

## Peer Review File

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### Reviewer A

**Comment 1:** I congratulate the superb anesthesiologists and surgeons of the Shanghai Chest Hospital for collecting a large series of CRR patients and compared the results of HFJV and cross-field ventilation. The finding of non-inferior results of HFJV and that there was a case that HFJV actually helped a patient who did not do well on cross-field ventilation confirmed that HFJV is a valuable tool in the anesthetic technique in these challenging surgeries. This is a great contribution to the literature in this field.

Only minor English editing needed.

**Reply 1:** Thanks for your appreciation of our work. As you mentioned, we performed a series of CRR in past several decades and accumulated some experience in CRR. Recently, we made some endeavors to introduce minimally invasive procedures that urged anesthesia and airway management to change accordingly. HFJV combined our modified exchange tube indeed provides more surgical field without interrupting surgical manipulation and are used more than ever in eligible patients. Because these procedures are performed infrequently at most centers, there are lack of standard in airway management, especially in the era of VATS. We hope we can share our experience with thoracic surgeons and anesthesiologists.

**Changes in the text:** We checked and fixed the typos and grammar mistakes. Thank you for pointing it out.

### Reviewer B

Carinal resection is a technically challenging procedure. Although it has been performed for over 70 years, only recently have acceptable morbidity and mortality rates been achieved. Airway management is especially paramount in tracheobronchial surgery. Cross-field ventilation through an additional port remains a universally accepted strategy during VATS carinal resection. Authors presented a unique experience in usage of HFJV as well as cross-field ventilation during complex carinal procedures in 32 patients. There are some minor shortcomings:

**Comment 2:** Consider moving Patient characteristic section from Results to Methods and combine with appropriate sections. Readers have to read 4 pages to see important numbers.

**Reply:** Thanks for your advice.

**Changes in the text:** We combined the patient characteristic section and deleted “Patient characteristic” in Methods section.

**Comment 3:** Page 7, line 158: Could you explain more about criteria for VATS vs. open approach?

**Reply:** CRR is a relatively challenging procedure in surgical field. The rise of minimally invasive surgery has made it possible to be performed under VATS with careful selection. CRR can be accomplished under VATS based on institutional experiences. Our selection criterion are as follows: when tracheal lesions are in the lower third of the tracheal or distal lesions involving the carina, and lesions relatively limited, or length of tumor less than 2 cm and tracheal resection less than 3 cm, and predicted tension on the site of the anastomosis is favorable.

**Changes in the text:** We added the changes in Methods, Page 8, line 199-205.

**Comment 4:** Page 9, line 192: how many patients (%)? (combine with line 232 as mentioned before)

**Reply:** 32 (39%) patients were included in the final analysis.

**Changes in the text:** We added the percentage in Result section, patients' demographics. Result, Page 12, line 290-295.

**Comment 5:** Page 11, line 233: how many male/female? p value?

**Reply:** We have the data of sex in Table 1. P value=0.267.

**Changes in the text:** We added all P value in Table 1.

<b>Sex (Male,</b>	<b>8 (36.4%)</b>	<b>6 (60%)</b>
<b>N %)</b>		

**Comment 6:** Page 12, line 262: p value?

We added all the P value in Table 1.

Variables	Cross-field ventilation group (n=22)	HFJV group (n=10)	P-value
Age, years	44±15	51±15	<a href="#">0.180</a>
Sex (Male, N %)	8 (36.4%)	6 (60%)	<a href="#">0.267</a>
Height (cm)	162.14±8.55	167.30±10.07	<a href="#">0.140</a>
Weight (Kg)	65.0±13.16	66.9±12.24	<a href="#">0.702</a>
ASA (II/III), n	8/14	5/5	<a href="#">0.699</a>
<u>Pathologic diagnosis</u>			<a href="#">1.000</a>
Squamous cell carcinoma	4( <a href="#">18.2%</a> )	1( <a href="#">10%</a> )	
Adenoid cystic carcinoma	18(81.8%)	9(90%)	
Surgical type, n (%)			<a href="#">0.001*</a>

**Comment 7:** Page 13, line 269-274: move to Conclusion

**Reply:** We agree with you and moved this sentence to Conclusion in Abstract.

**Comment 8:** Page 13, line 281: reference?

**Reply:** Thank you for pointing it out.

**Changes in the text:** We added ref 1.

**Comment 9:** Page 13, line 286: VATS abbreviation has never been defined before

**Reply:** Thank you for pointing it out.

**Changes in the text:** We have changed “under thoracoscopic-assisted procedures” in line 86 to “using video-assisted thoracoscopic surgery (VATS)”.

**Comment 10:** Please check your Figure 1, pictures and description don't match.

And some correction in the text:

**Reply:** We revised Figure 1. Please check the resubmitted version.

Page 23. Fig B. The distal end of the modified exchange tube which was placed in the left main bronchus.

**Comment 11:** line 86: consider paraphrasing, “under thoracoscopic-assisted procedures” sounds odd: using thoracoscopic-assisted techniques

**Reply:** Thank you for pointing it out.

**Changes in the text:** We have changed “under thoracoscopic-assisted procedures” to “using video-assisted thoracoscopic surgery (VATS)”.Page 5, line 92-93

**Comment 12:** Page 5, line 107: “to control oxygenation”

**Reply:** We deleted the “of”.

**Changes in the text:** Please check the revision in Page 6, line 126.

**Comment 13:** Page 8, line 176: consider paraphrasing “the airway was switched back to ventilating from above”: the tube was positioned above the anastomosis

**Reply:** We changed the sentence.

**Changes in the text:** We revised the sentence. “HFJV continued until the anastomosis was complete, and then switched back to LMA or ETT until the end of anesthesia.” in Page 9, 238-240.

**Comment 14:** Page 8, line 187: consider paraphrasing “HFJV didn’t interrupt the surgical sutures”: HFJV didn’t interrupt the bronchial anastomosis part / bronchial suturing.

**Reply:** We changed “HFJV didn’t interrupt the surgical sutures” to “HFJV didn’t interrupt the bronchial suturing”. Page 9, 236.

**Comment 15:** Page 11, line 233: “There were no significant differences”

**Reply and Changes in the text :** We changed to “There was significant difference of surgical approach two groups ( $P < 0.05$ )”. Page 12, line 297-298.

**Comment 16:** Page 13, line 288: either “under” or “in”

**Reply and Changes in the text:** Thanks for your careful review and we deleted “in”. Page 14, line 369.

**Comment 17:** Page 14, line 319: consider change “about” to “approximately”

**Reply and Changes in the text:** We changed “about” to “approximately”. in Page 16, line 420.

**Comment 18:** Page 15, line 329: “there are limited significant experience to determine which airway management approach should be preferred”

**Reply and Changes in the text:** “Because open or thoracoscopic CRR was performed infrequently at most centers, there were limited experience for anesthesiologists to select the more appropriate airway management.” Page 16, 434-436

**Comment 19:** Page 15, line 331: comma is unnecessary

**Reply and Changes in the text:** We delete the comma. Page 17, 451.

## **Reviewer C**

The authors describe a retrospective study in single institution to compare HFJV with

cross-field intubation in CPR. As HFJV provides an advantage during tracheal anastomosis even in VATS, it may be potentially adopted as a routine airway method. This manuscript presented interesting data about the HFJV with AUC of SpO<sub>2</sub> during operation, but I have some questions about the study.

**Comment 20:** Firstly, SpO<sub>2</sub> is important parameter during operation, but the accumulation of CO<sub>2</sub> result from insufficient ventilation is also the problem with HFJV. Do you monitor CO<sub>2</sub> using capnometer or blood gas during HFJV? Is it any difference between HFJV and conventional cross-field ventilation ?

**Reply:** Thank you for your question. We admit that ETCO<sub>2</sub> or PaCO<sub>2</sub> is good indicator to detect accumulation of CO<sub>2</sub>. During either HFJV or conventional cross-field ventilation, ETCO<sub>2</sub> monitoring becomes inaccurate; therefore, we intermittently draw blood gas to check PaCO<sub>2</sub>. Since this was a retrospective study, we couldn't accurately compare PaCO<sub>2</sub> between the two groups because the blood samples were not drawn at fixed time.

**Changes in the text:** We added the discussion of this part in Discussion. Page 16, line 421-429.

**Comment 21:** Additionally, I want to know the basic ventilator setting of HFJV such as driving pressure, inspiratory time and the fraction of inspired oxygen(FiO<sub>2</sub>) to perform safety management.

**Reply:** Thanks for your question. We have all the information at **Methods section, the fourth para:** Ventilation was switched to HFJV when the airway was incised, then HFJV parameters were set to 1 LUMEN CAT MODE and the initial parameters were set as follows: FiO<sub>2</sub> Jet 90%, frequency 100-120, I: E as 1:2 and PHF 0.9-1.2bar. Page 9, line 235-236.

**Comment 22:** Secondly, I consider peri-operative information such as the details of operative methods and surgical complications should be evaluated to compare HFJV with cross-field intubation.

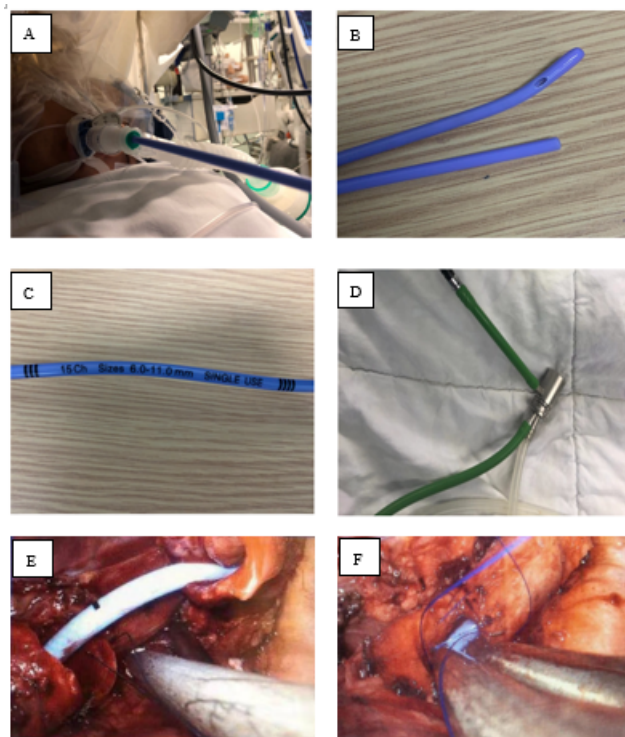
**Reply:** Thanks for your question and we agree with you on this point. Because of the inherent limitation of retrospective study, we couldn't retrieve more surgical information including the time to first anastomosis. For the surgical complications, we have information in "other outcomes in result section": "There was no significant difference in post-operative hospital stay: 9 [7, 11.5] days in cross-field ventilation and 9 [7, 10.5] days for HFJV. One death and one continuous air leak were observed in the cross-field group while no severe complications occurred in the HFJV group. " We aim to conduct a clinical trial to compare the details of operative methods and surgical complications, but it would be time consuming.

**Comment 23:** Finally, what are the measures to be taken when SpO<sub>2</sub> is 85% or less during VATS surgery? Do you have any criteria and preparations for switching from HFJV to cross-field intubation?

**Reply:** The threshold of “safety zone” has no definite answer and more dependent on institutional cooperation and experience. In CRR, SpO<sub>2</sub> below 80% or less is our safety limit. When SpO<sub>2</sub> could not be kept above 80%, anesthesiologists on site might adjust the HFJV parameters (Methods, the fourth para) and meanwhile surgeons will help check the distal end of HFJV catheter. If it also failed, we would switch to cross-field intubation or insert another ETT into right bronchus.

**Comment 24 :** Additionally, in Fig-1, alphabet(A, B,G,H,I,J)in the figure legends doesn't match with the figure.

**Reply:** Please check this revised version.



**Figure 1.** HFJV combined with an exchange tube

- A. The proximal end of the exchange tube connected to LMA or ETT.
- B. The distal end of the modified exchange tube which was placed in the left main bronchus.
- C. The length and outside diameter of the modified exchange tube.
- D. The proximal end of the exchange tube was connected to HFJV adaptor.
- E. During the anastomosis of posterior tracheal wall, the exchange tube could be continuously in place, without interfering with surgical exposure.
- F. During the anastomosis of anterior tracheal wall, HFJV could still continue in place.

## Reviewer D

Dr. Wu et al presented an interesting study to evaluate the efficacy of HFJV. The study design was retrospective. The authors deserved recognition of establishing a new method of ventilation in carinal resection operations. They should be applauded to carry out safe anesthesia with the novel method for very complex operations.

However, there are several areas in the manuscript needed to be addressed.

**Comment 25.** Carinal resection and reconstruction is almost never an emergent surgery. However, more than 50% of cases were excluded. The reasons for exclusion were not specified. Does over 50% of patients have operation under ECMO, which seems to be very high percentage?

**Reply:** Thank you for helping us clarify the problem. We searched keywords in anesthesia information system (2018/1/1-2021/9/30, elective surgery, carinal surgery or carinal resection and reconstruction, HFJV or cross-field ventilation). In all screened patients, more than 50% of cases were excluded because the surgeries were not classical CRR or partial carinal resection.

**Changes in the text:** We clarify the question in Result, 1<sup>st</sup> para, Page 12, line 290-

296.: “Between January 1, 2018 and September 30, 2021, 82 patients who underwent carinal surgeries were screened from the hospital information system. Among them, 4(4.8%) patients with severe airway obstruction required extracorporeal circulation and 46(56%) patients only received sleeve lobectomy or partial carinal resection without the need of cross-field ventilation or HFJV, 32 (39%) patients were finally included in the analysis.”

**Comment 26.** Selection bias was not addressed. What determined patients receiving cross-field or HFJV?

There are over a dozen surgical approaches in carinal resection and reconstruction. There are multiple patient factors could influence occurrence of intra-operative hypoxia including baseline pulmonary function, BMI, smoking history etc. The sample size is so small and unbalanced that it is impossible to control variables to make statistical analysis meaningful.

**Reply:** Selection cross-field or HFJV is determined by multi-department discussion. Selection bias may exist because patients in cross-field may receive more complicated procedure. Classical CRR is not performed frequently so the sample size was our major limitation. Age, gender, BMI were comparable between the two groups, but other confounders can't be adjusted including baseline pulmonary function, smoking history, etc.

**Changes in the text:** Page 18, line 452-456: We addressed the limitation in Discussion section: Due to its small overall sample size and limited cases of HFJV, selection bias may exist and some confounders like smoking history or pre-operative FEV1 could not be adjusted. Moreover, HFJV was performed by different anesthesiologists and parameters for optimal oxygenation during one-lung ventilation was not standardized. Therefore, large randomized prospective trials are needed for further confirmation.

**Comment 27.** AUC need to better described and explained. AUC should be expressed

as time x (oxygenation level deviated from either 90% or 80%). For example, if patients spent two minutes at oxygenation of 88%, the AUC will be  $2 \times 2\% = 4 \text{ min.}\%$ . Instead, authors only used min (page 11, line 244). Please see your reference 18 to verify.

**Changes in the text:** We re-described AUC in Methods section. Page 11, line 255-258.

“The primary outcome was the severity of intraoperative hypoxemia represented by area under curve (AUC). Intraoperative hypoxemia was defined as  $\text{SpO}_2 < 90\%$  lasting at least for one minute [14]. After removing artifacts, the AUC  $\text{SpO}_2$  was calculated as the area below 90% (AUC was calculated with respect to the x-axis or y-axis. In this analysis, x-axis represented time interval and y-axis represented the  $\text{SpO}_2$  actual value deviated from either 90, AUC was the integration of areas below the 90%). The anesthesia information system recorded  $\text{SpO}_2$  every 10 seconds. The original data were processed by Python and we calculated AUC of intraoperative  $\text{SpO}_2 < 90\%$  based on a previous trial [15].”

**Comment 28.** Typical cross field ventilation would cause fluctuation of oxygenation depending on ventilation or apnea that results in hypoxia. The severity and duration of hypoxia are frequently determined by the comfort level of anesthesia and surgical teams rather than the method of ventilation, i.e cross-field. During HFJV, since the ventilation is constant, the hypoxia is more determined by patient and ventilation method. With intra-operative hypoxia as primary outcome, it is imprudent to establish one method is better than the other to maintain oxygenation level esp in retrospective study.

**Reply:** Cross-field ventilation is still the golden standard in CRR. As you mentioned, the severity and duration of hypoxia may be determined by the comfort level of the team, so the incidence of hypoxemia is still a major issue due to tolerating periods of apnea. We tried to investigate the safety and feasibility of HFJV in CRR, therefore we selected intra-operative hypoxia as primary outcome. Whether HFJV as a means in one-lung ventilation could achieve equivalent or superior effect compared to cross-field ventilation has not been answered. Although this is a small sample-size study, we do think that our result can provide a novel perspective in air management in CRR.

**Comment 29.** It is impractical to establish either superiority or non-inferiority of HFJV to cross field with intra-op hypoxia as primary outcomes in 32 patients. The study is more suitable as feasibility study of case series to give more detailed description of patient characteristics such as BMI, PFT etc, intra-operative ventilation, oxygenation, hemodynamic parameters and surgical approaches. HFJV has its utility in thoracic operations, and we should collect as much experience as we can.

**Reply:** CRR is not frequently performed at most centers, therefore we had the limitation in sample-size. For rare procedures, even a small sample may provide new insight in perioperative airway management. We admitted that this was an exploratory study, and we hope a multicenter clinical trial may give the answer in the future.



