Peer Review File
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Reviewer A

A novelty of this study is that the authors have established their original risk score for predicting ECMO support during lung transplant procedures. I have some comments as follow.

Comment 1: Please present a new table on data to compare the patient valuables between the low-, moderate-, and high-risk groups.
Reply 1: thank you for the reviewer's valuable advice. According to the risk score, we divided the original data into three groups of data with low, moderate and high risk, and then carried out statistical analysis. The results are shown in Table S2.
Change in the text 1: we added some data in Table S2 and sincerely hope it can fulfill the reviewer's requirement.

Comment 2: If the authors would like to elucidate benefits of their original risk score, they should perform a validation test prospectively using this risk score. Then they should compare the post-operative outcomes between the development and validation groups. A risk score can improve post-operative outcomes by predicting ECMO support during transplant procedures?
Reply 2: Thank you for the reviewer's valuable advice. We agree with the reviewers' opinions that performing a validation test prospectively using this risk score, and we are also going to plan to do so. However, due to the particularity of lung transplant patients, the amount of surgery is insufficient in the short term, and the prospective experiment cannot be completed at present. In addition, our validation group was also an independent dataset for verification, and the test efficiency was good enough to validate the development group.

Comment 3: Please correct "postoperative graft dysfunction (PGD)" to "primary graft dysfunction (PGD)" (line 180).
Answer 3: Thank you for the reviewer's correction. PGD is the meaning of primary graft dysfunction.
Change 3: we have corrected to "primary graft dysfunction (PGD)" in page 8 line 195.

Reviewer B

The reviewer is honored to review an article about the study on a risk score for predicting ECMO support before lung transplantation. This is a unique study and is also a clinically useful study. The paper is well written and easy to understand, but there are several points to be clarified and/or revised, as follows:

Comment 1: In the abstract, "Logistic" should be "logistic". Please do not use an abbreviated form when it is used only once, such as CKMB".
Reply 1: thank you for the reviewer's correction. The "Logistic" should be "logistic", and we should not use an abbreviated form when it is used only once and is first used. The CKMB was used more than once in the manuscript.
Changes in the text 1: we had corrected the "Logistic" to "logistic", and changed the first occurrence of CK-MB to its full name in page 2 line 33 and line 36.

Comment 2: In the study design, the authors excluded patients who received urgent intraoperative ECMO (n=3). Based on the concept of this study, this population should be included in this study. Please explain the reason why the authors excluded this population form the study.
Reply 2: thank you for the reviewer's valuable advice. Please forgive us for not explaining clearly. The main purpose of this study was to identify risk factors for predicting ECMO support in lung transplantation and develop accurate and convenient risk scores to identify high-risk patients who required intraoperative ECMO support. The study mainly established a model based on the patient's basic characteristics and preoperative parameters after anesthesia. Patients with emergency ECMO supoort referred to those who had received a lung transplant on one side but needed to establish ECMO support urgently due to unstable hemodynamics or inability to maintain oxygenation during surgery. Fessler finds that patients who received emergency intraoperative ECMO support due to complications had a worse prognosis than those who did not need it[1]. If such patients were included, it would be contrary to the primary purpose of prediction in this study and biased the results.
Changes in the test 2: we had explained clearly in page 5 line 81.
1. Fessler J, Sage E, Roux A, et al. Is Extracorporeal Membrane Oxygenation Withdrawal a Safe Option After Double-Lung Transplantation?[J]. The Annals of Thoracic Surgery, 2020,110(4):1167-1174.

Comment 3: In Table1, p value of 0.000 is correct? <0.0001 or so might be fine.
Reply 3: thank you for the reviewer's important suggestion. And please forgive our carelessness, when P =0.000, it should be expressed as P <0.001.
Changes in the text 3: we had changed the P value of 0.000 to <0.001 in table 1.

Reviewer C

Thank you for the opportunity to review your very well written manuscript. The use of intraoperative ECMO during lung transplant is not systematized and this is a first effort toward evidence based protocols for patient selection and timing. I only have two questions, which I hope the authors can address:

Comment 1: How many/what other variables were test in the multivariate model?
Reply 1: thank you for the reviewr's questions. In the developmental data set, parameters such as basic characteristics and preoperative parameters after anesthesia were first included in the univariate analysis, and then the variables were screened out in the multivariate analysis. There were 11 variables in the multivariate model. They included the variables of sex, diabetes, smoking history, diagnosis, the values of proBNP, the values of left and right lung perfusion, plasma albumin (ALB), creatine kinase isoenzyme-MB (CKMB), pulmonary artery systolic pressure before surgery after anesthesia (PASP), and cardiac Troponin I (cTnI).

Comment 2: What is the hypothesis regarding the influence of gender and if related to chest size, should this variable be included?
Reply 2: thank you for the reviewer's commention. Our model predicted that women were high-risk of ECMO. Gender-associated differences could play a role in terms of graft survival, organ size, metabolic demands, circulating hormones, and receptors. Villavicencio confirmed that male sex, Karnofsky class greater than 50, double lung transplantation, and transplantation year were predictors of improved survival [2]. And Christie and associates [3] analyzed organ and recipient gender on the incidence of primary graft failure. Female donor gender was associated with the development of graft failure. ISHLT Lung Transplant Registry data also demonstrated a significant risk for female to male [4]. However, There are relatively sparse data on the prediction of gender in the use of ECMO in lung transplantationas. Further experiments may need to be explored the relation of gender and ECMO.

We don't think it's related to chest size. Because donor-recipient size matching is estimated in the preoperative evaluation of lung transplantation, the chest volume of each patient is matched with the size of the transplanted lung. In our center, the donor and recipient predicted total lung capacity was calculated as follows:
Male: (0.09 x Height (cm)) - 8.618
Female: (0.071 x Height (cm)) - (0.007 x Age (years)) - 5.965[5]. We believe that such a match will balance the influence of chest size, therefore, this factor is not included in our study.

2. Villavicencio MA, Axtell AL, Spencer PJ, et al. Lung transplantation from donation after circulation death. United States and single-Center experience. Ann Thorac Surg. 2018, 106(6): 1619-27.
3. Christie JD, Kotloff RM, Pochettino A, et al. Clinical risk factors for primary graft failure following lung transplantation. Chest. 2003, 124 (4):1232-41.
4. International Society of Heart and lung Transplantation Registry; Sato M, Gutierrez C, et al. The effect of gender combinations on outcome in human lung transplantation: the International Society of Heart and Lung Transplantation Registry experience. J Heart Lung Transplant. 2006, 25(6):634-7.
5. Riddell, P., et al., A simplified strategy for donor-recipient size-matching in lung transplant for interstitial lung disease. The Journal of heart and lung transplantation, 2021. 40(11): p.

1422-1430.