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Re: Manuscript no. 47181

Title: Independent Lung Ventilation: Implementation Strategies and Review of Literature

Dear Editor,

We thank you for the opportunity to submit this revised version. Below we provide a point by point response to the reviewer's comments in blue font. Also, we attach the revised manuscript with changes in red font.

In addition, we have made the requested alterations in format, specifically, running title, changing reference format, adding OCID, conflict of interest form, (decomposable) figures in .ppt format, adding author contribution, author affiliations in specified format, core tip and audio core tip.

We look forward to a favorable response.

Sincerely,

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Reviewer comments:

The manuscript is well written and widely describe the reality of the ILV in the actual ICU world.

1. My suggestion is to include some pediatric data being this manuscript a review (Di Nardo et al. Independent lung ventilation in a newborn with asymmetric acute lung injury due to respiratory syncytial virus: a case report. J Med Case Rep. 2008 Jun 19;2:212. ; Plotz FB, Hassing MB, Sibarani-Ponsen RD, Markerhorst DG. Differentiated HFO and CMV for independent lung ventilation in a pediatric patient. Intensive Care Med. 2003; Di Nardo et al. Single lung ventilation associated to ECMO: an alternative approach to manage ventilator-induced lung injuries in infants. Minerva Anestesiol. 2019 Jan;85(1):90-91;)

Response:

Thank you so much for drawing our attention to this. We have now added pertinent references to the introduction. Also, we have added information on lung isolation in pediatrics. However, we have refrained from providing a detailed discussion on pediatric lung isolation and independent lung ventilation. Since, this review mainly focuses on adult population and a detailed discussion on pediatric ventilation strategies would be beyond the scope of this review. However, we have added references which will guide interested readers to the appropriate articles.

Introduction, page 6, para 1

These are mostly confined to case reports or small case series, but span a variety of patient populations, including medical^[1-3], surgical^[4-6], pediatric^[7-10], and trauma^[3, 11].

Discussion, page 10, para 1

Since the smallest available DLT (26F, outer diameter- 8.7mm) is recommended for patients between 8 and 10 years of age^[23], endotracheal intubation with two single lumen tubes is the only way to achieve ILV in younger pediatric patients^[9].

2. I would suggest to Stress the importance of this technique where ECMO is not available (low income countries...most of the literature comes from India for example)

Response:

Agreed. That is an important consideration. We have added the following in discussion and conclusion to reiterate this point.

Discussion, page 9, para 2

In addition, ECMO requires a dedicated team and advanced institutional capabilities, which might not be available in resource poor locations.

Conclusion, page 20, para 1

ILV is likely the most optimal way to provide lung protective ventilation in patients with severe unilateral lung pathology, thereby avoiding ECMO, which is more invasive and unavailable in resource poor locations.

3. I would be moderate to suggest ILV for the management of PGD; there is only one paper of Snell G, but actually the use of more marginal donor lungs often compromises bronchial healing and increase postoperative complications. The preferred strategy is to move directly to VV-ECMO being ILV a long treatment with chances of further injuries to the lung.

Response:

We understand your concerns. We have now added the following sentence to inform readers about these concerns.

Discussion, page 8, para 3

ILV has been reported to be useful in patients who develop primary graft dysfunction following single lung transplantation, resulting in a poorly compliant graft lung and a native lung with markedly different lung mechanics^[5, 21]. However, the data on single lung transplantation is from one center, and other factors including the role of early extracorporeal membrane oxygenation (ECMO), and effect of double lumen tube (DLT) on bronchial anastomotic healing needs to be considered.

4. Among the modes of ventilation you should be spent a word on HFOV.

Response:

We have now added the following on HFOV.

Discussion, page 16, para 2:

These include assist control volume or pressure ventilation, pressure support ventilation, or high frequency oscillatory ventilation...

... Though various studies have shown no mortality benefit with using high frequency oscillatory ventilation in severe ARDS^[30], its role when preferentially applied to the diseased lung in ILV is uncertain.