Editorial Commentary

Awake prone positioning in COVID-19 patients: is there any benefit?

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The advent of the coronavirus disease 2019 (COVID-19) pandemic presented an unprecedented challenge to the medical field, necessitating innovative approaches to address the severe respiratory symptoms linked to the virus. Influenced by its success in treating acute respiratory distress syndrome (ARDS), prone positioning as a rescue maneuver, after the lack of improvement under optimal ventilatory settings, was used for COVID-19 patients. However, it's noteworthy that COVID-19 pneumonia diverges from traditional ARDS in several key aspects. Autopsies of COVID-19 pneumonia fatalities have revealed distinctive features like hyaline membrane changes and micro-vessel thrombosis, uncommon in classic ARDS cases (1-4). Furthermore, the anatomical presentation of COVID-19 pneumonia differs, with predominant bilateral, peripheral, and multilobar ground-glass opacities on computed tomography (CT) scans, deviating from the characteristic involvement of dependent lung regions observed in ARDS (5). Consequently, the efficacy of prone positioning in ameliorating ventilation-perfusion mismatch might not be as pronounced due to the atypical location of lung abnormalities. In the context of ventilated patients with COVID-19 pneumonia, research suggests that prone positioning may not significantly alter the respiratory system and lung mechanics. This indicates that lung aeration tends to remain preserved in COVID-19 pneumonia patients and might even trend towards deterioration due to ventilation in the prone position (6). Paradoxically, this finding suggests that despite severe lung damage, lung mechanics might present as normal during COVID-19 pneumonia, and trans-pulmonary pressures could remain below detrimental thresholds (6).

The effectiveness of prone positioning as a therapeutic approach for COVID-19 patients remains a topic of debate due to conflicting findings from various studies. In a randomized trial involving awake patients across fifteen hospitals in North America, patients were assigned to either prone positioning or standard treatment, both groups showing similar clinical outcomes, including mortality rates, need for mechanical ventilation, and respiratory failure worsening (7). Another meta-trial spanning six countries indicated that awake-prone positioning reduced treatment failure and intubation needs in hypoxemic respiratory failure cases without significant mortality improvement (8). Conversely, a meta-analysis encompassing mechanically ventilated patients showed no reduction in mortality, intensive care unit (ICU) stay, or mechanical ventilation duration in prone positioned patients (9,10). Some of the studies included in this meta-analysis had limitations that were addressed (11-13).

The study conducted by Nay *et al.* (14) aimed to assess the effectiveness of prone positioning as a treatment for less severe hospitalized COVID-19 patients. The study was conducted as a randomized trial with patients from France and Monaco, from August 2020 to January 2022 and involved 268 awake patients who were admitted for

COVID-19 in 15 medical wards at 12 hospitals. Patients were randomly assigned to either the prone positioning group or the usual care group. In the prone positioning group, patients were placed in a prone position for a minimum of two sessions with a cumulative time of at least 150 minutes during the daytime. Prone positioning was allowed at night if it was the patient's natural sleeping position. Patients in the usual care group were kept in the semi-sitting position in bed or a chair during the daytime. The results showed that the patients in the prone positioning group received at least one session of prone positioning, with 74.8% of patients proned on the day of enrollment. The median time spent in the prone position per day during the daytime was 138 minutes. Some patients experienced intolerance or refusal, resulting in 12.1% of patients having at least one day without prone positioning. Thirty-one-point-one percent of patients in the prone positioning group laid prone for more than 2 hours each day during the daytime. Patients in the usual care group did not use prone positioning during the daytime, except for one patient. The primary outcome was the rate of non-invasive ventilation (NIV), intubation, or death within 28 days. In the intention-to-treat population, the rate of this outcome was 14.1% in the prone positioning group and 12.9% in the usual care group. The difference was not statistically significant (adjusted odds ratio 0.43; 95% confidence interval: 0.14–1.35; P=0.15). The risk of NIV tended to be more frequent in the prone positioning group, primarily driven by patients with a body mass index below 30 kg/m^2. The researchers concluded that among COVID-19 patients hospitalized in medical wards and requiring supplemental oxygen, prone positioning did not significantly reduce the risk of NIV, intubation, or death. Overall, the study did not find a significant benefit of prone positioning in reducing the risk of severe outcomes in less severe hospitalized COVID-19 patients. The findings suggest that while prone positioning might have some effects on certain secondary outcomes, it did not demonstrate a clear advantage in the primary outcome of reducing the need for NIV, intubation, or death.

The study conducted by Nay *et al.* underscores both the limitations and strengths inherent in their research (14). Notably, the inability to blind patients and caregivers due to the nature of self-proning introduces potential bias. Participants' awareness of the study would be less likely to influence outcomes like non-invasive mechanical ventilation, intubation, and death, given the nature of the outcomes. However, caregivers had been conscious that assigned intervention can potentially affect their behavior and perception of treatment effects given the absence of well-defined intubation criteria. This could lead to variability in decisions on intubation, potentially favoring one group over the other. Moreover, the study lacks information on participants' COVID-19 vaccination status and other treatments like Remdesivir, which could introduce confounding variables that influence outcomes. However, the study boasts several strengths. The utilization of randomization and stratification based on oxygen impairment and body mass index enhances the study's credibility by minimizing biases and ensuring balanced baseline characteristics. By addressing the limitations of prior research, the study's design and methodology significantly enhance the robustness of their investigation into the effects of prone positioning. Notably, the study's focus on a clinically relevant question, whether prone positioning offers benefits to less severe COVID-19 patients, adds practical value to its findings. Despite the constraints, the research presents a comprehensive perspective on the potential advantages of prone positioning in managing COVID-19 cases.

In conclusion, while the question of whether prone positioning offers benefits to COVID-19 patients remains open, the current body of evidence suggests a lack of substantial advantages for both intubated and non-intubated individuals. However, the available research is not yet conclusive, and further extensive studies are required to provide a more definitive answer. Therefore, the use of prone positioning in COVID-19 treatment should be approached with caution. Decisions regarding its application should be highly individualized and based on a thorough evaluation of each patient's specific clinical condition. As our understanding of COVID-19 continues to evolve, ongoing research will be crucial in guiding informed medical decisions and refining treatment strategies.

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