Peer Review File

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Reviewer A Comments:

This manuscript by authors from 4 University institutions in the USA deals with an extensive review paper on new developments in lung transplantation that emerged over the last two decades. These developments are important to know and understand for anaesthesiologists and their trainees involved in lung transplantation.
We thank the authors for writing this extensive and complete review on current knowledge and increasing evidence in lung transplantation.

Major Comments:

1) Title and content of the paper:
The current paper is too long and too descriptive. Some sentences are difficult to read and to follow, not really focused.
We thank the reviewer for this comment and we have edited for length and readability.

The content does not fit with the title of the paper. Two options for revision are possible:
- Choosing a new title such as “new developments in lung transplantation important to anaesthesiologists” or “perioperative anaesthesiologic care in lung transplantation”.
We thank the reviewer for this comment and have made recommend changes to the title

- Narrowing the manuscript down by focusing on “state of the art in anesthesia for lung transplantation” by deleting the paragraphs on LAS, ECD, DCD, ECLS, TTE, PGD.

We thank the reviewer for this comment and have narrowed down the manuscript with the concept of “state of the art”. As such, we have removed the sections detailing lung allocation scoring and primary graft dysfunction as suggested.

2) Anaesthetic monitoring during lung transplantation:
The authors focus on the useful information obtained with TTE/TEE during lung transplantation; however, other useful methods for monitoring the patient are currently missing and not discussed.
We appreciate the reviewer comments and we respect the reviewer's opinion. We defer to add further description this time, as previous standard of care monitors have been well described and we believe an update on these is not warranted at this time.

Minor Comments:

Line 53: canine ….. ?
We have changed the word canine to dog

Line 80-81: strange construction of this sentence.
We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 92: please explain the meaning of the LAS-number, how to interpret this?
We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 95: "figure 1" in the text refers to "table 1" and should include criteria used to determine "waitlist urgency". However, "table 1" includes 2 criteria (CI at rest prior to any exercise and mean pulmonary artery pressure) that are used to determine "probability of survival after transplant" and not "waitlist urgency". So please adapt the referral in the text or adapt table 1.
We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 136: add the word "prior" to living organ donor.
We thank the reviewer for this and we have made the suggested change, adding the word "prior"

Line 168-169: it is not clearly indicated that you aim for comparing outcome between lungs from DBD vs DCD donors.
We appreciate the reviewer's criticism and have deleted this paragraph per another reviewer's

recommendation.

Line 215-216: remove this sentence or add some explanation.
We thank the reviewer for this comment and the sentence was removed as suggested.

Line 218: EVLP is absolutely not a "physiological" condition.
We thank the reviewer for this comment and have removed the word physiologic from this sentence.

Line 290: replace "single ventilation technique" by "one-lung ventilation technique".
We thank the reviewer for this comment and have changed to one-lung ventilation technique.

Line 447: I would not say that a restrictive fluid management is recommended. The main factor is that fluid overload or maybe better "hypervolemia" should be avoided because this might lead to increased extra-vascular lung water / pulmonary edema and subsequently PGD. Also, we know from thoracic surgery and major surgery in general (in the light of goal-directed therapy) and from the ICU that an "optimal" fluid strategy should be recommended, as both hypervolemia and hypovolemia are associated with worse outcome. Both under- and over-resuscitation are associated with increased complication rate.
We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 451: It should also be emphasized that the need for allogeneic blood transfusion is often driven by intra-operative surgical blood loss and is often "out of the anesthesiologists hands". Off course a restrictive transfusion strategy should be applied whenever possible to reduce the immune modulation.
We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 453: remove "thromboelastography" as it is a form of point-of-care testing.
We thank the reviewer for this comment and have made the recommended changes.

Line 456-465: remove this paragraph as it is already extensively discussed before.
We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 479-481: "a more restricted physiology is anticipated"…. Please explain wat you mean or rather

remove this sentence. Also relocate the statement about adaptation "to the donor lung size" to the paragraph about lung-protective ventilation and tidal volumes.

We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 483-484: the method that should be used to recruit the transplanted lungs is undefined so remove the specification '15 sec 30cmH2O'.

We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Reviewer B Comments:

I would like to thank the authors for drafting this excellent manuscript outlining the brief history and development of lung transplant organ allocation, advancement in donor pool expansion, trend of extracorporeal life support use, utilization of TEE, and PGD prevention ventilation. The manuscript is very well written and organized, and I only have some minor suggestions.

One appropriate addition to this article I could think of would be some discussion regarding extended cold static lung preservation strategy at 10 C led by the Toronto group. Although this is still in early stage of investigation, early results seem promising and may potentially lead to some further expansion of donor pool as well as a transition of lung transplantation to a daytime, more elective procedure.

We thank the reviewer for this comment and have added this as appropriate.

The precision of language can also be improved, for example (not limited to what listed below):
Line 327: "cath lab" can be deleted.
Line 473: "PGD into to intraoperative lung transplantation" is unclear.
Line 476-477: I think authors meant to say "reduced" instead of "extended" I:E ratio.

We thank the reviewer for these comments and we have responded in the following manner:

Line 327: We have deleted "cath lab" as recommended

Line 473: We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Line 476-477: We thank the reviewer for this comment and we have removed this paragraph as suggested by reviewer A.

Reviewer C Comments:

I was honoured to be have the opportunity to review the manuscript by Ashley Virginia Fritz and colleagues entitled "Anesthesia for Lung Transplantation: Innovations in the 21st Century". This is a well-written highly interesting review focusing on major advances regarding critical issues of lung transplant activity. The authors should be congratulated for their outstanding work. They present an excellent manuscript that for sure will be helpful for the transplant community.

We thank the reviewer for the generous and respectful comments. We appreciate their time, consideration, and honest feedback.

Reviewer D Comments:

The authors submitted a review article on the topic of anaesthetic management in lung transplantation. However, most of the text needs to be revised before the article can be considered for the publication. There seems to be a significant difference in the quality of the text between the last paragraph (PGD) and the rest of the text (which needs to be improved).

1. The whole text needs to be improved to be written in the style typical for review articles. Despite it is not a systemic review, the majority of the texts lacks standard discussion and comparison with the studies and does not refer to exact numbers and results from these studies. The review article is missing references on several occasions. Also, the authors do not refer to the studies in a standard fashion.

We appreciate the reviewer's comments and we have edited the manuscript for length and content as suggested.

2. The whole text needs to be improved for English language and grammar.

We appreciate the reviewer's comments and we have reviewed the manuscript and made appropriate

changes to grammar and language as requested.

3. Abbreviations need to be re-checked, spelled out when used for the 1st time, and corrected as the use of some abbreviations is not standardized (SLT, BOLT…).
We appreciate the reviewers' comments and we have reviewed the manuscript and made appropriate changes standard abbreviations as requested.

4. L 43, "end stage lung disease" should be end-stage.
This change was made to reflect the suggested edit.

5. L 45, "extra corporeal life support" should be extracorporeal and abbreviated (ECLS).
This change was made to reflect the suggested edit.

6. L 52, "The birth of lung transplantation" -- please re-phrase as only subject can be born, abbreviate LTx.
We thank the reviewer for this comment and this change was made to reflect the suggested edit.

7. L 70, please re-phrase "donation after circulatory death donors??" and abbreviate (DCDs).
We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

8. L 71-74, missing references as these statements do not refer to any literature. Here I suggest to add a few more such as:
a. Marczin N et al. International consensus recommendations for anesthetic and intensive care management of lung transplantation. An EACTAIC, SCA, ISHLT, ESOT, ESTS, and AST approved document. J Heart Lung Transplant. 2021 Nov;40(11):1327-1348.
b. Sef D et al. Midterm outcomes of venovenous extracorporeal membrane oxygenation as a bridge to lung transplantation: Comparison with nonbridged recipients. J Card Surg. 2022 Apr;37(4):747-759.
c. Loor G et al. Effect of mode of intraoperative support on primary graft dysfunction after lung transplant. J Thorac Cardiovasc Surg. 2022 Feb 4:S0022-5223(22)00119-2.
We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

9. L 80, please re-phrase "lower acuity patients while patients who were higher acuity or shorter life".
We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

10. L 95, where is Figure 1?

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

11. L 106, please re-write “waitlist times” as it is incorrect.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

12. L 113, please re-phrase “one year post-transplant” as “1-year” is standard.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

13. L 113-116, please re-write or delete as this is not correct and while we consent patients with estimated higher risk we do not aim to “predict postoperative mortality”.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

14. L 117, A major change in the US but not in the rest of the world, please re-phrase.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

15. L 124, what is OPTN?

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

16. L 133, “is formulated with the patient’s blood type”, please re-phrase.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

17. L 136, “and is 25% of the total allocation score”, please re-phrase.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

18. L 139, please re-phrase.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

19. L 141, please re-phrase “the mounting supply”.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

20. L 144-145, “annually, continues to rise”, please correct. “reexamined their historically rigid donor criteria.”, please re-write.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

21. L 147-148, “donation and donation after circulatory death (DCD) donors”, please re-phrase, abbreviation already mentioned. Please re-phrase “source of lungs”.

We thank the reviewer for this recommendation, and we have edited the sentence to read “Donation after brain death is most common whilst donations after circulatory death have largely been avoided due to the fear of warm ischemia time and associated allograft dysfunction.”

22. L 150, “However, lungs are unique.” Please delete.

We thank the reviewer for this comment and have deleted the phrase as recommended.

23. L 155, please re-phrase “from intensive care unit (ICU) DCD donors”.

We appreciate the reviewer’s comment and have removed “from the ICU”

24. L 156, please re-write ”The first controlled DCD (cDCD) donor transplant of the modern era”.

We appreciate the reviewer’s comment and have removed “of the modern era” from the sentence.

25. L 159, please re-phrase “pronounced in Europe”.

We appreciate this recommendation and have changed pronounced to “common”.

26. Lines 161-167, please delete as readers are familiar with this.

We have deleted this paragraph as recommended by the reviewer.

27. L 169, please refer to the study in a standard manner and not “A 2015 meta-analysis” and please refer to the correct results and comparison.

Please see #29

28. L 171-173, please refer to the correct results with numbers and not only “significantly increased”…

Please see #29

29. L 175, “Also, one analysis”, please refer to the study in appropriate way.

We appreciate the reviewer’s comments and have re-worded L169-175 to read “The inability to randomize donors and recipients limits the available outcomes data to observational cohort studies and subsequent meta-analyses, but there is likely no difference in 1-year mortality, primary graft dysfunction, PGD or acute rejection between DCD and DBD donors.(28-30) However there may be

increased anastomotic airway complications in the DCD cohort 2.07 (95% CI = 1.09–3.94; p = 0.026) and there was conflicting data on 5 year survival (29), but when (31) Overall, the current evidence suggests that cDCD donors are a viable and safe source with equivalent short term and potentially, long term outcomes."

30. I suggest here to add a table that will simplify for readers an overview of the important outcomes from all these important studies.

We respect and appreciate the reviewer comments and will defer to add a table at this time.

31. L 183, what is uDCD? Please spell out.

We thank the reviewer for this comment and have spelled out "uncontrolled DCD"

32. L 189, please re-phrase "the same group, from Madrid".

We thank the reviewer for this comment and have changed the sentence to "Recently, De la Cruz et al. reviewed all lung transplants from"

33. Lines 191-193 need to be completely re-written, please compare the results precisely in a standard manner. It is "90-day" and not "90 day".

We appreciate this comment from the reviewer and have changed the sentence to read "Recently, De la Cruz et al reviewed all lung transplants from 2013-2019 (239 DBD, 29 cDCD and 14 uDCD donors)(34) and found no difference in outcomes amongst the three groups including, 30-day, 90-day, 1 and 3-year survival, PGD at 3 and 72 hours, chronic lung allograft dysfunction (CLAD) incidence, airway complications, need for extracorporal membrane oxygenation (ECMO), or hospital or ICU length of stay.(34)"

34. L 193, a sentence cannot be started with the number.

We thank the reviewer for this recommendation and have removed the sentence per another reviewer's recommendations.

35. L 196, please re-phrase "Another group from Spain".

We thank the reviewer for this criticism and have changed the sentence to read "Others have reported"

36. L 197, please re-write or delete "similar, excellent long term outcomes." Where are the numbers, results?

We thank the reviewer for this comment and have re-written this section

37. L 198-200, which "work" in donor identification is needed?! EVLP already exists! Either re-write or delete.

We thank the reviewer for this comment and have re-written this section

38. Lines 201-211, The authors must remove the paragraph about MAID and euthanasia as this is serious ethical concern and is completely irrelevant to the topic of this article.

We respect the reviewer's comments and have removed this paragraph.

39. L 216, please re-write "donor, most recently 37%".

We thank the reviewer for this comment and have removed this from the sentence.

40. L 219-220, please remove the sentence "EVLP is multifaceted." Pls be precise and re-write "up to 12 hours or
more".

We thank the reviewer for this comment and have removed the phrase "EVLP is multifaceted". We have changed the sentence to read "EVLP significantly extends the safe organ preservation time to up to 12 hours"

41. L 223, 225, please re-phrase "lung refusals in one study", "Indirectly, by having EVLP available".

We thank the reviewer for this comment and have changed the sentences to read "EVLP may directly increase lung transplant volume by recuperating organs that initially did not meet donation criteria into acceptable organs for transplant.(42) Many centers with active EVLP programs report increases up to 70% in transplant volume and utilization because of EVLP."

42. L 227, "significant increases", please refer exactly to the results.

We thank the reviewer for this comment and have re-written this section

43. L 230-234, please re-phrase "Two are fixed", "Van Raemdonck's ISHLT registry study", "Campo-Canaveral de la Cruz's study".

We thank the reviewer for this comment and have re-written this section

44. L 238, ECD organs?

We thank the reviewer for this comment and have further clarified extended donor criteria for clarity.

45. Lines 243-246 need to be re-written for some weird wording (in spite, worst donor ration, Leveraging the benefits…) and please refer to the results and numbers.

46. L 253-256, Needs to be removed as the authors need to refrain from the opinion and refer to the evidence citing the particular references. DCD donors are associated with more post-transplant ECMO and AKI (Sef D et al. Utilization of extracorporeal membrane oxygenation in DCD and DBD lung transplants: a 2-year single-center experience. Transpl Int. 2020 Dec;33(12):1788-1798.) and more BOS in the long-term follow-up (Sabashnikov A et al. Long-term results after lung transplantation using organs from circulatory death donors: a propensity score-matched analysis. Eur J Cardiothorac Surg. 2016 Jan;49(1):46-53.) and such findings need to be discussed within the review article.

We thank the reviewer for this comment and have re-written this section

47. L 262-267, some weird wording (end stage pulmonary disease exacerbations, provide a reasonable pre-existing operative ECLS…), please re-write.

We thank the reviewer for this comment and have re-written this section.

48. L 276, please be precise and re-write "half are supported", median cannot be 6-29 days.

We thank the reviewer for this comment and have re-phrased this sentence. "The average duration of ECMO was between 6-29 days (depending on the study), half of patients supported with a VV configuration and numerous patients were ambulatory and awake until transplantation"

49. L 281, please re-phrase "being awake and the ability to participate".

We thank the reviewer for this comment and have re-written this sentence.

50. L 289, L 297, please re-phrase, again weird wording (full CPB, Historically ECLS…), "single-stage" is wrong.

We thank the reviewer for this comment and have re-written this sentence.

51. L 301, 303, please re-phrase, also the authors probably refer to SIRS?

We thank the reviewer for this comment and we have removed this sentence.

52. L 309, "some retrospective single center data"? Please avoid such statements.

We thank the reviewer for this comment and have re-written this sentence.

53. L 312, L 315, L 316 “Benefits over no ECLS”, “added inflammation and coagulopathy”, “is from the Hoetcher et al.”, please avoid such weird wording and re-phrase.

We thank the reviewer for this comment and have re-written this sentence.

54. L 327, what is the meaning of “septostomy procedures cath lab”? Please re-write “describes the use a hybrid-ECMO-CPB”.

We thank the reviewer for this comment and have re-written this sentence.

55. L 335-336, please re-write, institutions have “protocols”….

We thank the reviewer for this comment and have re-written this sentence.

56. L 346, “Two survey studies of lung transplant anesthesiologists from around the world…”, please re-write.

We thank the reviewer for this comment and have removed this sentence.

57. L 352-353, please remove this line as unnecessary.

We thank the reviewer for this comment and have removed this sentence.

58. L 355, which “other pathology”?! “Many patients’ last echo”?!, “Many patients have PH RV dysfunction…” please re-write.

We thank the reviewer for this comment and have removed this sentence.

59. Lines 362-367, please remove as it is a repetition of well-known basic practice.

We thank the reviewer for this comment and have removed this sentence.

60. L 370, “never did”, please re-phrase.

We thank the reviewer for this comment and have re-worded this sentence.

61. L 376, “Anastomotic complications are rare”, this is not correct, please provide the numbers.

We thank the reviewer for this comment and have added the incidence of anastomotic complications.

62. L 397, “all four PVs”, what if the patient has 5 PVs, please correct.

We thank the reviewer for this comment and have removed the word “four”.

Reviewer E Comments:

Thank you for your efforts to create such a thorough review of the topic. The discussion is very in depth, and the reference list is impressive. However, there are a significant number of grammatical issues that need to be addressed.

1. Line 52: add noun after “Soviet...” (surgeon? scientist? doctor? etc)..

We have changed the sentence to read “In May of 1947 Vladimir Demikhov reported the first successful lung transplantation in a dog”

2. Line 61: What were the reasons for COPD PH and CF to be considered contraindications?

We appreciate the reviewers comments and have changed the sentence to read “The early indication for lung transplant was end-stage pulmonary fibrosis. Over time, chronic obstructive pulmonary disease (COPD), pulmonary hypertension, and cystic fibrosis were added as indications for lung transplant.(3)”

3. Line 68: this is the first time “lung allocation score” is used- define “LAS” here instead of later in the text.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

4. Line 72: consider adding postoperative support as another important use for ECLS.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

5. Line 86: define “LAS” above.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

6. Line 115 "etc" should not be used in the main text of formal writing.

Consider "variables such as...".

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

7. Line 132-135: incorrect use of semicolons.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

8. Line 144: remove comma after “annually,”.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

9. Line 151 and 152: over use of “additionally”.

We have removed this word as recommended by the reviewer and appreciate the comment.

10. Line 159: “>” should not be used within main text of formal writing.

We appreciate this recommendation and have changed the text to read “greater than”.

11. Line 167: reference?

We appreciate the reviewer’s criticism and have deleted this paragraph per another reviewer’s recommendation.

12. Line 169 and 171: Meta analysis of what data? What were the study groups?

We appreciate the reviewer’s comments and have re-worded L169-175 to read “The inability to randomize donors and recipients limits the available outcomes data to observational cohort studies and subsequent meta-analyses, but there is likely no difference in 1-year mortality, primary graft dysfunction, PGD or acute rejection between DCD and DBD donors.(28-30) However there may be increased anastomotic airway complications in the DCD cohort 2.07 (95% CI = 1.09–3.94; p = 0.026) and there was conflicting data on 5 year survival (29), but when (31) Overall, the current evidence suggests that cDCD donors are a viable and safe source with equivalent short term and potentially, long term outcomes.”

13. Line 193-195: was this improvement statistically significant? Unlikely if n=14 as per ln190.

We thank the reviewer for this recommendation and have removed the sentence.

14. Line 207: add "no difference IN..."

We thank the reviewer for this recommendation and have added “no difference in”

15. Line 255: remove comma after "technology,".

We thank the reviewer for this comment and have removed the comma.

16. Line 274-277: be consistent with past and present tense.

We thank the reviewer for this comment and have fixed the sentence “tense”.

17. Line 280: add "and" before sequential.

We thank the reviewer for this comment and have added the word “and”.

19. Line 295: mPAP>25 is not severe pulmonary hypertension.

We thank the reviewer for this comment and have removed the word severe.

20. Line 307: in light of? "in lieu of" implies instead of.

We thank the reviewer for this comment and have changed the wording to reflect “in light of”.

21. Line 313-314: these are not benefits over "no ECLS" as implied at the beginning of the sentence; these benefits are only applicable when comparing to CPB.

We thank the reviewer for this comment and have changed the sentence to reflect comparison between.

22. Line 318: was this all types of ECMO (VV, VA, post operative?).

We thank the reviewer for this comment and have made the appropriate change in the text.

23. Line 321: this only applies to VA ECMO.

We thank the reviewer for this comment and have made the appropriate change in the text.

24. Line 327: add "in the" before cath lab; add "of" after "use".

We thank the reviewer for their comment and have changed the sentence to read: “These are termed alternative ECMO techniques and include the use of additional ECMO cannulas, non ECMO mechanical support devices and atrial septostomy procedures for LV venting”

25. Line 352: change “Pre-transplant” to lower case.

We thank the reviewer for their comment and have changed the letter to lower case.

26. Line 359: add “PH-ASSOCIATED…”.

We thank the reviewer for their comment and have changed the sentence to include PH associated.

27. Line 359: change “track” to “tract”.

We thank the reviewer for their comment and have changed the word to tract.

28. Line 369: describe the survey more (respondents, specifically intraop TEE or preoperative TTE?); consider adding "et al."

We thank the reviewer for their comment and have further described and added "et al".

29. Line 372: "anastomosis" should be plural.

We thank the reviewer for their comment and have changed the word to plural.

30. Line 395: consider adding "et al."

We thank the reviewer for their comment and have add et al.

31. Line 399: add "…<2.5mm HAS BEEN associated…).

We thank the reviewer for their comment and have changed the wording to read "has been associated with graft failure".

32. Line 410: noun/verb mismatch (cutoff or cutoffs vs exist or exists).

We thank the reviewer for their comment and have changed the verb to match the noun by changing verb to exists.

33. Line 442: Table 2 should be referenced in this paragraph.

We thank the reviewer for their comment and have added the reference to Table 2 in the paragraph.

34. Line 451: change to "in particular" or "particularly".

We thank the reviewer for their comment and have deleted the word.

35. Line 452: is this ratio reversed? Higher PRBC volume is associated with PGD risk.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A

36. Line 459: add "…dynamic LV OUTFLOW tract…"; also this concept is not mentioned at all in the TEE section.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A

37. Line 456 to 465: Consider removing this paragraph. The argument for TEE preventing PGD is a stretch

and distracts from the other PGD discussion topics. Line 462-465 has already been discussed in other sections and has limited to no TEE involvement.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A

38. Line 470: Include a sentence(s) noting that VA ECMO may require TIVA depending on the specific circuit.

We thank the reviewer for this comment and have removed this section as suggested by reviewer A

39. Line 473: "…, PGD into to intraoperative lung transplantation…"?

We thank the reviewer for this comment and have removed this section as suggested by reviewer A

40. Line 477: replace ":" with "..inspiratory TO expiratory"

We thank the reviewer for this comment and have removed this section as suggested by reviewer A

41. Line 483-484: this needs a reference and there is no verb for the subject (e.g. "is recommended").

We thank the reviewer for this comment and have removed this section as suggested by reviewer A.

RE-review Comments:

1. The authors need to clarify in the abstract whether this is a review or perspective article.

Reply: We thank the authors for this comment and have made the changes as requested.
Changes in text: We have clarified in the abstract that this article is a review article.

2. Please abbreviate LTx for lung transplant.

Reply: We thank the authors for this comment and have made the changes as requested.
Changes in text: LTx.

3. Line 52, "1963 to 1983 40 lung transplants" – no punctuation used.

Reply: We thank the authors for this comment and have added punctuation.
Changes in text: ","

4. Line 61, “A once extraordinary” – please correct.

Reply: We thank the authors for this comment and have made the changes as requested. Changes in text: deleted above phrase and added “lung transplantation” .

5. Line 77, there is no such term as “living lobar donation” – please correct. DCD is spelled out 2nd time – please delete.

Reply: We thank the authors for this comment and have made the changes as requested. Changes in text: deleted living lobar donation and deleted the spelling out of DCD.

6. Line 78, please abbreviate DBD and DCD. Most of the paragraph seems opinionated – please add references.

Reply: We thank the authors for this comment and have made the changes as requested. Changes in text: abbreviated DBD and DCD as requested. There are citations throughout this paragraph. A specific citation was added to this sentence.

7. Line 83, please remove that DCD donor do not experience HD instability – incorrect, any donor can become unstable in ICU. Also, missing references in the same paragraph and seems opinionated, please correct

Reply: We thank the authors for this comment and have made the changes as requested. Changes in text: deleted HD instability and included “experience less.” There are citations throughout this paragraph.

8. Line 90, please correct “outcomes data”

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: changed word to outcome.

9. Line 94, “in the DCD cohort 2.07 (95% CI = 1.09 – 3.94; p = 0.026) and there was conflicting data on 5 year survival, but when (18)” – not clear how the authors reported this study.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have removed the conflicting data.

10. The inability to randomize donors and recipients limits the evidence about DCD LTx, but in the recent study of 105 LTx with robust donor data (doi: 10.1111/tri.13754) - DCD donation was associated with increased need for postoperative ECMO ((32.0% vs. 7.5%) and the difference remained considerable after adjustment for the pre- and intraoperative covariates: RR = 4.11 (95% CI 0.95-17.7), P = 0.058) Furthermore, incidence of delayed chest closure, postoperative chest drainage after DCD donation. This is important to add to your discussion about DCD. As this should be a review article, all perspectives need to be considered.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have made the requested corrections and added this to the text.

11. Line 105, “including, 30-day” – please correct. “post-death”.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have made the requested corrections and removed “post-death” .

12. Line 110, “the Belgium experience of 22 DCD-V donor” – Belgium is a large country therefore cannot be represented by 22 donors, please correct.

Reply: We thank the authors for this comment and have made the changes as requested per prior reviewer comments.

Changes in text: We have deleted this paragraph per request of prior reviewer stating that any reference to DCD-V (category V DCD) should be removed for ethical considerations.

13. EVLP when used in DCD LTx can be associated with more pulmonary edema on the chest X-ray immediately after LTx and longer mean time to extubation in the DCD LTx. Vilavicencio et al. have recently demonstrated in a propensity-matched analysis (doi: 10.1016/j.athoracsur.2018.07.024). Please add to your discussion about EVLP as this is a clinically relevant drawback. Discussion cannot be from only single perspective.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have made the added suggestions.

14. Lines 140-142, is there any systematic review or meta-analysis that supports the use of EVLP? If there is no such strong evidence, please remove this statement.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have deleted the sentence as suggested.

15. Line 144, please remove “physiologic” as EVLP can not reproduce physiologic environment at all. Missing reference.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have added “laboratory monitoring” and deleted “of physiologic parameters”. Reference was added.

16. Line 176, “in ECMO bridge to transplant patients” – please correct.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have changed the sentence to read “in ECMO when used as bridge to transplant”.

17. Lines 187-191, pls use either single-lung ventilation or one lung ventilation, I suggest single-lung.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: changed the text to read “single-lung”.

18. Lines 194-201, the whole paragraph is missing references, otherwise this seems like opinion.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have added citations.

19. Line 204, please abbreviate PGD.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: changed PGD to include abbreviation and spelling and edited as such throughout the text.

20. “Data remains controversial however, CPB” – please correct.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have deleted that sentence.

21. Line 209, “full respiratory (VV)” – there is a mistake with the abbreviation, please correct. Again - “hemodynamic support (VA)”

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We corrected the abreviation to read VV-ECMO and VA-ECMO.

22. What is “termed alternative ECMO techniques”?

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have deleted the word termed and added “alternative ECMO techniques”

23. Line 229, please correct or delete as the statement is very imprecise.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: Deleted the sentence as suggested.

24. Line 232-3, please use reference at the end of the sentence

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: we have moved the reference to the end of the sentence.

25. Lines 239-242 – the sentence is too long, please add reference.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have changed the sentence format and added the reference 56 and 74.

26. Line 252, correct to "right-sided".

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have added the hyphen.

27. Lines 253-255, missing references.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: Citations were added 86 and 87 references.

28. Line 262, Correct to "case-by-case".

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have added the hyphens.

29. "2 to 33 percent" – please correct to %.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have added the percent symbol.

30. Lines 273-276, seem like another author started abbreviations – PV and PA have been already used.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: We have added abbreviation to PV and PA earlier in text and corrected in rest of text.

31. Line 279, missing reference.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: Citations were added (86 and 91).

32. Line 298, no need to abbreviate PVR.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: deleted abbreviation for PVR.

33. Line 309, "A systematic review found " - please re-phrase.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: The sentence was changed to read "Kumar et al reported…"

34. Lines 315-318, missing references.

Reply: We thank the authors for this comment and have made the changes as requested.

Changes in text: Citations were added (102 and 86).