*, Nay *et al.* published a randomized controlled trial (RCT) comparing PP to usual care in hypoxemic COVID-19 pneumonia patients (13). They conducted the RCT for mild to moderate COVID-19 pneumonia patients in medical wards diagnosed within 72 hours and requiring face masks or standard nasal prongs, with a median oxygen pressure to fraction of inspiratory oxygen of 173–178. Patients were randomly assigned to the self-PP or usual care group, with a median PP duration of 90 minutes. The primary outcome of this study is the ratio of treatment failure, expressed as a composite endpoint that includes the need for non-invasive ventilation (NIV), tracheal intubation, or death within 28 days of randomization. Secondary outcomes include the rates of tracheal intubation, NIV, and a decrease in the World Health Organization ordinal scale at 28 days.

The results indicated that self-PP did not meet the primary outcome. Subgroup analysis showed that PP decreased the probability of endotracheal intubation or death [hazard ratio: 0.10, 95% confidence interval (CI): 0.01–0.81, P=0.031] in patients with initial oxygen saturation ($SatO_2$) ≥95%. This was a negative study, and the paradoxical effect of the intervention on the combined outcome of intubation or death seems implausible, showing significance in less severe patients ($SatO_2$ ≥95%) and no effect in more severe patients, based on single patient events in the intervention group.

This study has several limitations. First, close observation of self-proning is challenging due to the medical staff system in medical wards. Second, the study did not provide detailed information about chest high-resolution computed tomography (HRCT) findings. The most recruitable HRCT findings for chest

^ ORCID: 0000-0003-3335-5409.

consolidation are bilateral and dependent without traction bronchiectasis (14). Therefore, the effectiveness of self-proning might not be evident in patients with pneumonia in unilateral or non-dependent areas. Third, the median duration of self-PP in this study was 90 minutes, which may be too short for recruiting consolidation. The duration of prone positioning in COVID-19 patients treated with mechanical ventilation is usually longer than 16 hours, which is a key issue. Two recent studies showed the benefit of prolonged PPV in intubated COVID-19 patients (15,16). However, the optimal duration of PP for mild to moderate COVID-19 pneumonia patients remains to be determined. Therefore, more time might be required for a positive effect of PP in mild to moderate COVID-19 pneumonia patients. Prolonged PP places patients in an unusual posture for conscious patients. Therefore, striking a balance between effectiveness and patient's tolerability is a crucial issue. Fourth, the criteria for NIV or tracheal intubation may vary at each institution, especially NIV criteria due to the absence of guidelines for NIV indications in COVID-19 pneumonia. Fifth, the study allowed patients to change positions freely during the nighttime. PPV of critically ill COVID-19 patients is typically conducted overnight. During nighttime, secretion is often increased, especially in pneumonia patients. Therefore, a nighttime protocol might be required. However, a meticulous protocol is challenging for conscious patients during nighttime. Daytime PP may be more realistic. Sixth, almost all patients received corticosteroids, but the study did not provide detailed information on the type, dose, or duration of corticosteroids. Different doses or durations of corticosteroids may have different effects on each patient. A recent meta-analysis of awake prone positioning, which included 17 clinical trials (2,931 patients), only reported a lower rate of orotracheal intubation [risk ratio (RR): 0.83, 95% CI: 0.70 to 0.99] but not for mortality (RR: 0.90, 95% CI: 0.45 to 1.82) (17). I propose that a sufficient duration of self-PP is required to reduce the orotracheal intubation rate for mild to moderate COVID-19 pneumonia patients.

Non-pharmacological management of COVID-19 pneumonia is crucial due to the limited availability of specific drugs for COVID-19 pneumonia. Even with the findings from this paper, more sophisticated research with a standardized protocol will be required to clarify the true effectiveness of PP for mild to moderate COVID-19 patients.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Journal of Thoracic Disease*. The article has undergone external peer review.

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1342/prf

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1342/coif). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Kishaba T. Prone position versus usual care in hypoxemic COVID-19 patients in medical wards: a randomised controlled trial. J Thorac Dis 2023;15(11):6379-6381. doi: 10.21037/jtd-23-1342

