LETTER TO THE EDITOR

Author Response: Can Early Use of High-flow Nasal Cannula with Improved Study Design Make a Statistically Significant Difference in the Rate of Intubation in Patients with Post-traumatic Lung Contusion?

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Keywords: Acute lung injury/acute respiratory distress syndrome, Endotracheal intubation, High-flow nasal cannula oxygen therapy, Lung contusion, PaO_2/FiO_2 ratio.

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Dear Editor,

We appreciate the opportunity to respond to the critical appraisal by Sharma S, et al. regarding our recently published manuscript: "Impact of the Early Use of High-flow Nasal Cannula in Patients with Post-traumatic Lung Contusion: A Randomized Clinical Trial".[1,2] We acknowledge the reviewers' insightful critique and welcome the discussion on this important topic, as it allows for a deeper understanding of the challenges and potential benefits associated with the early application of nasal cannula in patients with post-traumatic lung contusion. Likewise, we appreciate the reviewers' efforts in analyzing our study with a critical lens and providing thought-provoking perspectives that will contribute to the ongoing dialogue in this field. Our study evaluated early high-flow nasal cannula (HFNC) therapy in post-traumatic lung contusion. To maintain clarity and avoid an overly lengthy manuscript, not every detail was included; however, key aspects such as patient selection, treatment protocols, and escalation criteria were carefully considered. We would like to clarify several key points:

Per protocol, hemodynamically stable patients underwent chest computed tomography within the first hour of emergency admission. Exclusion criteria eliminated confounders such as facial trauma, airway obstruction, chronic lung disease, hemodynamic instability, impaired consciousness, emergency surgery, flail chest, or non-respiratory intubation. In the intensive care unit, lung contusion diagnosis was established, though manifestations could take 24–48 hours to develop.[3] A reassessment protocol included repeat imaging for unexplained or worsening hypoxia to monitor lung injury progression.

Before randomization, oxygen was administered in the Emergency Department (ED) using a simple mask at 10 L/min to maintain saturation above 94%. Upon ICU admission, oxygen delivery was standardized: The Venturi mask group received oxygen titrated according to standard settings (such as 60% at 15 L/min), while the HFNC group started at 60% FiO_2, adjusted as needed.

Patients with a PaO_2/FiO_2 ratio of 200–300 met the Berlin criteria for mild ARDS and were managed with low-flow nasal prongs at FiO_2 30–40%, as higher concentrations offered no added benefit and posed a hyperoxia risk. High-flow nasal cannula was reserved for more severe cases, while those maintaining oxygenation at lower FiO_2 levels recovered spontaneously within 3–5 days without advanced interventions. Patients with PaO_2/FiO_2 <100 were excluded as they typically require invasive ventilation. The study focused on moderate hypoxemia to evaluate responses to different interventions.

This study was open labelled. Randomization was conducted via a blind card polling method for unbiased allocation. Escalation was based on worsening hypoxia and increased work of breathing (WOB) to prevent self-inflicted lung injury. Regarding sample size calculation based on Frat JP et al.,[4] we used data from patients with a PaO_2/FiO_2 ratio below 200, as shown in Table 2 of Frat's study we applied the adjusted odds ratio from the same Table: 2.14 (95% CI: 1.08–4.22) using the Hsieh formula.[5]

Intubation was less frequent in the HFNC group (three cases, all on day two) compared to the Venturi mask group (nine cases: two on day one, four on day two, two on day three, and one on day four). However, this difference was not statistically significant, as disease progression primarily dictated the need for intubation, with supportive interventions rather than therapeutic measures being applied. Notably, the study postulates that the PEEP effect of HFNC may help mitigate self-inflicted lung injury.[6] These findings seem logical, as lung contusion typically presents within hours of trauma, with a peak of hypoxemia occurring around the second day post-injury.[7] Although daily intubation data were recorded, formal time-to-event analysis was not conducted due to violation

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of key assumptions for survival analysis, including non-proportional hazards and insufficient event frequency for robust estimation across time points.

Adequate analgesia was ethically ensured for all patients as a fundamental component of trauma management, with thoracic epidural analgesia being the primary regional technique, particularly for those with rib fractures. However, in cases of hemodynamic instability or increased risk of epidural hematoma especially in patients receiving anticoagulation or massive transfusion continuous erector spine plane block or thoracic paravertebral block was preferred.[8,9]

Mobilization was unhindered for HFNC patients due to long pipeline oxygen connections. Venturi mask users had brief disconnections during oral intake or hygiene, but documenting these in 120 patients was impractical. Also, patients were advised to keep their mouths closed to optimize positive end-expiratory pressure, but continuous adherence monitoring was unfeasible. Persistent mouth opening with nasal flaring and accessory muscle use signaled worsening respiratory failure.

The study patients exhibited a smooth recovery of hypoxemia without significant weaning failure from HFNC or Venturi mask, which is the usual course of lung contusion.[10] Strict adherence to infection control policies, combined with the absence of patient risk factors, ensured that no cases of nosocomial pneumonia occurred. Mortality in this cohort was due to trauma-related complications, not respiratory issues. All patients completing the intensive care unit course were tracked through the thoracic surgery outpatient clinic, ensuring no censoring.

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