EDITORIAL COMMENT

The Primary Graft Failure of Lung Transplantation for the PH Patients*

Hideyuki Kinoshita, MD, PhD

Lung transplantation (LT) is the established treatment option in end-stage irreversible pulmonary diseases, including pulmonary vascular disease. Patients with pulmonary hypertension (PH) have a greater short-term risk after transplant (lowest 3-month and 1-year survival rate), but have improved long-term survival compared with patients with other lung disease.[1] In LT recipients who die within the first year, the most common causes of death are infections and graft failure.[1] Particularly in patients with PH, primary graft failure is associated with an increased risk of death during the early postoperative period.[2] The use of extracorporeal membrane oxygenation (ECMO) support during and after transplantation improves survival, and ECMO is one of the advances in LT for patients with PH.[3,4]

In this issue of *JACC: Asia*, the paper by Jiao et al[5] showed that changes of mean pulmonary artery pressure (ΔmPAP) at the time of ECMO support and ECMO wean-off were related to post-LT survival after adjusting for potential confounders, and recipients with ΔmPAP ≤35 mm Hg had a higher mortality rate. In previous reports, PH fell immediately after LT, from 76 ± 14 mm Hg to 31 ± 11 mm Hg ($P < 0.05$), according to intraoperative transesophageal echocardiography data.[6]

The idea of the relationship with ΔmPAP during ECMO and mortality after LT is interesting. Surprisingly, patients with ΔmPAP ≤35 mm Hg had a higher mortality rate not only in the short-term but also long-term, up to about 2 years. The reason why ΔmPAP during ECMO affects the mortality of patients with LT is not elucidated in this paper. From the data that mPAP at the time of ECMO support did not correlate with mortality, there is a possibility that mPAP at the time of ECMO wean-off is correlated with post-LT survival. Although heart failure post-LT, duration of intensive care unit stay, time on intubation post-LT, and primary graft dysfunction were correlated with mortality,[5] these data suggest that poor condition of the transplanted lung could cause the decrease of the ΔmPAP during ECMO support and correlate with poor mortality after LT. Additionally, Jiao et al[5] demonstrate that the case volume of the LT center was correlated with mortality. ΔmPAP >35 mm Hg showed increased risk of post-LT morbidity only in low case volume (<50 cases/year) LT centers; however, ΔmPAP >35 mm Hg was associated with a reduced risk of post-LT morbidity in high-case volume (≥50 cases/year) LT centers.[5]

There are some limitations to this paper, eg, the ratio of idiopathic pulmonary arterial hypertension patients was too small, and a few too many patients were excluded because of lack of data. However, overall, Jiao et al[5] suggest that surgical procedure and postoperative management could affect primary graft failure, decreased ΔmPAP during ECMO, and mortality after LT.

Considering clinical relevance, to reduce the occurrence of early graft dysfunction, we must have a better understanding of the pathophysiological changes after transplantation for PH. From previous reports, the main cause of primary graft dysfunction in these patients was not residual PH, but left ventricular failure.[7,8] Left ventricular dysfunction results in elevated left-sided filling pressures and pulmonary edema, and the postoperative prolongation of veno-arterial ECMO after transplantation effectively prevents primary graft dysfunction. With the strategy of prolonged continuation of ECMO support for 3 to 7 days, the improvement of 1-year survival rates was

reported after LT for severe PH patients.[9] However, ECMO has frequent risks, such as bleeding, renal failure, sepsis, leg ischemia, and central nervous system complications.[10]

Recently a new strategy to prevent primary graft dysfunction of the LT for severe PAH patients treated with epoprostenol before LT has been reported.[11] The tapering pretransplant use of epoprostenol rather than abrupt discontinuation after transplantation improved the occurrence of primary graft dysfunction and perioperative outcomes.

The perioperative outcome of LT for patients with severe PH remains poor because of the primary graft dysfunction from left ventricular failure. To improve the outcome of LT for PH patients, management of the PH before LT, the timing of LT, and management of ECMO and medication after LT is important, and we must have a better understanding of the pathophysiological changes as to the cardiac function after transplantation for severe PH patients.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

ADDRESS FOR CORRESPONDENCE: Dr Hideyuki Kinoshita, Department of Community Medicine Supporting System, Kyoto University Graduate School of Medicine, 54 Kawahara-cho, Shogo-in, Sakyo-ku, Kyoto 606-8507, Japan. E-mail: Kinos@kuhp.kyoto-u.ac.jp.

REFERENCES

1. Christie JD, Edwards LB, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: twenty-seventh official adult lung and heart-lung transplant report—2010. *J Heart Lung Transplant*. 2010;29:1104–1118.

2. Whitson BA, Nath DS, Johnson AC, et al. Risk factors for primary graft dysfunction after lung transplantation. *J Thorac Cardiovasc Surg*. 2006;131:73–80.

3. Pereszlenyi A, Lang G, Steltzer H, et al. Bilateral lung transplantation with intra- and postoperatively prolonged ECMO support in patients with pulmonary hypertension. *Eur J Cardiothorac Surg*. 2002;21:858–863.

4. Moser B, Jaksch P, Taghavi S, et al. Lung transplantation for idiopathic pulmonary arterial hypertension on intraoperative and postoperatively prolonged extracorporeal membrane oxygenation provides optimally controlled reperfusion and excellent outcome. *Eur J Cardiothorac Surg*. 2018;53:178–185.

5. Jiao G, Huang J, Wu B, et al. Association of pulmonary artery pressure change with post-lung transplantation survival: retrospective analysis of China Registry. *JACC: Asia*. 2022;2:819–828.

6. Katz WE, Gasior TA, Quinlan JJ, et al. Immediate effects of lung transplantation on right ventricular morphology and function in patients with variable degrees of pulmonary hypertension. *J Am Coll Cardiol*. 1996;27:384–391.

7. Birsan T, Kranz A, Mares P, et al. Transient left ventricular failure following bilateral lung transplantation for pulmonary hypertension. *J Heart Lung Transplant*. 1999;18:304–309.

8. Avriel A, Klement AH, Johnson SR, et al. Impact of left ventricular diastolic dysfunction on lung transplantation outcome in patients with pulmonary arterial hypertension. *Am J Transplant*. 2017;17:2705–2711.

9. Tudorache I, Sommer W, Kuhn C, et al. Lung transplantation for severe pulmonary hypertension—awake extracorporeal membrane oxygenation for postoperative left ventricular remodelling. *Transplantation*. 2015;99:451–458.

10. Zangrillo A, Landoni G, Biondi-Zoccai G, et al. A meta-analysis of complications and mortality of extracorporeal membrane oxygenation. *Crit Care Resusc*. 2013;15(3):172–178.

11. Ohsumi A, Aoyama A, Kinoshita H, et al. New strategy to resume and taper epoprostenol after lung transplant for pulmonary hypertension. *Gen Thorac Cardiovasc Surg*. 2022;70(4):372–377.