Author’s response to reviews

Title: Extended use of Extra Corporeal Membrane Oxygenation as Bridge to lung transplantation in two patients

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Reviewer reports:

Reviewer #1: Authors presented two cases of patients who were on ECMO more than 200 days and underwent lung transplantation. One case survived after lung transplantation. However, one case died intraoperatively because of bleeding.

I have the following concerns.

1. The cause of intraoperative death was not related to ECMO. It was related to fibrotic scar tissue. It is not reasonable for the authors to conclude that they should turn down for lung transplantation for similar patients.

Thank you for your comments and time to review our manuscript. We did not mean that the ECMO was the cause of the death. We, meant that when a patient has developed a non-breathing, non-moving chest, it seems that the whole chest as well as the hilum and mediastinal structures underwent fibrotic transformation, that ultimately if the patient gets operated with a very high likelihood will result in death and organ waste. We believe that regardless of surgical approach we would have faced the same outcome. Some regard it as a flaw that we performed a sternotomy instead of a thoracotomy, but we wanted to have the option to go intrapericardially with the resection if complicated. We agree that the death had nothing to do with the ECMO itself.

2. Patients on ECMO are very higher risk for lung transplantation and have various background. It is difficult to standardize the patients' background.
Thank you for the comment, and we fully agree, otherwise we would not have allowed such a long bridging period with ECMO to lung transplantation, since it is almost certainly against all guidelines and current practice regimes. We just wanted to point out that under some circumstances one should decline listing and lung transplantation (which we did not, but in aftermath should have done in second case). Although this does not mean that we should not have tried, we still think it was right in the first place to get the patient to recover on ECMO, and even list the patient, but upon deterioration we should have delisted, which is the lesson we have learned.

Reviewer #2: Skansebo et al. provide a very well written account of 2 patients on long term ECMO as bridge to LTx. The authors seem to want to lead the reader into the idea that we can understand the limits of ECMO. Unfortunately, the 2 patients presented, though both on long-term ECMO, are very different in almost all aspects. This makes it very hard to draw conclusions towards the authors idea of the limits reached. They also "spring" the idea of cost into the discussion without a single economic data point in the case discussions. Furthermore, the costs for the survivor: ECMO, med flight to Sweden, days on ECMO, LTx, ECMO 2, kidney transplant far exceed the cost of the patient that died. The authors do not describe either patients pre-operative ventilatory status or whether they had tracheostomies, were they intubated etc. Nor is right heart function or the need of atrial septostomy discussed and is a concern with long-term v-v ECMO. Was V-V ECMO done with single double lumen cannula or other strategy?

Thank you for your comments and time to review our manuscript. We agree that both recipients are different in most aspects, however we wanted to make a point out of the fact that the older female against odds survived and the younger male succumbs. We have omitted the “limits reached” from the title, and do understand that the reviewer mean that conclusions drawn from only 2 cases have to be careful. We agree that we have mentioned costs maybe a little flamboyant, and therefore we omit these comments. Both patients were of course in the ventilator before they were receiving ECMO, and both were eventually also tracheotomized in order to manage secretion in the airways, which has been added to the manuscript. Both of them were on vaECMO initially but one of them were over time converted to vvECMO.

The authors have provided 2 references and neither help the reader adjudicate risk in these high risk patients - ECMO is not the issue, the patients comorbid diseases are, and there is literature to guide teams through this 'fog'.

Thus, I do not have a clear sense of the take home points with the 2nd patient regarding single lung transplant after prior contralateral pneumonectomy. The authors failed strategy of median sternotomy for recipient explant does not translate to centers that would have employed peripheral bypass and approached a complicated explant via thoracotomy. The idea that median sternotomy offered options was likely misguided; as exposure and extra pleural dissection is impossible, and this is often required for such cases. The authors don't acknowledge or consider that their surgical approach was potentially flawed. Another issue that they don't directly address
in assessing risks of the patients based on the presumed functional respiratory capacity pre/post transplant. If their deceased patient was truly non-ventilatory for their extended time on ECMO and with a contralateral pneumonectomy - post transplant weaning from ventilatory support would have been prolonged, if even possible, with pneumonia a likely outcome. These patients tend to perform like a patient with a paralyzed diaphragm, have post pneumonectomy like syndrome and without formal chest wall and diaphragm decortication, thoracic compliance is potentially a limiting issue to wean from positive pressure ventilation. The authors need to focus on the 800lbs gorilla in the room - post pneumonectomy and non ventilated patient - best case scenario is 30% mortality (F. Le Pimpec-Barthes 2014). Obviously, it is difficult to adjudicate these factors, but readers need to appreciate why patient 1 did well is because her greatest risk was dialysis before LTx (different than new dialysis after transplant) and the second patient was a futile adventure due to surgical misadventure that was likely due, in part, to a poor surgical strategy given the history. But, that even if transplant was successful, the patients thoracic comorbidities would have likely been unsurmountable given the experience of others - need references of prior pneumonectomy and LTx. I certainly commend the authors for their valient and superb care of these complicated patients, but I do not believe readers are better informed regarding the limits of ECMO as bridge to LTx based on the information presented and the conclusions drawn by the authors.

Thank you for your comment, and we do realize that our approach can be questioned, however, we still believe that our approach was an acceptable one, but vaECMO from groin and thoracotomy would have been an option. We do not believe that any approach would have been successful anyway, since pathology was so advanced. The reference given by Le Pimpec-Berthes does not help, its not on lung transplantation. We agree, that the non-ventilated chest may very well have been unsurmountable, but have not found any such references in the literature, which increased our effort to honestly describe this one. But we do agree that this patient had more than one contraindication to LTx (dialysis, fibrotic chest and pneumonectomy). We are not proud of this outcome, and recognize that we should have declined transplantation, and at a certain level we should have delisted the patient when progress occurred, but we did not, and there are lessons to be learned here for others.

Reviewer #3: Thank you for your interesting case reports describing patients with extensive preoperative extra-corporeal membrane oxygenation courses prior to lung transplantation. I believe this manuscript is interesting from a perspective of lessons learned. However, I do not believe a conclusion is feasible in any manner giving both the rarity of such extended use of ECMO and the anecdotal expected limited survival. It can be inferred that such a pre-operative course is of extremely small sample size. I do agree that these cases highlight complex decisions involving medical, ethical and allocation of limited resources. The institution will have to establish their goals in regards to the nature and aggressiveness they choose to resuscitate and subsequently transplant patients understanding the dangers of such an operation on a marginal
patient, likely serially transfused and transplanting a delicate organ(s) known to reject. The cases described may not necessarily support the conclusion of "some patients do survive."

Thank you for your comments and time to review our manuscript. We have modified our conclusion in the abstract to instead “we have shown that a patient can survive extremely long duration of ECMO…”

Please also take a moment to check our website at for any additional comments that were saved as attachments. Please note that as Journal of Cardiothoracic Surgery has a policy of open peer review, you will be able to see the names of the reviewers.