Peer Review File

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Reviewer A

The authors are to be commended for undertaking this study. As noted, it has been previously discussed by Li and Porteous, however, the impact of diastolic dysfunction on PGD needs to be further elucidated through investigation.

The most recent ISHLT consensus on ECLS in lung transplantation, Part II, https://pubmed.ncbi.nlm.nih.gov/39453286/ , discusses this as well, including the importance of echocardiography in perioperative lung transplantation. It discusses the prolongation of ECLS due to LVDD in group 1 PAH patients, and this is further developed in Part III, https://pubmed.ncbi.nlm.nih.gov/40455186/ , which is focused on postoperative considerations and a structured TTE exam to wean VA ECMO.

The authors should expand their discussion to discuss the literature focused on these issues, and the inclusion of both of these manuscripts in JHLT will be important for them.

Otherwise, could the authors please consider inclusion of high quality echo images, and perhaps creation of tables to discuss some more practical aspects of their echo exam? This, combined with expansion of the discussion, will improve the paper ahead of publication.

Reply: We are very grateful to the editor for his valuable suggestions, especially on the importance of supplementing high-quality echocardiography images. The key role of echocardiography in the decision of ECMO weaning after LTx has been supplemented and elaborated in detail in the discussion section. For details, please refer to lines 225-233. However, regarding the suggestion of supplementing ultrasound image data, we need to explain the following to you: For the strict protection of patients' privacy, this study is a retrospective analysis, and all case data need to be exported through a specific application process. Limited by this process and the current data state, there are many missing values of postoperative echocardiography data, so it is difficult to obtain high-quality original ultrasound image data that meets the publishing requirements in a short time. Therefore, we regret to say that this study may not be able to include such images in this submission. In order to make up for this shortcoming as much as possible and enhance the clinical reference value of the paper, we made an in-depth analysis: we paid special attention to the influence of LVDD and preoperative cardiac parameters on the duration of postoperative ECMO, and made a detailed comparative analysis. The results showed that there was no statistically significant difference in postoperative ECMO use time (see Table 1&S4 for specific data). Once again, we thank the editor for his careful review and constructive comments, and understand the benefits of high-quality images to the paper. We will focus on improving the collection and management process of image data in the future research, in order to better present relevant ultrasound images in the follow-up work.

Reviewer B

General comments to the editor
This is a single-center retrospective study evaluating the impact of preoperative left ventricular diastolic dysfunction (LVDD) on primary graft dysfunction (PGD) and mortality after lung transplantation, in a cohort of 344 patients. The topic is highly relevant, as it addresses a relatively underexplored predictive factor with direct implications for recipient selection and preoperative optimization. The study presents a robust sample size and consistent results, demonstrating an independent association between LVDD and the risk of PGD.
On the other hand, the association with mortality loses statistical significance after adjustment,

which should be communicated more cautiously. In addition, there are some methodological limitations that deserve further discussion. I consider the article suitable for major revision, as it has publication potential if the following issues are addressed.

Major points
Conclusions on mortality
In the abstract and conclusions, the interpretation of LVDD as a prognostic factor must be more cautious. After adjustment, LVDD is not an independent predictor of mortality, and this needs to be clearly stated to avoid misleading interpretations.

Reply: For details, please refer to lines 11-15 , lines 211-213, lines 315-318 .

Discussion of limitations
The discussion of methodological limitations should be expanded:
Retrospective design, subject to selection bias.
Diagnosis of LVDD included indirect parameters (TRVmax calculated).
Significant baseline differences between groups, particularly the prevalence of pulmonary hypertension, which may act as a confounder.
These issues should be highlighted more clearly to ensure transparency.
Reply: For details, please refer to lines 262-266 .

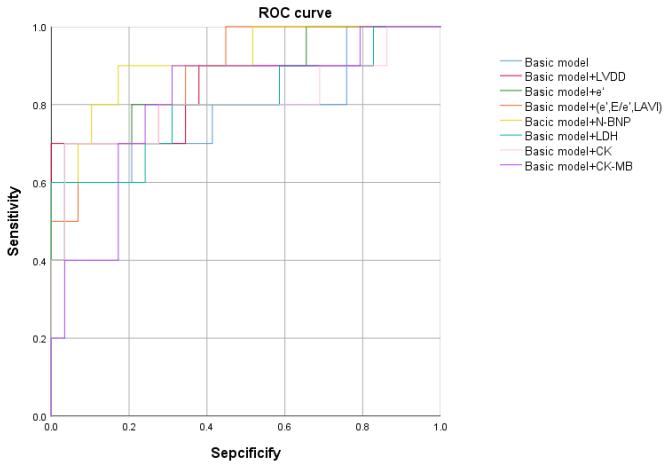
Clinical impact
The clinical implications should be balanced. The suggestion to optimize diastolic function before transplantation is interesting, but should be framed as a hypothesis rather than a definitive recommendation.
Reply: For details, please refer to lines 315-318 in conclusion.

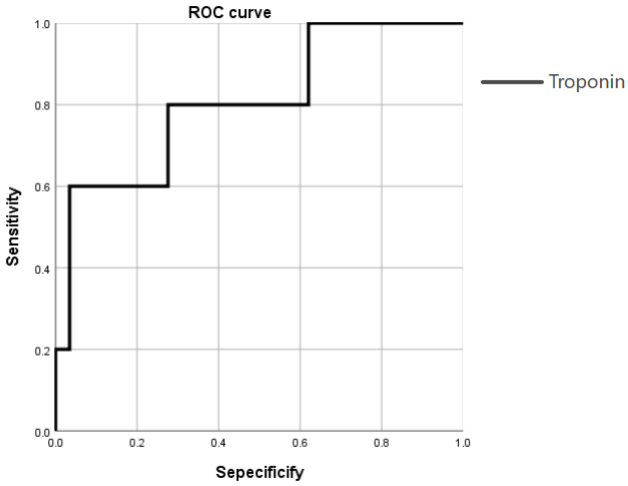
English language revision
The manuscript is understandable but contains grammatical and stylistic errors that impair readability. Professional English editing or review by a native speaker is recommended.

Minor points
Standardize abbreviations (LTx, LVDD, PGD) throughout the manuscript.
Reply: For details, please refer to abbreviation table.

Some tables are overly detailed; consider simplifying or highlighting only the most relevant data.
Reply: According to your opinion, we have deleted the contents of the form. For details, please refer to Table1.

ROC (AUC) results could be summarized more concisely, combining text and figure to reduce redundancy.
Reply: We made ROC curves of nine indexes, in which the missing value of N-BNP index exceeded 30%, but considering the importance of BNP, we still made statistics on the patients with complete data, as shown in the following figure. Because there are only 84 cases of troponin, we analyze the ROC curve separately, as shown in the following figure. If you consider thet problem of missing values and the ROC curve result is not accurate enough, then we can delete this part or pu in supplementary materials. For details, please refer to Figure 4.





Correct minor typographical and formatting errors (e.g., “perdict” → “predict”).
Reply: For details, please refer to line 315.

Conclusion
This manuscript addresses a relevant issue with a substantial cohort and clinically meaningful findings. However, the conclusions must be more balanced and the methodological limitations more thoroughly discussed. I recommend major revision, with potential for acceptance after substantial revisions.

Reviewer C

I appreciate the opportunity to review this article, which brings for discussion a very important point. The authors did a good job, trying to bring the most relevant data from their own experience and compare to the literature. The results are supporting the author's hypothesis.
There are, however, points that need to be addressed:

1-if this is a retrospective analysis of their own results, the authors should show the PGD3 rates at 72 hours, which is the most important timepoints. PGD 3s are different according to when it happen.

Reply: Thank you very much for providing such professional advice. When we collect PGD data, we all use PGD that occurs within 72h. We add the PGD acquisition time to the original text, in lines 100-101.

2-Line 138, Surgical Data: I would like to know more about the author's strategies regarding

ECMO intraop. Is it always done? If not, what is the criteria?

Reply: For those who have severe cardiac dysfunction before operation and the heart can not tolerate the stress of transplantation, V-AECMO mode is usually chosen for circulatory support. If the patient has severe oxygenation disorder, V-VECMO mode is preferred to provide respiratory support. Whether ECMO is finally enabled or not and the mode selection is by no means determined by a single clinical factor. Through the standardized multidisciplinary team (MDT) collaborative process, experts from transplant surgery, anesthesiology, critical care medicine, cardiovascular medicine and respiratory medicine jointly assessed the pathophysiological status, surgical risks and support treatment needs of patients, and reached a consensus decision after full discussion. Intraoperative ECMO support should be dynamically adjusted according to real-time monitoring indicators (such as hemodynamics, oxygenation index, organ perfusion) to ensure that intervention measures are synchronized with the patient's condition evolution.

3-Line 174, you reported 5 cases of cardio-cerebral death. What is this? Some type of DCD? Can you please clarify?

Reply: I sincerely thank the editor for his careful review of the details of donor classification. With regard to the five cases of DBCD donors mentioned in this paper, we make the following professional clarification based on their clinical features: DBCD refers to that after the establishment of DBD diagnosis, the donor's family members did not give up rescue until the diagnosis of DCD (irreversible cardiac arrest occurred before organ acquisition), which is not completely consistent with the conventional DBD and DCD, so we list them separately for discussion. **For details, please refer to Table S1.**

4-It may be particular to you center, but why do you have a significant predominance of males in either donors and recipients?

Reply: In this study, it was observed that the high proportion of male donors and recipients in lung transplantation is closely related to the gender distribution characteristics and social exposure factors of end-stage lung disease. From the perspective of end-stage lung disease factors, the incidence of COPD in men is higher than that in women, and most of them are male practitioners in high-dust industries such as coal mines and buildings, and the incidence of silicosis/pneumoconiosis in men is significantly higher than that in women. From the perspective of living habits, the proportion of male smokers and the duration of smoking are also significantly higher than those of female smokers, which are the reasons for the serious imbalance of the sex ratio of the recipients. In addition, the risk of accidents and cardiovascular and cerebrovascular accidents in male population is higher, which may be the reason for the imbalance of gender ratio in donor population.

5-Your 1-year postoperative mortality is high. Can you hypothesize why? Maybe the profile of your patients? I would be glad to hear you explain why, in comparison to, for example, ISHLT data, your numbers are different. I feel it is important to understand how centers do, sometimes they tackle incredible sick patients.

Reply: The one-year survival rate after lung transplantation in our center is different from the international authoritative data, which can be attributed to the proportion of high-risk recipients, the patients' own economic factors and the quality of donors: most of the patients undergoing

lung transplantation in our center are patients with end-stage lung disease, and their cardiopulmonary function reserve is poor, and the proportion of mechanical ventilation and multiple organ dysfunction before operation is obviously increased; Due to the economic constraints of patients after operation, the quality of postoperative recovery may not reach the ideal situation, which is closely related to postoperative mortality. Finally, because the proportion of organ donation in China is not high compared with that in the world, and it is limited by the shortage of donors, it is necessary to accept marginal donors in a higher proportion (such as donors with critical oxygenation function and elderly people); These are the reasons that lead to the mortality rate higher than international standards one year after operation.

6-Following this, and taking into consideration lines 218 - 221, I am curious to understand what are the causes of death of these recipients? Do the 2 groups differ in COD?

Reply: As a single-center retrospective analysis, this study is limited by the fact that the exact cause of death of some cases (especially those who died outside the hospital) has not been completely archived. In order to restore the clinical reality as much as possible, we supplement the information through the following ways: organizing multidisciplinary experts (including transplant surgery, critical care medicine and infectious diseases) to carry out traceability assessment of traceable cases;
Based on the above assessment, the main cause of death in 1-3 years after operation is infectious diseases, followed by multiple organ failure. We fully understand your concern about the difference in COD between the two groups, but we need to be frank. The specific definition of "COD" in the question needs to be further clarified. If you can provide a clear definition or classification framework of COD, we will further dig into whether there are differences in COD between the two groups if conditions permit.

7- Line 7, I think you bring very valid points, especially higher death rate and PGD 3. I would be careful regarding mechanical ventilation and ICU LOS because for these 2 items, there is statistical difference but not much clinical relevance, since the difference is quite small.
Reply: For details, please refer to lines 175-178,lines 249-252.

8- Your Discussion is well done, and you summary as well. Be careful with some typos, like line 336 “perdict”
Reply: For details, please refer to line323.
In summary, it is a pleasure to review your paper and I would be happy to reassess your project after a thorough review. I do think that there are points that you need to clarify, as I highlighted before. As your conclusion supports your data and hypothesis, in order to generalize, we need to better understand the points I highlighted before.