Reviewer's report

Title: Nine Veno-Venous ECMO Challenges and Controversies

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Reviewer: Steven J Lisco

Reviewer's report:

I thank the editors and the authors for the opportunity to review. The stated objective of the paper is to review nine challenges and controversies and discuss their current future implications on the treatment of ECMO patients. I would submit the following thoughts to the authors divided as required by the journal.

Major compulsory revisions:

1) There are too many grammatical and syntax issues to list. This paper needs extensive review and frankly unification of the writing styles. It appears that the authors divided the sections of the manuscript amongst themselves; however there appears to have been very little attempt to unify the writing styles. I would suggest that the senior authors work to correct this issue as it makes the manuscript very difficult to read.

2) The background section contains much of the same information that is considered in the discussion of the many challenges of ECMO. For instance, the discussion on the absence or presence of a reservoir in the circuit is discussed almost verbatim in the first paragraph of Challenge five. Please remove this discussion from the background section.

3) Challenge number one does not delineate a controversy; instead it just summarizes the recommendation from ELSO and from Brodie, et al. I would suggest that the authors spend time in this section discussing issues where they may themselves struggle. For instance, what age is too old for ECMO? What BMI is too high? Why do they consider an extended time at high FiO2 or high PEEP relative contraindications to ECMO? This should be referenced and discussed. How moribund is too moribund? Large ECMO centers lament these questions almost daily yet the authors spend little time on this important issue and fail to provide the reader with any recommendations except to EOLIA and CESAR without saying why these are valuable studies.

4) Challenge number two is very unorganized. The first paragraph talks about the utility of using ultrasound and Seldinger technique but does not say why or if this is controversial. Additionally, it is not referenced. The last paragraph in this section would seem to be better placed as the second paragraph. The authors would probably be better served here to discuss the routine use of two cannula prior to discussing the advantages and disadvantages of a double lumen cannula.

5) Challenge number three provides a brief discussion on membranes and pumps. There is little discussion of what the challenge is here. Are there different
membranes currently available which may be better than others? Certainly, the authors are not telling the reader that the challenge is not to use a bubble oxygenator, however this is the implication. Additionally, the authors could spend more time on a discussion of the pros and cons of using a roller pump vs. a centrifugal pump. Is there a time when one is better than the other? Do they have a recommendation? Is there literature to support a recommendation? What do the authors use in their institution?

6) Challenge number four conveys very little information except mention of the Maquet Cardiohelp system. Is this the only portable device? Clearly it is not. This section should be deleted if it cannot be developed further. Why is transport a challenge. It seems intuitively obvious but no mention is made about why one device might be better than the next. What devices are in development? Are there patient conditions that make transport prohibitive?

7) Challenge number five attempts to provide the reader with recommendations but is confusing and needs major revision. The last two sentences of the first paragraph are confusing. Is the lack of a reservoir an advantage or not? Do the authors mean to say that it is not a disadvantage if there is adequate peripheral or central IV access to infuse volume as required based upon patient condition? You might consider rewriting this section as follows: The lack of a reservoir on the ECMO circuit may be overcome by assuring that the patient has central or peripheral IV access adequate to allow rapid infusion of needed fluids. Similarly, in the absence of a reservoir caregivers must rely upon pharmacologic or mechanical diuresis to correct states of volume overload. The next two paragraphs are likely best as one. There is no need for a discussion of blood age in this manuscript. I would remove that sentence. Also, relevant in this section, but unmentioned is how the authors assess volume status in the ECMO patient. There is mention of pump chattering but certainly the authors utilize additional adjuncts to facilitate decisions related to fluid balance. This would be the ideal place for a discussion on use of echocardiography in the ECMO patient.

8) Challenge number six is the most complete of all the “challenges.” There is first a discussion of standard of care then the novel use of alternatives and reasons why these might be better than standard. Additional discussion on the risks of direct thrombin inhibitors might be an added plus here.

9) Challenge number seven is incomplete. This should be a very interesting discussion on the issues facing caregivers considering extubation of the ECMO patient. There is much written on this topic and I would think that for an anesthesiology journal this area would have been better developed. What are the reasons for extubation? When would you consider it and when not? Does pulmonary compliance make a difference? Etiology of respiratory failure (hypercarbic vs. hypoxic respiratory failure)? Do you extubate early or late in ECMO care? If late how do you manage sedation or weaning of sedation? What are signs that extubation might be a bad idea? What role does cardiac performance play in making this decision?

10) Challenge number eight is a discussion on the use of NMBs in ARDS not in ECMO. If it cannot be developed to apply to ECMO I would remove it or perhaps role it into the number seven.
11) Challenge number nine is a discussion of CESAR and only that study. Are there other studies that support one ECMO center over another? How many patients on ECMO per year are required to make a center expert or not? More could certainly be done with this section.

12) The summary seems to try to bring conclusion to many of the questions raised by the “challenges” not done in those respective individual sections. Much of this content would have been more interesting and better placed in the actual sections. Again, this section appears to be written by yet a different individual than each of the sections in the prior 8 pages. I think the summary would be better off shortened and much of this information added to earlier sections.

Given the extensive revision that this manuscript requires, I will withhold my comments on minor and discretionary revisions until appropriate. I encourage the authors to further develop this manuscript as described. I would ask them to consider when rewriting each section why each of the nine is truly a controversy for them at their own institution and then to convey to the reader how and why they make a particular decision when faced with each respective challenge. I again thank the authors for the privilege of reviewing their manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests