Reviewer's report

Title: Nine Veno-Venous ECMO Challenges and Controversies

Version: 2
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Reviewer: Daniel Chipman

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Overall, this review is clear and easy to read, although it is a somewhat basic overview of ECMO support. The authors identify challenges associated with ECMO, however they should consider providing more detail and insight, especially into the utilization of resources and eventual patient outcomes, as these are the true challenges. To many, the decision to provide ECMO may seem logical and straightforward without a clear understanding of all that is involved, including the physical and emotional strain on caregivers and family, tremendous utilization of resources and the eventual results. That being said, I think this paper is acceptable for publication and suggest only the following Discretionary Revisions:

1. The title makes reference to V-V ECMO, however considerable attention is given to V-A ECMO as well, possibly resulting in some confusion to the reader e.g., paragraph 4, line 11, "The degree of cardiac unloading is dependent on the flow rate and the position of the venous drainage cannulae."

2. In paragraph five, line 3, the authors indicate that lack of a reservoir is disadvantages in that reinfusion of fluids may only be be accomplished via central or peripheral venous access. It should be pointed out that, when additional volume is needed, rapid infusion may also be achieved via the ECMO circuit, providing immediate, central access.

3. In the section Challenge One, relative contraindications should also include advanced age and multi-system organ failure. One may also consider withholding ECMO support in the case of repeated suicide attempts without previous psychological treatment and/or support. These may be considered controversial, but should be mentioned to prompt further discussion.

4. In the section Challenge Two, disadvantages of a double lumen cannula should also include higher reinfusion pressure and the potential for recirculation of oxygenated blood back into the drainage lumen.

5. Insertion of a large, double lumen cannula into the internal jugular vein may result in cerebral venous congestion. Consideration should be given to placement of an additional cephalod drainage line.

6. With femoral vein to femoral artery V-A ECMO, a distal line e.g., 5 french catheter, is often inserted to prevent ischemia of the lower extremity.
7. In Challenge Three the authors correctly point out that improved pump and membrane design have minimized many of the problems associated with earlier experiences with ECMO. However it remains essential that pre and post membrane pressures are monitored to identify clot formation and the potential for membrane failure. With polymethylpentene hollow fiber membranes, once the difference in pressure across the membrane begins to increase it may progress more rapidly than previously seen in the older silicone plastic membranes, resulting in the need for emergent membrane replacement.

8. It is also important to monitor the actual blood flow through the circuit and not just pump revolutions per minute. As the authors explain, unlike the older roller pumps, current centrifugal pumps are influenced by both preload and afterload. Changes in either may significantly alter blood flow.

9. Challenge Seven: the airway should be more fully explained. Although the authors correctly indicate that patients awaiting lung transplant may be extubated and encouraged to participate in physical therapy, there is little doubt that patients with severe ARDS, requiring ECMO should remain intubated. However, mechanical ventilatory support may often be decreased to prevent ventilator induced lung injury.

10. In the section Challenge Nine: hospitals, it should be explained that improved pump and membrane technology, along with simplified circuit design have prompted many non-ECMO hospitals to place patients on bypass with the intention of transporting them to full ECMO centers. This takes the decision to provide ECMO out of the hands of the ECMO experts possibly resulting in patients who may have otherwise been excluded receiving ECMO support inappropriately.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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