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Critical Care Management Following Lung Transplantation

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Postoperative critical care management for lung transplant recipients in the intensive care unit (ICU) has expanded in recent years due to its complexity and impact on clinical outcomes. The practical aspects of post-transplant critical care management, especially regarding ventilation and hemodynamic management during the early postoperative period in the ICU, are discussed in this brief review. Monitoring in the ICU provides information on the patient's clinical status, diagnostic assessment of complications, and future management plans since lung transplantation involves unique pathophysiological conditions and risk factors for complications. After lung transplantation, the grafts should be appropriately ventilated with lung protective strategies to prevent ventilator-induced lung injury, as well as to promote graft function and maintain adequate gas exchange. Hypotension and varying degrees of pulmonary edema are common in the immediate postoperative lung transplantation setting. Ventricular dysfunction in lung transplant recipients should also be considered. Therefore, adequate volume and hemodynamic management with vasoactive agents based on their physiological effects and patient response are critical in the early postoperative lung transplantation period. Integrated management provided by a professional multidisciplinary team is essential for the critical care management of lung transplant recipients in the ICU.

Keywords: Lung transplantation, Postoperative care, Intensive care units, Artificial respiration, Hemodynamics

Introduction

Lung transplantation for patients with various end-stage lung diseases has become an increasingly standard therapy [1]. The first lung transplantation in Korea was performed in 1996, and the numbers have steadily increased thereafter, with approximately 150 lung transplantations reported annually since 2019 [2]. However, the number of patients transplanted from intensive care units (ICUs) with mechanical respiratory support has steadily increased based on the allocation system according to medical urgency, technical improvements, and reports of beneficial outcomes [3]. Therefore, the need for critical care before and after lung transplantation has increased in recent years, along with the multidisciplinary team approach [4,5]. Furthermore, critical care issues are involved in the management of early postoperative complications, as well as the safe bridging of candidates by mechanical respiratory support.

The spectrum of early postoperative complications after lung transplantation includes primary graft dysfunction, arrhythmias, infections, non-pulmonary organ failure, and anastomotic and pleural complications, as well as postoperative bleeding [6]. Therefore, prevention and adequate management of these complications in the early postoperative period may have a significant impact on lung graft function and clinical outcomes [7]. Some complications may be preventable or easy to recover from if managed appropriately. However, the management strategies are relatively unclear since robust evidence from systematic evaluations or clinical trials is not fully available in many situations [6,7]. In addition, other basic issues contribute to the increased difficulty of caring for recipients in the ICU, including mechanical ventilation (MV) support and hemodynamic management. Current practice in ventilation and hemodynamic management is mainly based on the results of observational studies, the underlying pathophysiology, and expert opinions, as high-quality evidence-based guide-

lines are not yet available [8]. Therefore, the practical aspects of post-transplant critical care management, especially ventilation and hemodynamic management during the early postoperative period in the ICU are addressed herein.

Multidisciplinary team

Recipients are routinely transferred to the ICU immediately from the operating room after successful transplant surgery. Generally, recipients are still intubated and some might even require postoperative extracorporeal membrane oxygenation (ECMO) support. Although weaning from both MV and ECMO is primarily in the hands of the intensivist, regular ICU rounds by the transplant team are very important in order to monitor the patient's clinical status and obtain a comprehensive update on the patient's progress, including graft and other organ function, early immunosuppressive therapy, wound and drain monitoring, nursing information, and physical therapy [9]. Ideally, at least 1 daily round should be attended by a thoracic surgeon, a transplant physician, and the intensivist as a team. An infectious disease specialist should be part of daily transplant team rounds, since infections are the most frequent complications in the early postoperative period. A clinical pharmacist should also be involved in the multidisciplinary team due to the complexity of immunosuppressive therapy, which has a narrow therapeutic index, leading to potential severe adverse drug events and drug–drug interactions in critically ill patients [10,11].

Postoperative monitoring in the intensive care unit

Patients typically arrive in the ICU with a pulmonary artery catheter (PAC) in addition to venous and arterial lines in place, chest tubes to drain pleural spaces, and an indwelling bladder catheter in place to fully monitor gas exchange, hemodynamics, the amount of mediastinal and pleural drainage, and urinary output. Patients should undergo a full physical examination, evaluation of hemodynamic parameters, and assessment of peripheral circulation and perfusion upon arrival in the ICU, in addition to communication among surgeons, anesthesiologists, intensivists, and transplant physicians regarding intraoperative events. Patients are generally hypothermic postoperatively. This can increase the pulmonary vascular resistance and the likelihood of bleeding and infection [12,13], and patients should be warmed using a forced air warming device. Moreover, an evaluation of the position of the endotracheal tube and the placement of lines, chest tubes, and drainage catheters is essential.

ICU monitoring is similar to intraoperative monitoring. Monitoring in the ICU is essential because it provides information on the patient's clinical status, diagnostic assessment of complications, and future management plans, while monitoring in the operating room is designed to assess acute changes in vital functions resulting from the patient's response to medication and surgical manipulation [14]. Therefore, arterial blood gas analyses should be performed regularly for the early detection of gas exchange abnormalities and acid-base imbalances. This will guide the appropriate adjustments for respiratory and metabolic support. In addition, venous blood samples are obtained to monitor the complete blood count, coagulation profile, renal profile, hepatic profile, and lactate levels. Bedside electrocardiography and portable chest radiography are routinely performed at our center.

A PAC is routinely used starting in the operating room even though there is a paucity of data on its use in the postoperative lung transplantation period [15]. One of the most common indications for PAC use is severe pulmonary hypertension, given its high reliability in measuring beat–to-beat pulmonary artery pressure [16]. Moreover, the PAC can be used to evaluate right ventricular (RV) function, which might be associated with the prognosis of lung transplantation [17]. However, several studies have suggested that RV function normalizes in adult patients after lung transplantation, even in patients with severe preoperative RV dysfunction [18-21]. Therefore, there is no need to monitor pulmonary hypertension or RV function postoperatively unless there are other problems that affect the pulmonary artery pressure. Furthermore, cardiac function could be evaluated with bedside echocardiography, including RV function [17]. Therefore, the PAC itself can only be beneficial after lung transplantation if its use guides therapies that improve patient outcomes [15].

Management of mechanical ventilation

The goals of MV following lung transplantation are to promote graft function, maintain adequate gas exchange, and prevent ventilator-induced lung injury [7]. There have been no large, multicenter trials to guide MV management after lung transplantation despite the critical role of MV in lung transplantation, and only a few studies have addressed appropriate MV after lung transplantation [22,23]. Despite wide variation in practice, the currently applied lung pro-

tective MV strategies in lung transplantation have been extrapolated from the practice guideline for MV patients with acute respiratory distress syndrome (ARDS), since experimental data suggest that all lung transplantation recipients are at risk of ventilator-induced lung injury [24]. In addition, the benefits of lung-protective ventilation extend to surgical patients at risk for ARDS [25]. Interestingly, however, a recent survey addressing MV practices after lung transplantation has shown that many of the reported practices did not conform to the consensus guidelines on ARDS management [23].

Although low tidal ventilation (usually 6 mL/kg of predicted body weight) has been the preferred strategy even in lung transplantation, a survey on MV following lung transplantation indicated that recipient characteristics most commonly determine tidal volume [22]. Titrating the tidal volume to the donor-predicted body weight rather than the recipient-predicted body weight reduces the risk of delivering insufficient or excessive tidal volume in size-mismatched allografts [26]. However, undersized allografts might receive higher tidal volumes than oversized allografts based on the donor-predicted body weight [27]. Therefore, adjustments of the adequate tidal volume should be made based on gas exchange over the next several hours following initial low-tidal volume ventilation. A driving pressure higher than 15 cmH_2O has recently been shown to be strongly associated with mortality in patients with ARDS; this corresponds to the pressure required for alveolar opening (tidal volume/respiratory system compliance) and is calculated as the plateau pressure minus positive end-expiratory pressure (PEEP) [28,29]. This pressure can be used as an indicator of ventilator-induced lung injury risk [30]. Therefore, although it remains unclear how to best reduce the driving pressure as part of lung protective ventilation strategy in practice, driving pressure-guided ventilation has been proposed as another technique to reduce postoperative pulmonary complications and improve recovery in thoracic surgery patients [31]. However, the use of a high PEEP to reduce driving pressure is generally avoided due to its potential negative effects on the healing of bronchial anastomosis and alveolar overdistension in grafts [5].

Weaning from MV is usually completed within 72 hours, and extubation is performed in the ICU in non-complicated patients after lung transplantation. The median MV duration after lung transplantation is 2 to 3 days [22]. MV weaning is usually intentionally performed slowly in patients with a high risk of severe graft dysfunction or inadequate gas exchange [32]. Lung allografts involve a disruption of the nerve supply as a consequence of harvesting from the donor. A weak cough, poor respiratory mechanics caused by deconditioning, and inadequate pain control lead to an inability to clear airway secretions. Therefore, early tracheostomy should be considered when more than 1 week elapses before weaning from MV [33].

Pulmonary vasodilator inhalation including nitric oxide (NO) has been proposed as a method to prevent ischemia-reperfusion injury after lung transplantation, but it did not prevent graft dysfunction in randomized controlled trials [34-36]. Therefore, the routine use of inhaled NO in lung transplantation is not recommended, but its selective use is recommended for patients with severe graft dysfunction showing severe hypoxemia and elevated pulmonary artery pressure [37]. Inhaled epoprostenol was recently reported to be equivalent to inhaled NO for preventing severe graft dysfunction [38]. However, it remains unclear whether either inhaled NO or epoprostenol conferred any benefit and whether their routine use to prevent graft dysfunction should be supported.

In patients with severe graft dysfunction, MV may be insufficient to provide adequate gas exchange, and high ventilator settings may be harmful to the allograft. ECMO support could be an efficient rescue therapy for this critical presentation [39]. It is generally accepted that early ECMO institution leads to improved salvage rates [40]. Several case series have shown that recipients with refractory graft dysfunction requiring ECMO experienced long-term survival similar to that reported in patients not supported with ECMO [41]. These data support the use of ECMO to manage severe graft dysfunction, particularly to correct refractory hypoxemia and to reduce additional damage from MV to the already injured graft. The high incidence of complications, such as bleeding, vascular injury, and neurologic deficits, has been a major concern when using ECMO in the postoperative period after lung transplantation, although the incidence of such complications has dramatically decreased in recent years [42]. Debate continues regarding the ECMO type that should be used. However, veno-venous ECMO is recommended to support most patients with severe graft dysfunction, even in the setting of hemodynamic compromise [43].

Management of hemodynamics

The initial hemodynamic management goal following lung transplantation is to maintain adequate organ perfusion, which is monitored by measuring lactate, urine output, and mixed venous oxygen saturation, if available.

However, transplanted lungs have varying degrees of pulmonary edema as a result of increased vascular permeability and disrupted lymphatic drainage [44,45]. In addition, increasing cardiac output with inotropes, with or without vasopressors, may also contribute to pulmonary edema by increasing the amount of flow through the lung allograft. Therefore, individualized management is required to maintain adequate perfusion pressure balance with the lowest possible cardiac output to reduce the exacerbation of pulmonary edema risk. Postoperative volume status management is actually an area of considerable heterogeneity in practice [23]. The implementation of a dedicated protocol that maintains specific hemodynamic targets has been shown to be associated with reduced graft dysfunction severity [46]. In addition, the use of fluid restriction strategies was found to be unrelated to increased vasopressor use or renal function deterioration [47]. These data suggest the potential benefits of more aggressive diuresis and fluid restrictions in the early postoperative period after lung transplantation.

Hypotension, which is common in the immediate postoperative setting, is generally caused by systemic inflammatory response syndrome from the surgical insult, with low systemic vascular resistance, medication-induced hypotension, hemorrhage, tamponade, and heart failure [4]. The management should be causally determined, including volume management and transfusions, vasopressor or inotrope application, bleeding diatheses correction, and surgical revisions. Patients with low systemic vascular resistance may need additional vasopressor treatment, with norepinephrine and vasopressin being the preferred agents. Vasopressin does not increase pulmonary vascular resistance since V1 receptors are not present in the pulmonary arteries. Several studies have demonstrated that vasopressin can effectively ameliorate systemic hypotension without increasing pulmonary vascular resistance [48]. Norepinephrine has been shown not only to slightly increase pulmonary vascular resistance, but also to improve RV function through its inotropic effects. This may indicate an advantage of norepinephrine in patients with impaired RV function requiring vasopressors [49], but it poses a risk of arrhythmia. However, the addition of vasopressin to catecholamine vasopressors was significantly associated with a lower atrial fibrillation risk [50]. Therefore, the choice of inotropes and vasopressors in postoperative lung transplantation care should be made with consideration of their effects on systemic and pulmonary vascular resistance (Table 1) and should be individualized based on patient response.

The risk of pulmonary edema is higher with transient diastolic dysfunction of the left ventricle (LV), which becomes incapable of handling a normal preload in the early postoperative period in patients with significant pulmonary hypertension before lung transplantation [51]. The small and "deconditioned" LV of patients with severe pulmonary hypertension is prone to developing diastolic dysfunction when exposed to a normal or high preload after transplantation, resulting in elevated left-sided filling pressures and pulmonary edema [52]. Bridging this period with veno-arterial ECMO has been described for the postoperative management of recipients with severe pulmonary hypertension as a way to specifically address these issues and allow time for recovery of the "deconditioned" LV, which can take several days [51-54].

Table 1. Physiological effects of inotropes and vasopressors for critical care management in lung transplantation recipients

Vasoactive agents	CO	SVR	PVR	Risk of arrhythmia
Inotropes				
Dobutamine				
Low dose (<5 μg/kg/min)	↑	↔ or ↓	↓	+
High dose (5–15 μg/kg/min)	↑ ↑	↓	↔	++
Dopamine				
Low dose (≤5 μg/kg/min)	↑	↔ or ↑	↔	+
Medium dose (5–10 μg/kg/min)	↑	↑	↑	++
High dose (10–20 μg/kg/min)	↑	↑ ↑	↑	+++
Milrinone	↑ ↑	↓ ↓	↓	+++
Vasopressors				
Norepinephrine	↑	↑ ↑	↔ or ↑	++
Vasopressin	↔ or ↑	↑ ↑	↔ or ↓	±[a]

CO, cardiac output; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance.
[a]Based on a recent systematic review and meta-analysis of 23 trials that included 3,088 patients with distributive shock, the addition of vasopressin to catecholamine vasopressors compared with catecholamine vasopressors alone was significantly associated with a lower atrial fibrillation risk [50].

Conclusion

The postoperative critical care management of lung transplantation recipients in the ICU is complex and can critically affect the clinical outcome. Therefore, appropriate monitoring and a multidisciplinary team approach are essential. The grafts should be appropriately ventilated with lung-protective strategies to prevent ventilator-induced lung injury, as well as to promote graft function and maintain adequate gas exchange. Hypotension and varying degrees of pulmonary edema are common in the immediate postoperative setting after lung transplantation. Ventricular dysfunction in lung transplant recipients should also be considered. Therefore, diuresis and adequate support with inotropes and vasopressors based on the physiological effects and patient response are critical in the early postoperative period after lung transplantation.

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Author contributions

All work was done by Kyeongman Jeon.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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References

1. Leard LE, Holm AM, Valapour M, et al. *Consensus document for the selection of lung transplant candidates: an update from the International Society for Heart and Lung Transplantation*. J Heart Lung Transplant 2021;40:1349-79.
2. The National Institute of Organ, Tissue and Blood Management. *Organ transplantation statistics* [Internet]. Seoul: The National Institute of Organ, Tissue and Blood Management; 2020 [cited 2022 Jun 30]. Available from: https://www.konos.go.kr.
3. Ko RE, Lee JG, Kim SY, et al. *Extracorporeal membrane oxygenation as a bridge to lung transplantation: analysis of Korean organ transplantation registry (KOTRY) data*. Respir Res 2020;21:20.
4. Fuehner T, Kuehn C, Welte T, Gottlieb J. *ICU care before and after lung transplantation*. Chest 2016;150:442-50.
5. Di Nardo M, Tikkanen J, Husain S, et al. *Postoperative management of lung transplant recipients in the intensive care unit*. Anesthesiology 2022;136:482-99.
6. Kao CC, Parulekar AD. *Postoperative management of lung transplant recipients*. J Thorac Dis 2019;11(Suppl 14):S1782-8.
7. Geube M, Anandamurthy B, Yared JP. *Perioperative management of the lung graft following lung transplantation*. Crit Care Clin 2019;35:27-43.
8. Marczin N, de Waal EE, Hopkins PM, 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;40:1327-48.
9. Schuurmans MM, Benden C, Inci I. *Practical approach to early postoperative management of lung transplant recipients*. Swiss Med Wkly 2013;143:w13773.
10. Monchaud C, Marquet P. *Pharmacokinetic optimization of immunosuppressive therapy in thoracic transplantation: part I*. Clin Pharmacokinet 2009;48:419-62.
11. Monchaud C, Marquet P. *Pharmacokinetic optimization of immunosuppressive therapy in thoracic transplantation: part II*. Clin Pharmacokinet 2009;48:489-516.
12. Polderman KH. *Mechanisms of action, physiological effects, and complications of hypothermia*. Crit Care Med 2009;37(7 Suppl):S186-202.
13. Geurts M, Macleod MR, Kollmar R, Kremer PH, van der Worp HB. *Therapeutic hypothermia and the risk of infection: a systematic review and meta-analysis*. Crit Care Med 2014;42:231-42.
14. Potestio C, Jordan D, Kachulis B. *Acute postoperative management after lung transplantation*. Best Pract Res Clin Anaesthesiol 2017;31:273-84.
15. Senoner T, Velik-Salchner C, Tauber H. *The pulmonary artery catheter in the perioperative setting: should it still be used?* Diagnostics (Basel) 2022;12:177.
16. McRae KM. *Pulmonary transplantation*. Curr Opin Anaesthesiol 2000;13:53-9.
17. Kusunose K, Tsutsui RS, Bhatt K, et al. *Prognostic value of RV function before and after lung transplantation*. JACC Cardiovasc Imaging 2014;7:1084-94.
18. 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;27:384-91.
19. Moulton MJ, Creswell LL, Ungacta FF, Downing SW, Szabo BA, Pasque MK. *Magnetic resonance imaging provides evidence for remodeling of the right ventricle after single-lung transplantation for pulmonary hypertension*. Circulation 1996;94(9 Suppl):II312-9.

20. Schulman LL, Leibowitz DW, Anandarangam T, et al. *Variability of right ventricular functional recovery after lung transplantation*. Transplantation 1996;62:622-5.
21. Kasimir MT, Seebacher G, Jaksch P, et al. *Reverse cardiac remodelling in patients with primary pulmonary hypertension after isolated lung transplantation*. Eur J Cardiothorac Surg 2004;26:776-81.
22. Beer A, Reed RM, Bolukbas S, et al. *Mechanical ventilation after lung transplantation: an international survey of practices and preferences*. Ann Am Thorac Soc 2014;11:546-53.
23. King CS, Valentine V, Cattamanchi A, et al. *Early postoperative management after lung transplantation: results of an international survey*. Clin Transplant 2017;31:e12985.
24. de Perrot M, Imai Y, Volgyesi GA, et al. *Effect of ventilator-induced lung injury on the development of reperfusion injury in a rat lung transplant model*. J Thorac Cardiovasc Surg 2002;124:1137-44.
25. Futier E, Constantin JM, Paugam-Burtz C, et al. *A trial of intraoperative low-tidal-volume ventilation in abdominal surgery*. N Engl J Med 2013;369:428-37.
26. Eberlein M, Reed RM, Bolukbas S, et al. *Lung size mismatch and primary graft dysfunction after bilateral lung transplantation*. J Heart Lung Transplant 2015;34:233-40.
27. Dezube R, Arnaoutakis GJ, Reed RM, et al. *The effect of lung-size mismatch on mechanical ventilation tidal volumes after bilateral lung transplantation*. Interact Cardiovasc Thorac Surg 2013;16:275-81.
28. Amato MB, Meade MO, Slutsky AS, et al. *Driving pressure and survival in the acute respiratory distress syndrome*. N Engl J Med 2015;372:747-55.
29. Bellani G, Laffey JG, Pham T, et al. *Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries*. JAMA 2016;315:788-800.
30. Tonetti T, Vasques F, Rapetti F, et al. *Driving pressure and mechanical power: new targets for VILI prevention*. Ann Transl Med 2017;5:286.
31. Ahn HJ, Park M, Kim JA, et al. *Driving pressure guided ventilation*. Korean J Anesthesiol 2020;73:194-204.
32. Diamond JM, Lee JC, Kawut SM, et al. *Clinical risk factors for primary graft dysfunction after lung transplantation*. Am J Respir Crit Care Med 2013;187:527-34.
33. Wang R, Pan C, Wang X, Xu F, Jiang S, Li M. *The impact of tracheotomy timing in critically ill patients undergoing mechanical ventilation: a meta-analysis of randomized controlled clinical trials with trial sequential analysis*. Heart Lung 2019;48:46-54.
34. Meade MO, Granton JT, Matte-Martyn A, et al. *A randomized trial of inhaled nitric oxide to prevent ischemia-reperfusion injury after lung transplantation*. Am J Respir Crit Care Med 2003;167:1483-9.
35. Perrin G, Roch A, Michelet P, et al. *Inhaled nitric oxide does not prevent pulmonary edema after lung transplantation measured by lung water content: a randomized clinical study*. Chest 2006;129:1024-30.
36. Botha P, Jeyakanthan M, Rao JN, et al. *Inhaled nitric oxide for modulation of ischemia-reperfusion injury in lung transplantation*. J Heart Lung Transplant 2007;26:1199-205.
37. Van Raemdonck D, Hartwig MG, Hertz MI, et al. *Report of the ISHLT Working Group on primary lung graft dysfunction part IV: prevention and treatment: a 2016 Consensus Group statement of the International Society for Heart and Lung Transplantation*. J Heart Lung Transplant 2017;36:1121-36.
38. Ghadimi K, Cappiello J, Cooter-Wright M, et al. *Inhaled pulmonary vasodilator therapy in adult lung transplant: a randomized clinical trial*. JAMA Surg 2022;157:e215856.
39. Hartwig MG, Walczak R, Lin SS, Davis RD. *Improved survival but marginal allograft function in patients treated with extracorporeal membrane oxygenation after lung transplantation*. Ann Thorac Surg 2012;93:366-71.
40. Wigfield CH, Lindsey JD, Steffens TG, Edwards NM, Love RB. *Early institution of extracorporeal membrane oxygenation for primary graft dysfunction after lung transplantation improves outcome*. J Heart Lung Transplant 2007;26:331-8.
41. Bellier J, Lhommet P, Bonnette P, et al. *Extracorporeal membrane oxygenation for grade 3 primary graft dysfunction after lung transplantation: long-term outcomes*. Clin Transplant 2019;33:e13480.
42. Na SJ, Jeon K. *Extracorporeal membrane oxygenation support in adult patients with acute respiratory distress syndrome*. Expert Rev Respir Med 2020;14:511-9.
43. Fan E, Del Sorbo L, Goligher EC, et al. *An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine clinical practice guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome*. Am J Respir Crit Care Med 2017;195:1253-63.
44. Kaplan JD, Trulock EP, Cooper JD, Schuster DP. *Pulmonary vascular permeability after lung transplantation: a positron emission tomographic study*. Am Rev Respir Dis 1992;145(4 Pt 1):954-7.
45. Cui Y, Liu K, Lamattina AM, Visner G, El-Chemaly S. *Lymphatic vessels: the next frontier in lung transplant*. Ann Am Thorac Soc 2017;14(Supplement_3):S226-32.
46. Currey J, Pilcher DV, Davies A, et al. *Implementation of a management guideline aimed at minimizing the severity of primary graft dysfunction after lung transplant*. J Thorac Cardiovasc Surg 2010;139:154-61.
47. Pilcher DV, Scheinkestel CD, Snell GI, Davey-Quinn A, Bailey MJ, Williams TJ. *High central venous pressure is associated with prolonged mechanical ventilation and increased mortality after lung transplantation*. J Thorac Cardiovasc Surg 2005;129:912-8.
48. Mizota T, Fujiwara K, Hamada M, Matsukawa S, Segawa H. *Effect of arginine vasopressin on systemic and pulmonary arterial pressure in a patient with pulmonary hypertension secondary to pulmonary emphysema: a case report*. JA Clin Rep 2017;3:1.
49. Legrand M, Zarbock A. *Ten tips to optimize vasopressors use in the critically ill patient with hypotension*. Intensive Care Med 2022;48:

736-9.
50. McIntyre WF, Um KJ, Alhazzani W, et al. *Association of vasopressin plus catecholamine vasopressors vs catecholamines alone with atrial fibrillation in patients with distributive shock: a systematic review and meta-analysis*. JAMA 2018;319:1889-900.
51. 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;99:451-8.
52. Hoeper MM, Benza RL, Corris P, et al. *Intensive care, right ventricular support and lung transplantation in patients with pulmonary hypertension*. Eur Respir J 2019;53:1801906.
53. Hoetzenecker K, Schwarz S, Muckenhuber M, et al. *Intraoperative extracorporeal membrane oxygenation and the possibility of postoperative prolongation improve survival in bilateral lung transplantation*. J Thorac Cardiovasc Surg 2018;155:2193-206.
54. 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;53:178-85.