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### Letter to the Editor

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# Non-invasive respiratory supports on inspiratory effort in Covid-19: how and when is it matter of selection?

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Dear editor,

Non-invasive respiratory support (NRS) strategy has been widely used in management of Covid-19 acute respiratory failure (ARF) in order to avoid mechanical ventilation. However, there is an increasing attention about the potential risk of developing Ventilator Induced Lung Injury (VILI) or Patient Self-Induced Lung Injury (P-SILI) during NRS and the debate is still ongoing.

We have read with great interest the study of Schifino et al. This study, to the best of our knowledge, is the first that makes a comparison between high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP) and non-invasive ventilation (NIV) in Covid-19 ARF, measuring respiratory mechanics parameters. The authors showed that the inspiratory effort progressively decreased in treatment with Venturi Mask (VM), HFNC, CPAP and NIV. Moreover, only NIV demonstrated to significantly reduce the tidal change in esophageal pressure ( $\Delta$ Pes) and so the inspiratory effort, leaving transpulmonary pressure constant, under the limit that have been considered safe in order to prevent lung damage. The authors also reported better gas exchange during CPAP and NIV with higher PaO2/FiO2 in comparison with VM [1].

Albeit several studies reported outcome data in patients with Covid-19 ARF treated with NRS, there is still a paucity of high-quality evidence and the main randomized control trials have shown in part contradictory results. The HENIVOT trial demonstrated no difference between helmet NIV (H-NIV) and HFNC in respiratory support-free days. This observation could be influenced by the absence of a control group receiving standard oxygen therapy. Nevertheless, two of the secondary outcomes (rate of endotracheal intubation and median number of days free of invasive mechanical ventilation) were respectively significantly lower and higher in patients treated with H-NIV than with HFNC [2]. In the Recovery trial, CPAP, but not HFNC, reduced the composite outcome of tracheal intubation or mortality within 30-days compared with conventional oxygen therapy [3].

The pathogenesis of lung damage in Covid-19 ARF and if it could lead to a "classical" form of acute respiratory distress syndrome (ARDS), are still matter of debate. The mechanisms of lung injury progression in Covid-19 ARF is an emergent issue and the high inspiratory effort could play an important role in this process.

The study of Schifino et al. adds important information in the comprehension of respiratory mechanics during NRS treatment in Covid-19 ARF. The study population was classified as moderate-severe ARDS in early phase according to PaO2/FiO2 and imaging. Moreover, the value of inspiratory effort was found quite lower than that reported in "classical ARDS" (1). Tonelli et al. have shown that the inspiratory effort in Covid-19 ARF was lower than in non-Covid-19 one, suggesting a complex pathogenesis of hypoxemia in the patient involving also low ventilation/perfusion (V/Q) ratio and microvascular impairment. Furthermore, as Schifino et al, they described a significant lower inspiratory effort during NIV treatment [4].

In addition, the tree patients of the study of Schifino et al. who failed NRS approach had higher value of inspiratory effort that did not show a reduction during NIV trial before intubation [1]. The conclusions of the study, in our opinion, underline the importance of early monitoring of respiratory mechanics during NRS treatment. The changes in the inspiratory effort, controlled through  $\Delta$  Pes, could be an interesting parameter to investigate in the monitoring of NRS response during Covid-19 ARF treatment.

In the study of Schifino et al., patients were treated and monitored in supine position, according with the early stage described in Computed Tomography scans. The use of awake prone position (PP), in combination with different NRS in ARF Covid-19 patients, was reported in literature with various results. Ehrmann et al., in a meta-trial of six randomised controlled open-label superiority trials, showed that awake

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Abbreviations: NRS, Non-invasive respiratory support; ARF, Acute Respiratory Failure; VILI, Ventilator Induced Lung Injury; P-SILI, Patient Self-Induced Lung Injury; HFNC, High-flow Nasal Cannula; CPAP, Continuous Positive Airway Pressure; NIV, Non-invasive ventilation; VM, Venturi Mask; H-NIV, Helmet non-invasive ventilation; ARDS, Acute Respiratory Distress Syndrome; PP, Prone Position;  $\Delta$ Pes, Tidal change in esophageal pressure; V/Q, Ventilation/Perfusion.

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PP in Covid-19 patients treated with HFNC significantly reduced the risk of intubation or death in comparison with standard care [5]. Yoshida et al. reported data about the respiratory mechanics changes during PP in awake ARDS patients. They showed that PP improves oxygenation, gives a more homogeneous distribution in lung aeration and reduces the inspiratory effort, dynamic lung stress and systemic inflammation [6]. PP could have a positive impact in respiratory mechanics for several reasons: recruitment of dependent lung regions, a more homogeneous distribution of V/Q ratio, alleviation of mediastinum's compression of dorsal lung regions and change in chest wall elastance. The aforementioned physiopathological changes induced by PP could improve oxygenation and consequentially the need of different NRS. Although the data in Covid-19 ARF patients are limited, awake PP could reduce the risk of effort-dependent lung injury in moderate-to-severe ARDS especially in patients with mainly consolidative patter and extended pulmonary involvement.

Further studies in respiratory mechanics are needed during NRS in Covid-19 ARF patients to better understand the early signs of excessive respiratory effort and their relationship with clinical outcomes in order to minimize the risk of VILI/P-SILI and progression of lung damage.

### **Declaration of Competing Interest**

the authors declare they have no conflict of interest.

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