

Peer Review File

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Reviewer A

The authors were able to demonstrate that HFNC improved respiratory condition in patients in immediate postoperative period after esophagectomy using ROX index as an objective indicator.

I would like the authors to elaborate on a few details:

Given that improved outcomes shown in patients that received HFNC was a decrease in the incidence of acute respiratory failure, the authors should describe in a more detail the circumstances of the cases that developed ARF in the historical cohort

Author's reply: thank you. Through your question, we realized that we did not sufficiently specify that the historical cohort included patients from May 2021 and then went backwards until we reached the required sample size (May 2020). Consequently, the only change in the treatment of these patients was the adoption of HFNC after May 2021.

However, to give further details as requested by the reviewer, we added some details in the revised version of the manuscript as follows: "The five patients to whom ARF was diagnosed developed low oxygen saturation ($SpO_2 < 92\%$) after 46 [40-54] hours from extubation. Bacterial pneumonia was diagnosed in 3 of them, and antibiotic treatment improved the condition. For the remaining two patients, a negative CT scan ruled out pulmonary embolism but revealed large right atelectasis, so fiberoptic bronchoscopy revealed bronchial obstruction due to secretions with subsequent improvement." Please, see page 14 lines 273-278.

How do the authors interpret that there was improvement in postoperative ROX index but no reduction in postoperative pneumonia?

Author's reply: The ROX index reflects the interplay between oxygenation and respiratory rate, finally giving a summary of respiratory function that can be preserved in the early stages of pneumonia. We should specify that we delivered HFNC 24 hours after extubation, and then patients received standard oxygen therapy as per our routine practice. We argue that 24h could not prevent the onset of pneumonia since it is usually suspected after 48-72h hours from surgery.

Was this the experience of a single surgeon?

Author's reply: yes, it is! The same surgeon (MV) performed all these esophagectomies.

At least 80% of the patients underwent open procedures and yet the authors presented low incidence of respiratory complications which is remarkable. Would HFNC be as useful for patients undergoing minimally invasive esophagectomy?

Author's reply: we have just started recruiting patients undergoing MIE in an ongoing study exploring this item (clinicaltrials.gov NCT05718284). We hope to answer the reviewer's question in a few months!

Reviewer B

In this article, the effect of the early use of HFNC after esophagectomy is analyzed.

I think this study is valuable because postoperative respiratory complications are troublesome and critical for the patients who underwent esophagectomy. However, it has a lot of points to be revised.

1. Page 5 "Surgical characteristics" section

Surgical procedure, especially for upper mediastinal manipulation, is very important because it affects postoperative respiratory status. The author should describe in detail.

Author's reply: thank you, we provided a more detailed description in the revised version as specified in page 8 lines 138-155.

2. Page 9 "Line 241-241. "In the remaining (35%), gas flow or temperature was reduced to achieve the patients' comfort."

Many patients could not handle the distress of HFNC. I think it is important for validating the efficiency of HFNC.

Author's reply: you are right! However, in our study, none of the patients in the HFNC cohort discontinued or refused the treatment because it was intolerable. Only a reduction in gas flow rate or temperature was adopted; we cannot exclude that if a higher gas flow rate would be tolerated, the efficacy of HFNC could have been improved.

3. Page 9, line 245-247.

I cannot find any statistical trend. Moreover, the number of "Surgical" complications does not coincide. × table 5 → ○ table 4

Author's reply: thank you for the comment. For statistical trend, we mean a tendency toward a statistically significant with a lower ARF rate in the HFNC than HC (p 0.06). Nonetheless, we modified the revised version of the paper accordingly. Regarding the number of complications, you are right!

We corrected the table. Please accept our apologies.

4. Page 19, Table 1. ARISCAT score and SpO₂/FiO₂

Are the P-values correct?

Author's reply: we corrected the p values as 0.70 and 0.60, respectively.

5. Page 20, Table 2.

Among 31 HFNC patients, 30 patients underwent neoadjuvant chemotherapy or chemoradiotherapy. Even if the clinical stage was I. neoadjuvant therapy is done?

Author' reply: yes, it is!

6. Page 21, Table 3. PEEP_{THOR}(cmH₂O)

Is the P-value correct?

Author's reply: yes, it is!

Minor

- nasal googles → nasal goggles

Author's reply: we modified accordingly!