



Critical Care Management Following Lung Transplantation

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ARTICLE INFO

Received July 15, 2022

Accepted July 18, 2022

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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 de-

vice. 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 cmH₂O 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 disrup-

tion 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.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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