Efficacy of repeated pronations in patients affected by COVID-19-related acute respiratory distress syndrome: think it twice!

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Abstract

Prone position is widely used to ameliorate gas exchange in severe COVID-19-related ARDS (CARDS), through its beneficial effects on shunt and dead space. However, the effectiveness of repeated pronation has never been explored in this category of patients. We then retrospectively analyzed the changes of the alveolar-arterial oxygen gradient (A-aO_2grad), as shunt index, and the ratio $EtCO_2/p_aCO_2$ ratio, as dead space index, during repeated pronation cycles in 7 patients with CARDS admitted to our intensive care unit. The A-aO_2grad decreased significantly more during the first pronation than the second (-43.6% *vs* -12.2% - p0.008) and, similarly, the improvement was maintained only after the first supination (-26.2% *vs* +9% - p0.04). The $EtCO_2/p_aCO_2$ ratio showed similar behavior but did not achieve statistical significance. Considering our findings, with the inherent limitations of the study, since pronation entails risks for the patient, as well as requiring a lot of effort from the nursing staff, further caution appears to be necessary in indicating pronation.

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Introduction

As part of management strategies for severe respiratory failure, prone positioning has been shown to improve the mismatch between ventilation and perfusion (V/Q) and, consequently, gas exchanges.[1] Dependent lung tissue is recruited and lung secretion drainage is promoted.[2-4]

Several multicenter studies and meta-analyses have shown that the application of long sessions in the prone position, together with lower tidal volume and continuous intravenous infusion of muscle relaxant, are the most important strategies leading to a reduction in overall mortality in patients with ARDS.[5,6]

However, the mechanisms leading to these effects are not fully understood.

The advantages of prone positioning are widely exploited for the treatment of COVID-19-related acute respiratory distress syndrome;[7,8] however, little is known about the efficacy of repeated cycles on lung shunt and dead space. Our aim is to analyze the efficacy of repeated pronation in early COVID-19-related pneumonia.

Materials and Methods

We conducted a retrospective study on patients admitted in the ICU of Bufalini Hospital in Cesena, Italy, from 03/03/2020 to 09/05/2020. We enrolled mechanically ventilated adult patients who underwent at least two cycles of prono-supination within the first five days of ICU hospitalization. As standard of care, we set minimum F_iO_2 to achieve $p_aO_2 \geq 70$ mmHg and minute ventilation to maintain pH ≥7.25 or p_aCO_2 <70 mmHg. We registered end-tidal CO_2 ($EtCO_2$) and arterial blood gas analysis just before every decubitus change and one hour after supination. Finally, we calculated shunt in terms of alveolar-arterial oxygen gradient (A-aO_2grad), computed as

$[(F_iO_2) \times (\text{atmospheric pressure} - H_2O \text{ pressure}) - (p_aCO_2/0.8)] - p_aO_2$

$EtCO_2/p_aCO_2$ ratio ($EtCO_2/p_aCO_2R$) was used as a surrogate of pulmonary dead space.

Results

Data were fully available for seven patients; only two of them underwent more than two prono-supination cycles, so these records were excluded from the analysis. Median pronation time was 23 (IQR 6) hours for the first cycle and 18 (IQR 4.5) hours for the second one (p=0.13). In order to better understand the effect of the single pronation maneuver, we have analyzed the variation of the indices cited above during the pronation (difference between end of supination and end of pronation) and between the same (difference between end of supination and one hour after end of pronation). Along the first pronation, median $A\text{-}aO_2$grad decreased from 369.3 (IQR 293) to 208.4 (IQR 146.4) mmHg and $EtCO_2/p_aCO_2R$ increased from 0.72 (IQR 0.26) to 0.84 (IQR 0.08); one hour after supination $A\text{-}aO_2$grad was 272.6 mmHg and $EtCO_2/p_aCO_2R$ was 0.83. The second cycle led to a median $A\text{-}aO_2$grad reduction from 298.8 (IQR 95.2) to 262.4 (IQR 147.6) mmHg, while $EtCO_2/p_aCO_2R$ raised from 0.81 (IQR 0.06) to 0.84 (IQR 0.11); $A\text{-}aO_2$grad and $EtCO_2/p_aCO_2R$ were, respectively, 325.8 mmHg and 0.76 one hour after supination. The major procedure-related complications were pneumothorax (1 case) and accidental ventilator disconnection with sudden severe desaturation (1 case), the former drained and the latter resolved with a recruitment maneuver.

Discussion

The inflammatory state consequent to SARS-CoV-2 infection leads to a pulmonary epithelial and endothelial damage, with deleterious effects on gas exchange and pulmonary vascular resistance (*i.e.*, V/Q ratio).[9] Pulmonary shunt and respiratory dead space are difficult to evaluate bedside, as their quantification requires advanced instruments and highly invasive devices. Hence, we focused on the variation of $EtCO_2/p_aCO_2R$ for respiratory dead space and $A\text{-}aO_2$grad for pulmonary shunt, which are more clinically suitable.[10,11]

$A\text{-}aO_2$grad decreased by 43.6% at the end of the first pronation, while the reduction was 12.2% with the second cycle (p=0.008, Mann-Whitney test). This trend is confirmed by the improvement of $EtCO_2/p_aCO_2R$ (+15.6% after the first cycle, +3.7% after the second one – p=0.16). It is interesting to note that the most marked improvement that occurs during the first pronation is reflected also at the moment of supination: the improvement of $A\text{-}aO_2$grad, meant as the difference between before the pronation and an hour after the supination, is significantly higher after the first cycle than the second (p=0.04) (Figure 1). Also from this point of view $EtCO_2/p_aCO_2R$ confirms the trend improvement, although not reaching the significance (p=0.10) (Figure 2).

The lesser duration of the second pronation does not seem to be correlated to its minor efficacy; indeed, there is no correlation between the pronation length and $A\text{-}aO_2$grad and $EtCO_2/p_aCO_2R$ in the first cycle (respectively, *Spearman's rho* 0.41 and 0.45), even less in the second one (respectively, *Spearman's rho* -0.19 and -0.45).

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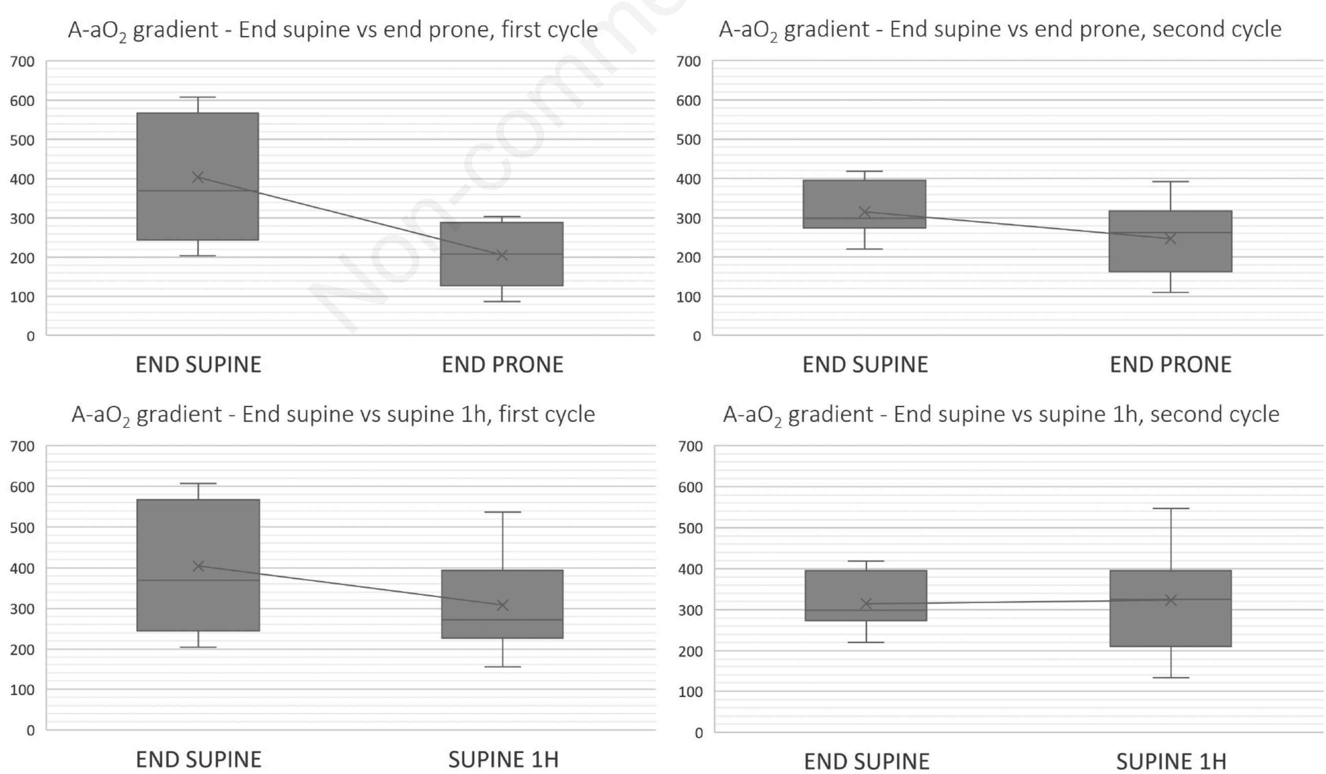

Figure 1. $A\text{-}aO_2$ gradient variations during the pronation and one hour after supination in the first and in the second prono-supination maneuver.

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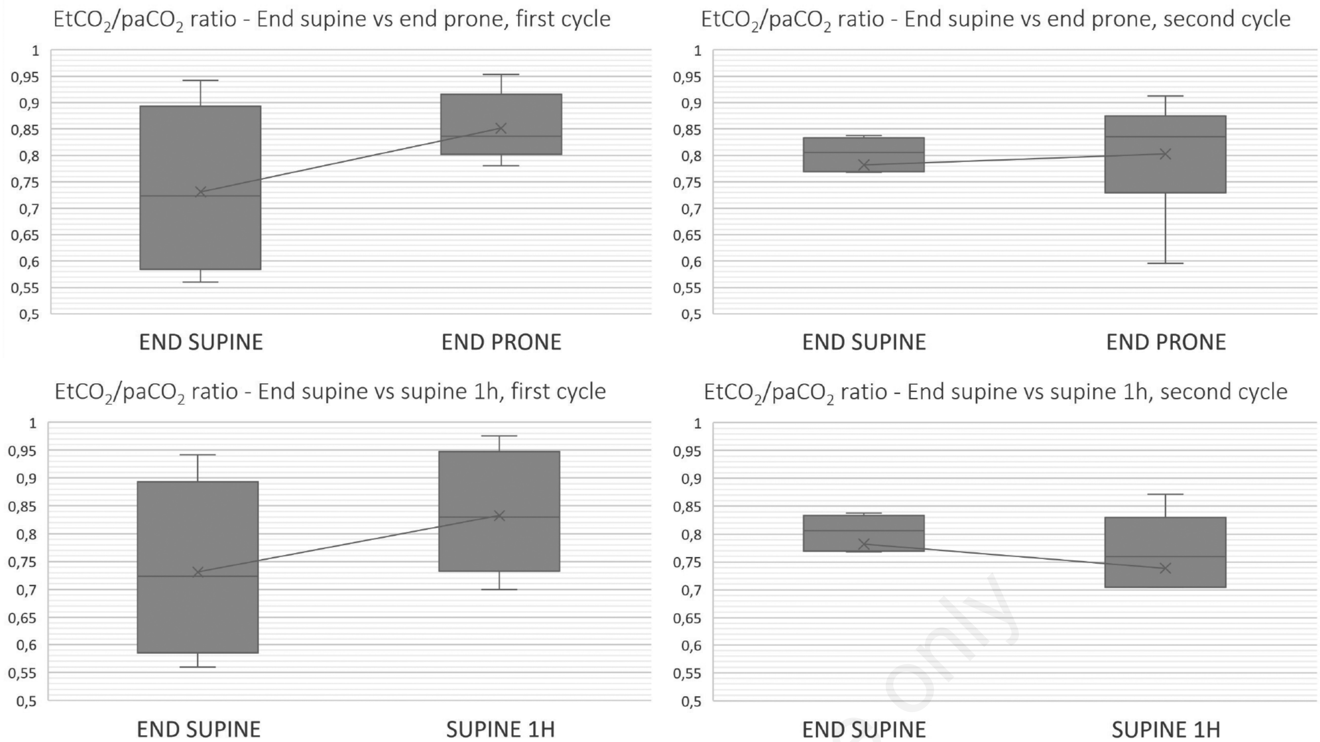

Figure 2. $EtCO_2/paCO_2$ ratio variations during the pronation and one hour after supination in the first and in the second prono-supination maneuver.

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Conclusions

The little amount of data limits the statistical significance of our study; nevertheless, our work gives new insights on the suitability of repeated pronation maneuvers. Although simple, the pronation is not free of complications and requires an additional burden in an over-ceiling work environment, such as during the COVID-19 pandemic.

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