Peer Review File

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Reviewer A

Comment: The idea for a meta-analysis investigating ECMO bridge to transplant is a decent one, however the execution in this case is not at a publishable level. I would highly recommend a complete re-write, with the help of a native English-speaker, and a much more thorough results section and nuanced discussion.

Reply: We greatly appreciate the reviewer's suggestions. Those suggestions are all valuable and very helpful for revising and improving our paper.

Changes in the text: We performed a high-density, extensive editing on this manuscript.

（highlighted in red in the manuscript）

Reviewer B

The authors demonstrated the mortality and prognostic factors in lung transplantation after ECMO bridging by systematic review and meta-analysis. I have some comments.

Comment 1: What is a novelty of this systematic review paper? We can find some review papers in which similar results were reported previously.

Reply 1: We greatly appreciate the reviewer's suggestions. Indeed, several review papers showed that patients undergoing long-term ECMO-supported lung transplantation who received bridging therapy had a worse prognosis that those who did not receive ECMO (1-2). However, our study aimed to deeply investigate the prognostic factors of lung transplantation after ECMO bridging therapy. Importantly, it was beneficial for establishing standardized nursing protocols and developing an evaluation index system of ECMO nursing in a scientific manner.

References:

1.Zheng H, Yan D, Wang P, et al. Survival with Lung Transplantation and Extracorporeal Membrane Oxygenation: A Systematic Review and Meta-Analysis. Minerva Respir Med 2022;61:6-15.
2.Wan X, Bian T, Ye S, et al. Extracorporeal Membrane Oxygenation as a Bridge Vs. Non-Bridging for Lung Transplantation: A Systematic Review and Meta-Analysis. Clin Transplant 2021;35:e14157.

Changes in the text: "we have modified our text as advised (see Page 14-15, line 257-

271)"

Comment 2: Please describe in more detail about the complications during ECMO.

Reply 2: Thanks for reviewer's suggestions. We have added relevant descriptions in our paper.

"The wide applications of ECMO may cause a series of complications during patient care. Generally, ECMO complications include infections, bleeding, thrombosis, hemolysis, renal injury and hepatic impairment. These risks and benefits should be heavily weighted in clinical practice. Indeed, we found that mortality was significantly higher in trials involving patients with complications during ECMO in our review. Our observation of complications including intracranial hemorrhages and bloodstream infection were tightly associated with mortality (risk ratio 2.24, 95% CI 1.45-3.44). During ECMO assistance, these were several elevated risks of complications including bleeding, thrombosis, and infections, which can impact patient prognosis."

Changes in the text: "we have modified our text as advised (see Page 16-17, line 305-328)"

Comment 3: There appear to be a lot of English mistakes, so could the authors ask an English native language expert to check the paper to ensure correctness of the spelling, grammar and syntax?

Reply 3: Thanks for the reviewer's comments. We have edited this manuscript for language, grammar, clarity, native tone, flow, and coherence.

Changes in the text: we have modified our text as advised. **（highlighted in red in the manuscript）**

Reviewer C

Overall this is an excellent paper. The authors clearly made a diligent effort looking for eligible studies, and found an impressive patient number.

I am recommending minor revisions, but this paper will be a valuable contribution to the field.

Comment 1: Line 5 – I think there is a typo here. Edit to the authors' style.
Reply 1: Thanks for the reviewer's advices. Our abstract has been edited in the standard form of the journal's instructions.

Comment 2: Line 20 - "Conclusions: Lung transplant patients with prolonged ECMO

support, worsening liver and kidney functions as well as complications associated with prognostic in lung transplantation after extracorporeal membrane oxygenation bridging therapy."

Difficult to understand. Does the author mean Lung transplant patients with prolonged ECMO support [are at high risk for] worsening liver…

Reply 2: We greatly appreciate the reviewer's suggestions.

Changes in the text: we have modified our text as advised.
The search identified eight trials encompassing 1,086 participants. The prognosis of patients undergoing lung transplantation with ECMO bridging was significantly associated with several factors: prolonged ECMO support (risk ratio 1.07, 95% CI 1.02–1.12, I^2 = 77%), deterioration in liver and kidney function (risk ratio 3.62, 95% CI 2.37–5.54, I^2 = 0%), and complications during ECMO (risk ratio 2.24, 95% CI 1.45–3.44, I^2 = 5%).
(see Page 3-4, line 46-52)

Comment 3: Line 56 – "These enhancements have facilitated the increased utilization of ECMO as an effective bridging therapy for patients with cardiopulmonary failure and is preferred over tracheal intubation (10-12)."

Would Briefly mention why. Avoidance of nosocomial pneumonia, ventilation-refractory hypoxia, ability to ambulate and participate with pre-operative rehabilitation, etc.

Reply 3: We greatly appreciate the reviewer's suggestions.
"These improvements have led to the growing use of ECMO as a preferred bridging therapy over tracheal intubation for patients with cardiopulmonary failure, primarily to avoid hospital-acquired pneumonia, ventilator-refractory hypoxia and to maintain walking ability and participation in preoperative rehabilitation (10-12). "
Changes in the text: we have modified our text as advised (see Page 7, line 102-108)

Comment 4: No discussion of the rate of bleeding on ECMO which remains the most common source of major complications. But this may be included in the composite reference to "complications." If so, would mention.

Reply 4: Thanks for the reviewer's comments. "The wide applications of ECMO may cause a series of complications during patient care. Generally, ECMO complications include infections, bleeding, thrombosis, hemolysis, renal injury and hepatic impairment. These risks and benefits should be heavily weighted in clinical practice. Indeed, we found that mortality was significantly higher in trials involving patients with complications during ECMO in our review. Our observation of complications including

intracranial hemorrhages and bloodstream infection were tightly associated with mortality (risk ratio 2.24, 95% CI 1.45-3.44). During ECMO assistance, these were several elevated risks of complications including bleeding, thrombosis, and infections, which can impact patient prognosis."

Changes in the text: "we have modified our text as advised (see Page 16-17, line 305-328)"

Comment 5: Finally, I would mention that the higher rate of mortality among patients needing ECMO support is not an apples-to-apples comparison against overall waitlist mortality. Since patients receiving ECMO are the most critical, the 2 groups are not comparable populations. It is more likely that a proportion of the 23% of patients who die on the waitlist (e.g. those eligible for ECMO) who would have had a 100% mortality, are now given a chance at pre-transplant survival. Of those, now 63% make it to surgery compared to what would have been nearly 0% in the high risk / critical patient sub group.

Reply 5: Thanks for reviewer's suggestions. Indeed, the higher rate of mortality among patients needing ECMO support is not an apples-to-apples comparison against overall waitlist mortality. However, we aimed to study the prognostic factors of lung transplantation after ECMO bridging therapy in patients for lung transplantation. Moreover, our review did not make a comparison between groups for overall mortality.