Peer Review File

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Reviewer A

It is better to explain why you chose VV instead of VA ECMO support (especially when patients experienced cardiac arrest preoperatively) and also how you menaged the heparin admistration to balance its need and the risk of major bleeding.

Please take a look at this article and consider to include it into references: Repair of traumatic avulsion of the right bronchus in children using extracorporeal membrane oxygenation support - Interact Cardiovasc Thorac Surg. 2021 May; 32(5): 834–836.
Published online 2020 Dec 24. doi: 10.1093/icvts/ivaa327

Reply: Thank you for your comments. We have read this article carefully and think it is very valuable. We have quoted this document in our article.
1. The explanation for why we chose V-V ECMO is as follows: our patient mainly has bronchial injury, and his cardiopulmonary function is actually normal, so we chose V-V ECMO, in addition, about V-V ECMO and.The indications for VA-ECMO have been explained in lines 76-89 of the article; as mentioned in your recommended article, the use of VA-ECMO is due to the fact that patients with chest trauma with airway injury may lead to right ventricular dysfunction, hyperventilatory pressure, massive blood transfusion and the use of catecholamines. VA-ECMO can lighten the load of the right heart and help it support and recover. Obviously, our patients are more suitable for VA-ECMO.
2. The answer to how to manage heparin administration to balance the demand for heparin with the risk of massive bleeding is as follows: because of trauma, V-A ECMO requires more anticoagulation, V-V ECMO requires less anticoagulation, these patients have lung injury, but heart function is good, so V-V ECMO is more appropriate. For the management of heparin anticoagulation, we maintain the APTT between 40 and 50 units by monitoring APTT (which is consistent with the recommendations of the guidelines). And these patients underwent emergency surgery with the support of V-V ECMO, and the risk of bleeding after the operation was lower. After operation, the bleeding was judged by detecting APTT, blood routine red blood cells and observing the drainage volume of the drainage tube. This is mentioned in the postoperative situation of our article(see page 4-5 ,line 122-126, (see page 7 , line 197-204.)
Changes in the text: page 3,lines 76-89; see page 4-5 ,line 122-126, (see page 7 , line 197-204.)

Reviewer B

Thank you for the opportunity to review this report of three cases of patients operated, for traumatic bronchotracheal repture, utilizing VV-ECMO.

My comments:

1. The indications and uses of ECMO are not satisfactorily described. For example, lines 31-32 you indicate that VV ECMO is used for cardiac and respiratory failure (this is incorrect). The introductory paragraph (lines 62-64) should also specificy whic types of ECMO you're referring to. Listed vaguely mixes the indications between VV and VA, in my opinion.

Reply:

Thank you for your valuable advice. We have introduced the indications and uses of VV and VA-ECMO at page 1-2 ,lines 31-36 and page 3-4 ,76-89. All three of our patients were treated with VV-ECMO, which was also explained in page 13 ,line 410-420 . (VV-ECMO) for primary respiratory failure that cannot be improved by conventional medical treatment and mechanical ventilation. Many patients consider using VV-ECMO only after deep sedation, muscle relaxants, prone position, inhaled pulmonary vasodilators and diuretics are ineffective. The main goal of supporting VV-ECMO patients is to promote lung rest through lung protective ventilation. Lung protective ventilation aims to reduce the triggers of mechanical ventilation-induced lung injury (VILI), such as volume trauma, pressure trauma, atelectasis trauma and biological injury. Our patients are mainly injured by bronchial and tracheal ventilation and can not breathe on their own, while VA-ECMO is mainly used in previous heart failure, incomplete reperfusion, poor myocardial protection during surgery or technically difficult surgery, it is obvious that our patients are more suitable for VV-ECMO.

Changes in the text: page 1-2 ,lines 31-36 and page 3-4 ,76-89.;page 13 ,line 410-420 .

2. For case 1, would you please clarify why the decision to cannulate VV was made (instead of VA) for a child having multiple cardiac arrests pre-operatively? Also, why not utilize cardiopulmonary bypass instead? In your opinion, what are the perceived benefits of VV ECMO over cardiopulmonary bypass? Also, given the number of cardiac arrests, concerns about neurologic outcome would be paramount. How did this child do? What do you mean by "good physical condition?"

Reply:

Thank you for your valuable advice, which was also answered in the previous review. our patient is mainly injured in the main pathway of the bronchus and trachea and is unable to breathe on his own. in fact, his cardiopulmonary function has no organic lesions. The main goal of supporting VV-ECMO patients is to promote lung rest through lung protective ventilation. Lung protective ventilation aims to reduce the triggers of mechanical ventilation-induced lung injury (VILI), such as volume trauma, pressure trauma, atelectasis trauma and biological injury.

This is in line with the conditions for the use of VV-ECMO; while VA-ECMO is mainly used for previous heart failure, incomplete reperfusion, poor myocardial protection during surgery or technically difficult surgery, it is obvious that our patients are more suitable for VV-ECMO. In addition, cardiopulmonary bypass is of course a feasible method, but our patient was in critical condition at that time. In order to save the patient's life and improve the prognosis, our VV-ECMO can be treated in the emergency department, while the cardiopulmonary bypass needs to be performed in the operating room, which increases the treatment time of the patient, so we choose to use VV-ECMO.

Compared with cardiopulmonary bypass, VV-ECMO has the following advantages:

(1). Non-invasive: VV-ECMO is a non-invasive circulatory support technique that provides oxygenation and circulatory support by inserting venous catheters. In contrast, cardiopulmonary bypass requires thoracotomy to achieve circulation by connecting arteries and venous ducts.

(2). Quick start: VV-ECMO can be started in a short time, usually only a few minutes, can be quickly started in emergency surgery, while cardiopulmonary bypass takes a long time to prepare and start in the operating room.

(3).Low side effects: VV-ECMO has fewer side effects compared with cardiopulmonary bypass. Cardiopulmonary bypass may lead to a variety of complications, such as platelet dysfunction, coagulation dysfunction, inflammatory reaction and so on.

(4).Adjustability: VV-ECMO can be adjusted according to the needs of patients, including blood flow, oxygenation index, etc., to meet different physiological conditions. On the other hand, cardiopulmonary bypass is relatively fixed and the adjustment range is small.

(5).Longer support time: VV-ECMO can provide cycle support for a long time and can be used continuously for weeks or even months. On the other hand, cardiopulmonary bypass is generally used only during operation, and the supporting time is short.

After the operation, we discussed that the neurology of the patient had a specific description of the patient's sedation state at that time, unable to accurately evaluate consciousness, the existence of two pupil light reflex, and the pathological sign was negative: page 8, 233-239 lines. During the follow-up, it was found that the child had speech expression disorder after trauma, the response was slightly indifferent, and the post-traumatic mental disorder was considered.

Changes in the text: page 1-2 ,lines 31-36 and page 3-4 ,76-89.;page 13 ,line 410-420 .

3. For case #2, why was single lung ventilation during the OR not utilized over ECMO? How did this person do (in more detail) at time of discharge?

Reply: Thank you for your question. According to the patient's assessment at that time, the rupture position of the patient made it impossible to insert a double-lumen tube and use one-lung ventilation, so we chose ECMO; in our comprehensive assessment. After comprehensive treatment, our patients discharged from the hospital, patient 2 and patient 3: Shenzhiqing, two

pupils and other equal circles, sensitive to light reflex, able to perform some physical activity. See article page 7,197-204 lines.

Changes in the text: page 7,197-204 lines.

4. For case #3, how too did this person do at time of discharge (in more detail, if available)?

Reply: After comprehensive treatment, our patients discharged from the hospital, patient 2 and patient 3: Shenzhiqing, two pupils and other equal circles, sensitive to light reflex, able to perform some physical activity. See article page 7,197-204 lines.

Changes in the text: page 7,197-204 lines.

5. I find the multidisciplinary discussion of the cases not easy to follow. The discussions and opinions of these varying team members can be summarized.

Reply: Thank you for your suggestion. We have made a summary description in the multidisciplinary discussion section. Specific page7-9，212-239 and 258-291 lines.

Changes in the text: page7-9，212-239 and 258-291 lines.

Reply:

6. The discussion also needs to have changes made regarding the discussion surrounding describing what ECMO is. For example, vague statements like "The main role of ECMO is to keep patients hemodynamically stable..." are incorrect. VA ECMO stabilizes the cardiac system (in addition to respiratory). The cannulation strategies are also too limited. There are multiple locations to cannulate VA vs VV.

Reply:

Thank you for your valuable advice. We revised it in page 13 ,line 399-409 of the article. The main goal of VV-ECMO use is to promote lung rest through lung protective ventilation. Lung protective ventilation aims to reduce the triggers of mechanical ventilation-induced lung injury (VILI), such as volume trauma, pressure trauma, atelectasis trauma and biological injury. And help critically ill patients recover, so as to provide enough time for definite treatment. It can be used as a treatment option for patients with acute biventricular heart failure complicated with respiratory failure, especially as an adjuvant therapy in the case of cardiac arrest.

Changes in the text:page 13 ,line 399-409

Reviewer C

In general:

- Please write V-V corresponding tot he international ECMO spelling

Reply: Thank you for your suggestion. We have made the modification.

Changes in the text: page1，26-27 lines.

Background:

- V-V ECMO does not act as an artificial heart and lungs support (line 32). It has nothing to do with cardiac support!

Reply: Thank you very much for your suggestion. What you said is right. We have cut it in the last suggestion.

Changes in the text: page1， 32-34 lines.

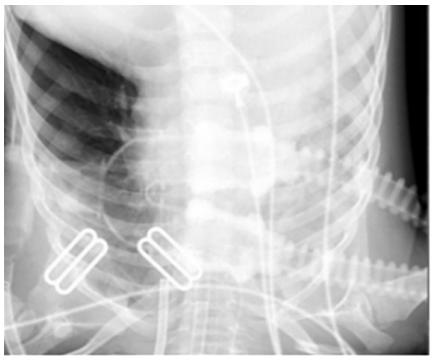
Case 1:

- what body weight did the child have?
- what is severe respiratory and circulatory dysfunction (line 96)? intubated? what FiO2, PEEP? What catecholamines?
- I do not see atelectasis in the CT scan in figure 1. Did you provide the correct images?
- which ECMO cannula size for the 4 year old child (line 104)?
- the cannulation text should be more compact, same things are repeated
- there is no consecutive timeline in the text. Preoperative conditions are told in the paragraph after the description of the surgical procedure. Please write the case report following a timeline so that the reader can understand what happened when.

Reply：

(1)Thank you for your suggestion. Here is a detailed reply to you. We did not find detailed data on the child's weight, FiO2, and PEEP. On admission, the patient was in a coma and underwent endotracheal intubation. A right thoracic closed drainage tube was placed, and there was a significant amount of gas escape. The respiratory movement on the right side was weakened, and there was fibrillation weakening on the right side of speech. Percussion of the right lung yielded a clear sound. The admission diagnosis was 1. Closed chest injury with right pneumothorax and bronchial rupture in the right middle lung lobe; 2. Traumatic shock. After admission, the patient experienced cardiac arrest and was administered epinephrine (0.3mg intravenous push every 3 minutes, with a total of 1.2mg). Subsequently, ECMO was initiated with a speed of 2500rpm, a flow rate of approximately 1.7L/min, no tube jitter, sweep gas at 3L/min, FiO2 at 100%, and tracheal intubation.

(2)The imaging provided in our article is the image of patient 2. The chest DR of patient 1 is shown below.



(3) During the process of VV ECMO, a right internal jugular vein to right femoral vein approach

was used for cannulation. Standard precautions and disinfection were followed, and a right femoral vein incision was made for cannulation. A Maquet arterial catheter of size 14F was inserted to a depth of 20cm, and a 15F (Changzhou Kangxin) Seldinger method was used to place the right internal jugular vein cannula to a depth of 7cm. The ECMO was set at a speed of 2500rpm with a flow rate of approximately 1.7L/min, and no tube jitter was observed. Sweep gas was set at 3L/min with a FiO2 of 100%, and tracheal intubation was performed. The use of heparin in ECMO during surgery is described in lines 138-142 on page 5.

Changes in the text: page5，138-142lines.

(4) We have adjusted it in chronological order.

Changes in the text: page 4-5，118-150 lines.

Case 2:

- Same points like in case 1: Clear timeline is missing, what happened when? You write the patient was resuscitated in the external hospital (line 129), so how can he come to your hospital with shortness of breath? Was he intubated and sedated or extubated and awake? At what time after intubation was the ECMO implanted? You describe in a detailed way which sutures were used for surgery but no details about ECMO implantation, timing, cannulas, flow. This doesn't fit.

Reply：Patient 2 was initially sent to an external hospital for treatment, where a chest X-ray indicated "multiple rib fractures and left pneumothorax" (specific report not available, as the patient was in critical condition and a complete CT scan was not possible). Closed chest drainage, cervical immobilization, endotracheal intubation, and mechanical ventilation were performed.Admission was diagnosed as"multiple rib fractures on the right side, left pneumothorax, acute respiratory failure, sternal fracture, and C6 vertebral body fracture,"admitted to ICU. After treatment, the patient's consciousness improved, with spontaneous eye opening and response to verbal stimuli. The patient required ventilator assistance with a FiO2 of 100% to maintain oxygen saturation at approximately 85%. Subsequently, the patient was transferred to our hospital for further treatment and was placed on mechanical ventilation .Under this ventilation mode, the following monitoring data were recorded: PEEP: 2cmH2O, f: 12bpm. After mechanical ventilation, the oxygen saturation increased to 87%. Ten hours after admission, the patient's oxygenation index dropped below 100mmHg, and bronchoscopy suggested possible left main bronchus rupture, indicating the need for ECMO support. After cannulation, membrane lung and tubing were connected, and ECMO treatment was initiated with an initial rotation speed of 3240/min, oxygen flow rate of 5L/min, and blood flow rate of 4.17L/min. Under this support mode, the oxygen saturation remained around 95%. The ventilator mode was adjusted to Bipap with PEEP: 2cmH2O, PIP: 13cmH2O, FiO2: 100%, and the oxygen saturation was maintained at 90-95%.

Changes in the text: page 5-6，154-175 lines.

Case 2:

- Main bronchus which side (line 149)? What was ruptured – trachea and bronchus?
- ECMO how many ours after intubation?
- No ECMO details mentioned like in the other cases
- Was the patient first extubated and then ECMO decannulated or first ECMO decannulated and then extubated? In my opinion, it would have made sense to let the patient wake up and extubate with ECMO support – how did you do it?

Treatment and follow up:

- what anticoagulation regime did you do during the surgery? Heparin bolus with ECMO implantation or start of anticoagulation strictly after surgery?
- I don't understand the sense of copying and pasting your two experts opinions (Dr. Kaserer and Dr. Sef) concerning ECMO treatment in your cases. The topics they mention are very true and important fort he treating team, but I see no literature citations and guidelines as a base for publishing it in a journal.

Discussion:

- Line 358: Why ist ‚the main role of ECMO to keep the patients hemodynamically stable'? In all of your cases, you yoused V-V ECMO, so the goal is to maintain oxygenation and decarboxylation, which is not mentioned in your sentence. I would like a clear defnition of V-A für circulatory support and V-V for respiratory support.
- Did you find any other literature and cases of ECMO used fort he above mentioned surgery? Why don't you describe it and compare it ithe your procedure?
- How do you know ECMO reduces the risk of emergency surgery? Do you have a proof or literature for this hypothesis? Of course, in your three cases it went well, but what about bleeding problems etc.? Have you got a comparison with other cases? I recommend the literature of Jusytna Swol for ECMO in trauma (see PUBMED).

Reply: thank you for your question. Here is our reply. (1)The patient was suffering from left main bronchial rupture, and was treated with closed negative pressure thoracic drainage, cervical brace fixation, endotracheal intubation and mechanical ventilation, and the therapeutic effect was not obvious. after being transferred to our hospital, ECMO was performed 8 hours after admission because of poor oxygen saturation. At that time, the patient was passive posture, conjunctival congestion, Bilateral pupils with equal size and shape, and the light reflex was slow. The oxygenation index of the patient was lower than 100mmHg after mechanical ventilation. Bronchoscopy showed that the left trachea might be ruptured, and there was ECMO indication. After the puncture was completed, after connecting the membrane lung and the tube, the patient was treated with ECMO, the initial speed was transferred to 3240/min, oxygen flow rate 5L/min, blood flow rate 4.17L/min, oxygen saturation was 95% in the above support mode, ventilator mode was Bipap,PEEP:2cmH2O,PIP:13cmH2O, oxygen concentration: 100%. Oxygen saturation is maintained at about 90-95%. After surgical treatment, the patient's condition was stable after extubation, the ECMO was removed, and the patient had spontaneous cough before extubation.

(2)We have responded to anticoagulant regimens and postoperative bleeding,because of trauma, V-A ECMO requires more anticoagulation, V-V ECMO requires less anticoagulation, these patients have lung injury, but heart function is good, so V-V ECMO is more appropriate. For the management of heparin anticoagulation, we maintain the APTT between 40 and 50 units by monitoring APTT (which is consistent with the recommendations of the guidelines). And these patients underwent emergency surgery with the support of V-V ECMO, and the risk of bleeding after the operation was lower. After operation, the bleeding was judged by detecting APTT, blood routine red blood cells and observing the drainage volume of the drainage tube. This is mentioned in the postoperative situation of our article(see page 4-5 ,line 122-126, (see page 7 , line 197-204.)

Changes in the text: page 4-5 ,line 122-126, page 7 , line 197-204.)

(3) Thank you for your suggestion. We have studied Jusytna Swol's article carefully and have added "Extracorporeal Membrane Oxygenation in Trauma" to our article.