

Peer Review File

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Reviewer A

Comment 1: A well written manuscript. I have few queries

Why did you choose aPTT as the means of assessing adequate anticoagulation (page 4 line 120) - is it not appropriate to use ACT rather than aPTT?

Reply 1: Thank you for your valuable comments. What is the more reliable assay to monitoring anticoagulation on ECMO is still debated and practice varies widely among centers. In this study, to reduce the risk of intraoperative bleeding, we applied a “low-intensity” regimen, aiming at aPTT values of 50-60 seconds. For lower levels of heparin infusion, aPTT seems preferable, as ACT at values lower than 225 loses its accuracy. aPTT was measured bedside with a portable device for timely assessment.

Change 1: P8L204-212: “To limit bleeding during surgery, heparin infusion was maintained at low intensity regimen and targeted to an activated partial thromboplastin time (aPTT) of 50-60s [5, 6]. Anticoagulation was measured at the bedside using a portable device (Hemocron Signature Elite, Werfen-Instrumentation Laboratory SpA, Milan, Italy). The aPTT was preferred to the ACT to allow a more precise assessment at lower levels of anticoagulation [14]. Heparin infusion was interrupted during ECMO removal or in case of bleeding. Heparin was continued after surgery and until ECMO was withdrawn and heparin infusion was suspended 30-60 minutes before de-cannulation with no reversal therapy”

P18-19: We add the reference associated at the anticoagulation management:

5. Stephen A Esper 1, Jerrold H Levy, Jonathan H Waters, Ian J Welsby. Extracorporeal membrane oxygenation in the adult: a review of anticoagulation monitoring and transfusion. *Anesth Analg*. 2014 Apr;118(4):731-43. doi: 10.1213/ANE.000000000000115.

6. McMichael ABV, Ryerson LM, Ratano D, Fan E, Faraoni D, Annich GM. 2021 ELSO Adult and Pediatric Anticoagulation Guidelines. *ASAIO J*. 2022 Mar 1;68(3):303-310.

14. J S Reiner 1, K S Coyne, C F Lundergan, A M Ross. Bedside monitoring of heparin therapy: comparison of activated clotting time to activated partial thromboplastin time. *Cathet Cardiovasc Diagn*. 1994 May;32(1):49-52. doi: 10.1002/ccd.1810320112.

Comment 2: one of the main difficulties of ECMO include capillary / venous congestion: how did the author manage this, during dissection of surgical field?

Reply 2: Thank you for your comment. In our series, we did not modify our standard dissection technique and we did not observe any issues about capillary and venous congestion that could increase the bleeding risk. We found that ECMO did not increase the risk of bleeding in the chest or in the neck and also we did not observe oedema, thrombosis, or bleeding or oedema at the site of outflow cannula.

Change 2: no changes.

Comment 3: Any specific note on reversal of anticoagulation at the end of surgical repair when ECMO is weaned off?

Reply 3: Thank you for your question. As We stated in the paragraph methods, reversal is used only in case of bleeding, but in our series we did not observe any case of surgical bleeding at the end of the procedures and then we did not use anticoagulation reversal.

Change 3: P8L211-212: “Heparin was continued after surgery and until ECMO was withdrawn and heparin infusion was suspended 30-60 minutes before de-cannulation with no reversal therapy”

Reviewer B

Comment 1: A well written paper which adds significantly to our knowledge about use of v- ECMO in airway surgery. I would like to know the sizes of used cannulae in both internal jugular vein and femoral vein. These could be added to the table 2.

Reply 1: Thank you for your precious comments and as you suggested, we add the cannulae size into the first column of the table 2 and also this sentence in material and methods: P7 L196 a multistage drainage cannula of 23 or 25 French and an infusion cannula of 17-19F were used according to the size of the patient and the vein diameter determined by ultrasound before cannulation.

Change 1: P7 L196 to P8L197-198: “a multistage drainage cannula of 23 or 25 French and an infusion cannula of 17-19F were used according to the size of the patient and the vein diameter determined by ultrasound before cannulation”.

Reviewer C

Comment 1: Thank you very much for sharing your experience. Obviously this center is highly specialized for tracheal surgery. Could you please share the decision making process in patients with 1- Case 7 and 8 and 9. These are highly complicated situations. Please explain the thought process.

Reply 1: Thank you for your valuable comment. As explained in the paragraph results (P9 and 10) and also into the tables (P21 and 22) the case 8 and 9 were two carinal resections and reconstructions with complete parenchymal preservation (Eschapassee technique). Case 8, in particular, presented tracheal chondrosarcoma recurrence previously treated with tracheal resection through right thoracotomy and in this case we chose the VV-ECMO support to obtain a clean field during the whole dissection and anastomoses in the setting of complete cardio-respiratory stability. The case 7 was a left main bronchus resection with bronchial anastomosis between the carina and the distal part of the left main bronchus with the whole preservation of the left lung in patient who could not tolerate single lung ventilation due to a previous right lower bilobectomy. This patient could not undergo to one-lung ventilation and then the only way to ensure adequate gas exchange was an ECLS support. We chose VV-ECMO technique because an hemodynamical support was considered not necessary.

Changes 1: we added the reference [15]

Comment 2: From your recommendation I understand that you suggest VV ECMO to all patients with a carina resection. Is this because of the clean operative field only?

Reply 2: Thank you for your thoughtful comment. We selected for ECMO airway surgery only extremely complex cases, for example patient without an adequate reserve, patients not able to tolerate single lung ventilation or patients scheduled for carinal resection with complete parenchymal preservation. VV-ECMO ensured a clean operative field in the setting of complete cardio-respiratory stability, which is highlighted more clearly in the discussion P12L304-309. On the other hand, due to the increased risk of bleeding and increased medical costs, we do not recommend VV-ECMO in every case of standard carinal resection such as carinal sleeve right pneumonectomy. In these cases we perform surgery with standard ventilation strategy such as one-lung ventilation and cross-field ventilation.

Changes 2: we modified the discussion as follows: P12L304-309

Comment 3: Pictures are not at the best quality. Please provide better pictures.

Reply 3: We send all pictures in the original form and in this way the quality should have been improved. Unfortunately, the picture of the endoscopic (fiber-optic bronchoscopy) aspect of the neo-carinal anastomosis has low quality due to the absence of high definition (HD) instrument used to catch this picture.

Changes 3: all the pictures are sent in the original form.

Comment 4: Please mention about the release maneuvers. The focus seems to be ECMO. rather than ECMO, tracheal repair techniques need to be defined here.

Reply 4: Thank you for your precious comment. The objective of our paper is to report and discuss the indication and the usefulness of VV-ECMO support in very selected cases of complex airway surgery. We tried to focus on this topic because, in our opinion, the literature is still lacking on this argument while there are in the literature so many papers concerning surgical techniques of trachea. Regarding the release manoeuvres during the carinal resection with parenchymal preservation (Eschapassee technique), we recently published a surgical case report in which we described every surgical steps of the procedure, including release manoeuvres. For patients who underwent to airway surgery under VV-ECMO for tracheal or main bronchus traumatic laceration, no release manoeuvres were applied. For other cases performed through thoracotomy, we released the airway with the hilar and pericardiac release and then we added this sentence and associated reference to the results (P10L259-260) “In the cases performed by thoracotomy, the tracheobronchial tree was mobilized by releasing the hilum and pericardium “ [He J, Zhong Y, Suen HC, Sengupta A, Murthy RA, Stoelben E, Carretta A, Toker A, Wang C, He J, Li S. The procedure and effectiveness of release maneuvers in tracheobronchial resection and reconstruction. *Transl Lung Cancer Res.* 2022 Jun;11(6):1154-1164. doi: 10.21037/tlcr-22-385. PMID: 35832456; PMCID: PMC9271432.]

Changes 4: we added P10L259-260 “In the cases performed by thoracotomy, the tracheobronchial tree was mobilized by releasing the hilum and pericardium”[16]

Comment 5: Please mention about the management of early postoperative period.

Reply 5: Thank you for your comment. We inserted a short paragraph on this argument in the materials and methods.

Changes 5: P8L213-220: “In the early postoperative period, standard clinical monitoring was performed, including serial blood gas analyses and daily chest X-rays in trans-thoracic patients. If necessary, flexible bronchoscopy was performed to remove secretions. The neck was always kept in a slightly flexed position, with some pillows being used. In selected cases of very complex airway anastomoses or in particularly frail patients, VV-ECMO was prolonged after surgery to ensure safe extubation and to maintain low pressure ventilation on challenging anastomoses. A flexible bronchoscopy was performed before discharge from hospital and on postoperative day 7 to assess regular healing of the anastomosis”.

Comment 6: Discussion needs to be short and focusing tracheal surgery rather than ECMO.

Reply 6: Thank you for your suggestion and we tried to short the discussion, but some arguments need to be deeply discussed (our results, the possibility to prolong VV-ECMO after surgery, indications, advantages, troubles and limits) and in particular we thought that the focus of the whole paper is the application of VV-ECMO to airway surgery and then our objective was to discuss on this.

Changes 6: we deleted these sentences:

“such as previous extensive contralateral lung resection, traumatic disruption of main airways or tumors involving the two bronchial systems precluding safe intubation and ventilation. There are then cases in which the use of ECLS, although not mandatory,”

We inserted this paragraph:

P12L304-320 “In three cases of carinal resection and reconstruction and one case of extended post-tracheostomy stenosis and prior left pneumonectomy, high-flow VV-ECMO achieved through a femoro-jugular cannula was highly effective, allowing apnoea for a median of three hours, avoiding

cross-field ventilation and facilitating surgery with faster and more precise suture placement, as well as stable cardiorespiratory conditions. In order to perform surgery without ventilation, a relatively high ECMO flow of about 4 l/min must be maintained. For this reason, we prefer double venous cannulation and especially the femoral-jugular setting is absolutely appropriate to avoid or minimize recirculation between inflow and outflow. Another significant advantage of ECMO, especially in this configuration, is the possibility of prolonging its use in the postoperative period, allowing the patient to be extubated immediately after the procedure and avoiding mechanical ventilation and the associated mechanical stress on the fresh suture line. In our experience, prolonged ECMO after surgery was required in four cases (cases 4, 5, 6 and 8).”

These results are also possible thanks to a very active collaboration between thoracic surgeons, anesthesiologists and the institutional ECMO team, where all elective cases of complex main airway surgery were discussed in a multidisciplinary meeting.”

We deleted this sentence: “They highlighted that the use of ECMO resulted in better surgical exposure, compared to conventional cross-field ventilation, due to a clean operative field without interfering tubes, which is important for complex resection and reconstruction of carina in a setting of stable cardiorespiratory conditions.”

We add this part of sentence: P13L343 “as in some cases of left carinal resection through sternotomy.”

We deleted this sentence: “VV-ECMO has demonstrated to be a safe and useful approach guaranteeing gas exchange for several hours even without lung ventilation (4 patients).”

We removed this paragraph: “Nowadays, VV-ECMO can be considered the gold standard ventilation strategy in major airway surgery when an ECLS is required [4, 5, 8, 18]. In three cases of carinal resection and reconstruction and in one case of extended post-tracheostomy stenosis and previous left pneumonectomy, high-flow VV-ECMO achieved through femoro-jugular cannulation was very effective allowing apnoea for a median of three hours avoiding cross-field ventilation and facilitating surgery with faster and more precise suture placement, as well as allowing completely stable cardiorespiratory conditions.

In order to perform surgery in the absence of ventilation, it is necessary to maintain a rather high ECMO flow, around 4 l/min. For this reason we prefer double venous cannulation and in particular the femoral-jugular setting is absolutely adequate avoiding or minimizing the re-circulation between inflow and outflow. Another substantial advantage of ECMO especially in this configuration, is the possibility to prolong its use in the postoperative period, allowing the extubation of the patient immediately after the procedure and avoiding the mechanical ventilation and its consequent mechanical stress on the fresh suture line. In our experience prolonged ECMO was required after surgery in four cases.

From our experience, based on 4 cases of carinal left pneumonectomy through median sternotomy, the VA-ECMO could be advisable instead for cases of carinal resection carried out by sternotomy, which requires aorta and superior vena cava mobilization with potential hemodynamic disturbance.”

Comment 7: Highlight BOx messages are more meaningful than the discussion. Please stay aligned with it.

Reply 7: Thank you for your valuable comment and We add the highlight box as the first part of the main text and in our opinion they are completely aligned with the results and discussion and this fact is assured by the use of the same sentences in the box and in the text. We modified the conclusion of the highlight box following the main text conclusion.

Changes 7: P5L135-139: “VV-ECMO enables the safe and precise performance of complex main airway procedures with minimal postoperative morbidity and could be the extracorporeal support of choice in cases that cannot be managed with conventional ventilation techniques.”

Reviewer D

Comment 1: Your manuscript describes well how the intraoperative use of VV-ECMO is an important extension for tracheobronchial surgery. You describe a significant experience of complex procedures, and I must congratulate you on your impressive operative results. As you state by yourself, the small number of cases included in your study depends on the rarity of the treated conditions. This is also the reason for the descriptive character of your study. However, to my point of view, your study lacks necessary requirements of original research and rather works as a case series. Moreover, I have difficulties in finding significant novelty in your results. I would recommend revising the paper according to the following recommendations and resubmit it as a case study/series.

Reply 1: Thank you for your valuable comment and precious advices. We completely agree with you regarding the small numbers of patients included in this study, but it reflects the rarity of this kind of airway surgical procedures performed with ECLS support such as VV-ECMO. Actually, the literature lacks of papers like this in which technical and post-operative results of VV-ECMO in complex airway surgery are completely elucidated and discussed and in our opinion this could be sufficient to consider this paper as an original article. The literature includes several papers of ECMO support in the peri-transplantation period, but few papers are about ECMO in elective thoracic surgery and the largest studies included mostly VA-ECMO [for example Lang G, Ghanim B, Hötzenecker K, et al. Extracorporeal membrane oxygenation support for complex tracheo-bronchial procedures†. *Eur J Cardiothorac Surg.* 2015 Feb;47(2):250-5; Rinieri P, Peillon C, Bessou JP, et al. National review of use of extracorporeal membrane oxygenation as respiratory support in thoracic surgery excluding lung transplantation. *Eur J Cardiothorac Surg.* 2015 Jan;47(1):87-94.].

Changes 1: no changes.

Comment 2: Introduction:

There seems to be an adjective missing in the first sentence. Maybe you meant “most important requirements”?

Reply 2: Thank you for your advice and We are completely agree with you and We changed the first sentence as follows.

Changes 2: P6L147: “The two most important requirements....”

Comment 3: Lines 90/91: “However, despite potential advantages, elective ECMO has been infrequently used in the thoracic surgical population.” Can you please give evidence for this statement?

Reply 3: Thank you for your suggestion, and we added the reference [Rinieri P, Peillon C, Bessou JP, et al. National review of use of extracorporeal membrane oxygenation as respiratory support in thoracic surgery excluding lung transplantation. *Eur J Cardiothorac Surg.* 2015 Jan;47(1):87-94.] to this sentence. The paper by Rinieri et al. reflects the French experience of ECMO in thoracic surgery apart from lung transplantation and the authors reported the outcomes of 36 patients included in a four-year period from 17 centers. I think that this paper well reflects the rarity of the use of ECMO in thoracic surgery excluding lung transplantation.

Changes 3: P6L163 added the reference [Rinieri P, Peillon C, Bessou JP, et al. National review of use of extracorporeal membrane oxygenation as respiratory support in thoracic surgery excluding lung transplantation. *Eur J Cardiothorac Surg.* 2015 Jan;47(1):87-94.].]

Comment 4: Methods:

Line 110: Do you really mean “haematosiis”? I assume you relate to haemostasis, don't you?

Reply 4: Thank you for your comment. Yes I mean haematosiis as a synonym of gas exchange. To reduce this inconvenient, I deleted this word from the paper.

Changes 4: haematosiis has been changed with gas exchange in the whole paper.

Comment 5: Line 114: Please introduce every abbreviation and complete the abbreviation list, e.g. HLS.

Reply 5: Thank you for your comment and We completely agree with you and then We implemented the abbreviation list as you suggested.

Changes 5: the abbreviation list has been implemented and completed.

P24 L584 to P25 L591:

ACT: activated clotting time

aPTT: activated partial thromboplastin time

HLS: Heart-Lung support

IQR: interquartile range

ICU: intensive care unit

HFJV: high flow jet ventilation

NSCLC: non-small-cell lung cancer

ARDS: acute respiratory distress syndrome

Comment 6: Line 120: Why did you use aPTT for monitoring instead of ACT?

Reply 6: Thank you for your question. Please see the Reply to Reviewer A.

Changes 6: P8L204-212: “To limit bleeding during surgery, heparin infusion was maintained at low intensity regimen and targeted to an activated partial thromboplastin time (aPTT) of 50-60s [5, 6]. Anticoagulation was measured at the bedside using a portable device (Hemocron Signature Elite, Werfen-Instrumentation Laboratory SpA, Milan, Italy). The aPTT was preferred to the ACT to allow a more precise assessment at lower levels of anticoagulation [14]. Heparin infusion was interrupted during ECMO removal or in case of bleeding. Heparin was continued after surgery and until ECMO was withdrawn and heparin infusion was suspended 30-60 minutes before de-cannulation with no reversal therapy”

P18-19: We add the reference associated at the anticoagulation management:

5. Stephen A Esper 1, Jerrold H Levy, Jonathan H Waters, Ian J Welsby. Extracorporeal membrane oxygenation in the adult: a review of anticoagulation monitoring and transfusion. *Anesth Analg*. 2014 Apr;118(4):731-43. doi: 10.1213/ANE.000000000000115.

6. McMichael ABV, Ryerson LM, Ratano D, Fan E, Faraoni D, Annich GM. 2021 ELSO Adult and Pediatric Anticoagulation Guidelines. *ASAIO J*. 2022 Mar 1;68(3):303-310.

14. J S Reiner 1, K S Coyne, C F Lundergan, A M Ross. Bedside monitoring of heparin therapy: comparison of activated clotting time to activated partial thromboplastin time. *Cathet Cardiovasc Diagn*. 1994 May;32(1):49-52. doi: 10.1002/ccd.1810320112.

Comment 7: Discussion:

Lines 193-195: “These outcomes are the direct consequence of a precise algorithm for patients’ selection and a very active collaboration between thoracic surgeons, anesthesiologists and institutional ECMO team.” What characterizes your precise algorithm for patient selection and the

very active collaboration? Please elaborate on what makes your approach special in comparison to other protocols for the intraoperative use of ECMO.

Reply 7: thank you for your suggestion. I modified the paper excluding the precise algorithm of patient selection because, as you noted, it could generate confusion to the readers.

Changes 7: P12L318-320: “These results are also possible thanks to a very active collaboration between thoracic surgeons, anesthesiologists and the institutional ECMO team, where all elective cases of complex main airway surgery were discussed in a multidisciplinary meeting.”

Comment 8: Line 263, 264: “From our experience, the VA-ECMO could be advisable instead for cases of carinal resection carried out by sternotomy, which requires aorta and superior vena cava mobilization with potential hemodynamic disturbance.” You didn’t describe a case of an intraoperative use of VA-ECMO for airway surgery. Can you collaborate on the experience the above-mentioned statement bases on?

Reply 8: Thank you for your comment. Our experience comes from some cases of carinal left pneumonectomy accomplished by sternotomy in which the aorta and superior vena cava should be mobilized and then these manoeuvres could lead some kind of hemodynamical instability and to maintain a full cardiorespiratory support VA-ECMO could be advisable/useful. I modified the sentence in this way: “VA-ECMO is advisable in heart failure or in cases where manipulation of the great vessels is expected, as in some cases of left carinal resection through sternotomy.”

Changes 8: P13L342-343 “VA-ECMO is advisable in heart failure or in cases where manipulation of the great vessels is expected, as in some cases of left carinal resection through sternotomy.”

Comment 9: Line 265: You give an enumeration of limitations but only list “first”. Please revise.

Reply 9: Thank you for your suggestion, I integrated the list of limitations with the heterogeneity of the diseases treated with airway surgery such as tumors, trauma, fibro-inflammatory disease and post-surgical stenosis.

Changes 9: P16L409-411: “Second, our study population could be considered heterogeneous in terms of pathology, as we included airway trauma, tumours, fibroinflammatory diseases and stenosis.”

Comment 10: Strobe checklist: Information is incorrect, e.g. sensitivity analysis is said to be described which is not applicable in the study design. Discussion on generalizability of the study results is at least very scarce.

Reply 10: Thank you for your comment. We modified the STROBE checklist as you suggested.

Changes 10: We modified the STROBE check-list as you suggested.

Comment 11: Abbreviation list is incomplete.

Reply 11: Thank you for your advice. We implemented the abbreviations list.

Changes 11:

P24L584 to P25L591 ACT: activated clotting time

aPTT: activated partial thromboplastin time

HLS: Heart-Lung support

IQR: interquartile range

ICU: intensive care unit

HFJV: high flow jet ventilation

NSCLC: non-small-cell lung cancer

ARDS: acute respiratory distress syndrome

Comment 12: Please revise the paper with a native speaker. Unfortunately, the paper seems rather carelessly prepared right now considering a noteworthy number of spelling mistakes as well as mistakes in grammar, syntax and wording (e.g. emergent patient).

Reply 12: Thank you for your comment. We reviewed the whole paper and we corrected some typos such as emergent that has been changed with emergency, some other typos in the tables have been corrected. Moreover, the paragraph discussion was completely revised and modified to increase the readability.

Changes 12: emergent-> emergency, several modifications of the discussion

Reviewer E

Comment 1: The authors reported their experience in complex airway surgery utilizing VV-ECMO in 10 cases.

I congratulate the authors for sharing their experience with us in this challenge issue.

I liked the paper. Well written and can be read easily.

The paper with this experience report will help the other thoracic surgeons to plan their cases in a safe way.

Reply 1: Thank you for your valuable comment and effort.

Changes 1: no changes.

Reviewer F

Comment 1: VV ECMO is not the gold standard for complex airway surgery. Such statement may lead to unnecessary use of ECMO which comes with other risk such as vascular injury, bleeding etc and increase health care cost. It is an option to enable this complex surgery when conventional management such as cross field ventilation is not feasible. When indicated, ECMO should be implemented electively rather than as a salvage measure in an event of complete loss of airway or hemodynamic instability.

Reply1: Thank you for your valuable comment. We also think that VV-ECMO is not the gold-standard support for all complex surgery, but it could be a very useful tool in very selected cases. Our small numbers confirm this issue (10 patients operated on ECMO out of 73 patients). Considering your comment, we modified the discussion, the conclusions and the highlight box with a less strong sentences.

Changes 1: P4L90-92: "The use of intraoperative VV-ECMO allows safe and precise performance of main airway surgery with minimal postoperative morbidity in patients requiring complex resections and reconstructions and in cases that cannot be managed with conventional ventilation techniques."

P5L135-137: "VV-ECMO enables the safe and precise performance of complex main airway procedures with minimal postoperative morbidity and could be the extracorporeal support of choice in cases that cannot be managed with conventional ventilation techniques."

P16L414-419: "Despite all these limitations, our experience leads us to conclude that the use of intraoperative VV-ECMO in patients requiring complex resections and reconstructions, and in cases that cannot be managed with conventional ventilation techniques, allows for safe and precise performance of main airway surgery with minimal postoperative morbidity."

We believe that VV-ECMO should be part of the surgical armamentarium of teams that frequently deal with complex resections and reconstructions of the main airway.”

Comment 2: Hence, the most important point for this review will be: how to select this cases, and who need to be put on ECMO. A table summarising the difference between the 10 ECMO cases vs the rest may be good. Ie, difference with airway/carina resection anatomy, pt with previous lung resection on contralateral lung, duration of surgery, duration of hospital stay, relevant complications such as bleeding, vascular injury, airleak etc.

Reply 2: thank you for your precious comment. I think you are right in saying that the selection criteria are the focus and the true objective of our study. I think that the selection criteria could be considered clear reading the paragraph results and also joining the information of the results with that of the tables, the reader should have a clear idea on our selection criteria. In our opinion, the table 1 depicts all the aspects of our selection process. The comparison of complex airway surgical patients with a cohort of “standard” airway patients (tracheal stenosis, carinal right pneumonectomy, laryngo-tracheal resection) is not possible and not feasible because we consider and treat these two groups in a completely different way regarding functional aspects and perioperative and intraoperative management.

Changes 2: no changes.

Comment 3: Another table summarising the indications of ECMO in major airway cases will be good.

Reply 3: thank you for your comment, we believe that table 1 summarises the indications to ECMO in a clear way and also the paragraph “results” depicts all the information that the readers need regarding indications to VV-ECMO and to the surgical approach. I do not think that another table with general indications to VV-ECMO would be useful to the readers.

Changes 3: no changes.

Reviewer G

Comment 1: For those of us who perform complex tracheal surgery, the topic is good and very interesting. There are a large number of reports of cases of VV ECMO use in complex lung, airway and digestive surgeries due to benign and malignant pathology. This work with 10 cases is interesting. as well as the division they make within the indications, dividing them into mandatory and those in which they could obtain advantages, considering the latter as a controversial indication. However, the methodology is not very clear, they mention that their objective is to describe their experience with the use of VV ECMO in complex airway surgery and they should stick to it and should not conclude that the use of VV ECMO is a gold standard, even less so because the study is descriptive of only 10 cases, then they mention that in that time interval of their retrospective study they operated 73 patients, this last data is not interesting or is unnecessary because its objective is based on 10 patients

Reply 1: thank you for your precious comment and based on your advices, we changed the conclusion of the abstract in this way: “The use of intraoperative VV-ECMO allows safe and precise performance of main airway surgery with minimal postoperative morbidity in patients requiring complex resections and reconstructions and in cases that cannot be managed with conventional ventilation techniques.” and the conclusion of the main text as follows: “Despite all these limitations, our experience leads us to conclude that the use of intraoperative VV-ECMO in patients requiring complex resections and reconstructions, and in cases that cannot be managed with conventional ventilation techniques, allows for safe and precise performance of main airway surgery with minimal postoperative morbidity. We believe that VV-ECMO should be part of the surgical armamentarium of teams that frequently deal with complex resections and reconstructions of the main airway.” We

change also the paragraph methods (P7L178-180), enlightening that during the study period we reviewed all the patients undergoing to major airway surgery (n=73) and identified and analyzed the clinical data of those operated on with the VV-ECMO support. In our opinion, this sentence is useful to understand how rare is the VV-ECMO approach in elective airway surgery.

Changes 1: P4L90-92 “The use of intraoperative VV-ECMO allows safe and precise performance of main airway surgery with minimal postoperative morbidity in patients requiring complex resections and reconstructions and in cases that cannot be managed with conventional ventilation techniques.”

P16L414-419: “Despite all these limitations, our experience leads us to conclude that the use of intraoperative VV-ECMO in patients requiring complex resections and reconstructions, and in cases that cannot be managed with conventional ventilation techniques, allows for safe and precise performance of main airway surgery with minimal postoperative morbidity. We believe that VV-ECMO should be part of the surgical armamentarium of teams that frequently deal with complex resections and reconstructions of the main airway.”

P7L177-180 “We retrospectively reviewed the medical records of 73 patients who underwent main airway surgery at Careggi University Hospital of Florence between June 2013 and August 2022. The data of 10 patients (study group) who underwent main airway surgery under VV-ECMO support were collected and analyzed in terms of clinic-pathological, perioperative and follow-up outcomes.”

Comment 2: The introduction could be improved and include the technique (modalities) of VV ECMO that they use in their center. I also consider that in the methodology it should have been stated that they used the Strobe “check list” and highlighted it in the informed consent.

Reply 2: thank you for your comment, and then we included this sentence and its related references in the paragraph methods: “In our Institution is active the ECMO referral center for respiratory diseases with mobile ECMO team available 24 hrs/day for 365 days/year for retrieval in other hospitals in Tuscany and center of Italy”

We inserted the link to the STROBE checklist as you suggested.

Changes 2: P7L192-194: “An ECMO referral center for respiratory diseases is active in our institution with a mobile ECMO team available 24 hours/day, 365 days/year, to serve other hospitals in Tuscany and central Italy”

P7L182: “We present this article in accordance with the STROBE reporting checklist”