



Surgical Complications Affecting the Early and Late Survival Rates after Lung Transplantation

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Since the first lung transplantation in humans was performed in 1963, patient selection, standardized procurement, and surgical techniques have been developed and established for this procedure. However, despite these developments, surgical complications continue to be important factors influencing patient morbidity and mortality, and efforts should be made to decrease morbidity and improve survival rates by understanding, rapidly detecting, and appropriately treating surgical complications.

Keywords: Lung transplantation, Anastomotic leak, Airway obstruction, Pulmonary artery stenosis

Introduction

Lung transplantation is a complex process ranging from pre-transplant evaluation and donor and recipient management to surgery and recovery and rehabilitation of the patient after surgery. The complications of lung transplantation can be classified as surgical or non-surgical (medical). Surgical complications are especially significant because these can cause graft loss and mortality if not properly managed. According to the International Society for Heart and Lung Transplantation (ISHLT) 2016 consensus statement, 390 of 49,453 patients who underwent lung transplantation between January 1990 and June 2014 died because of technical complications between 0 and 30 days after surgery [1]. This article describes the surgical complications that can affect the early and late survival rates of lung transplantation, with a particular focus on their management.

Vascular complications

Vascular complications can be classified as bleeding or stenoses. These are usually preventable using appropriate surgical techniques [2]. Bleeding at the anastomotic site can be affected by the recipient's underlying disease and tissue fragility owing to long-term steroid use. If bleeding

at the anastomotic site is confirmed during surgery, it can be managed by reinforcement, and if necessary, a pledget using the pericardium or felt can be used. Reinforcing while maintaining the patency of blood vessels by loosening the blood vessel clamp is advantageous as it can prevent the obstruction that may occur due to suture of the back wall. Delayed bleeding can be diagnosed by the amount of chest tube drainage and chest X-rays, and treatment is determined based on the amount of bleeding and hematological test results, degree of lung compression, and hemodynamic compromise due to bleeding. In cases of massive hemorrhage or severe hemodynamic compromise, surgical re-exploration is required to control bleeding.

Vascular anastomotic stenosis is a rare complication that occurs in fewer than 5% of lung transplants [3,4], and vein stenosis is particularly critical. The surgical technique is important, and it is also critical to consider the blood vessel size of the donor and recipient during anastomosis. Delayed treatment of stenosis may be dangerous because it is associated with graft loss. Transesophageal echocardiography is used to check the patency of blood vessels, and contrast-enhanced computed tomography can be used to diagnose stenoses. If stenosis is detected during surgery, it can be corrected with sutures among other techniques, while arterial stenosis found after surgery can be corrected with percutaneous angioplasty and stent insertion [5-7]. Venous



stenosis more frequently requires anastomosis reoperations than percutaneous angioplasty [8].

Vascular non-anastomotic obstructions include kinking, external compression, or thrombi. Kinking contributes to inadequate redundant vessel lengths during anastomosis. During anastomosis, the lungs collapse, but after reperfusion, the lungs expand again; therefore, it is important to determine the appropriate length of a blood vessel that is tension-free and not redundant. Intravascular thrombi may interfere with pulmonary blood flow. Such a thrombus may occur because of inadequate perfusion and flushing during procurement. The diagnosis can be made with contrast-enhanced computed tomography, and kinking or external compression can be treated with percutaneous stent insertion (Fig. 1). Anticoagulant treatment can be attempted for thrombi. However, if this method is refractory or there is a severe obstruction, surgical treatment through re-exploration may be required.

Airway complications

The incidence of airway complications has decreased with the development of surgical techniques and advances in organ preservation, but the airway complication rate has been reported to be 2%–18% in several studies [9]. Donor bronchial ischemia is an important cause of airway complications since the bronchus receives blood from the pulmonary and bronchial arteries. Because the bronchial artery is transected during lung procurement, the blood supply is dependent on retrograde flow from the pulmonary artery [9]. The risk factors are multifactorial, including donor/recipient size mismatch, hypoperfusion, poor donor organ preservation, mechanical ventilation, primary graft dysfunction, ischemic time, and surgical technique.

According to the ISHLT 2018 consensus statement, the airway complications include ischemia and necrosis, dehiscence, stenosis, and malacia [9]. Their grading system is based on the initial bronchoscopic findings 2–3 weeks after lung transplantation.

Partial-thickness necrosis often resolves spontaneously

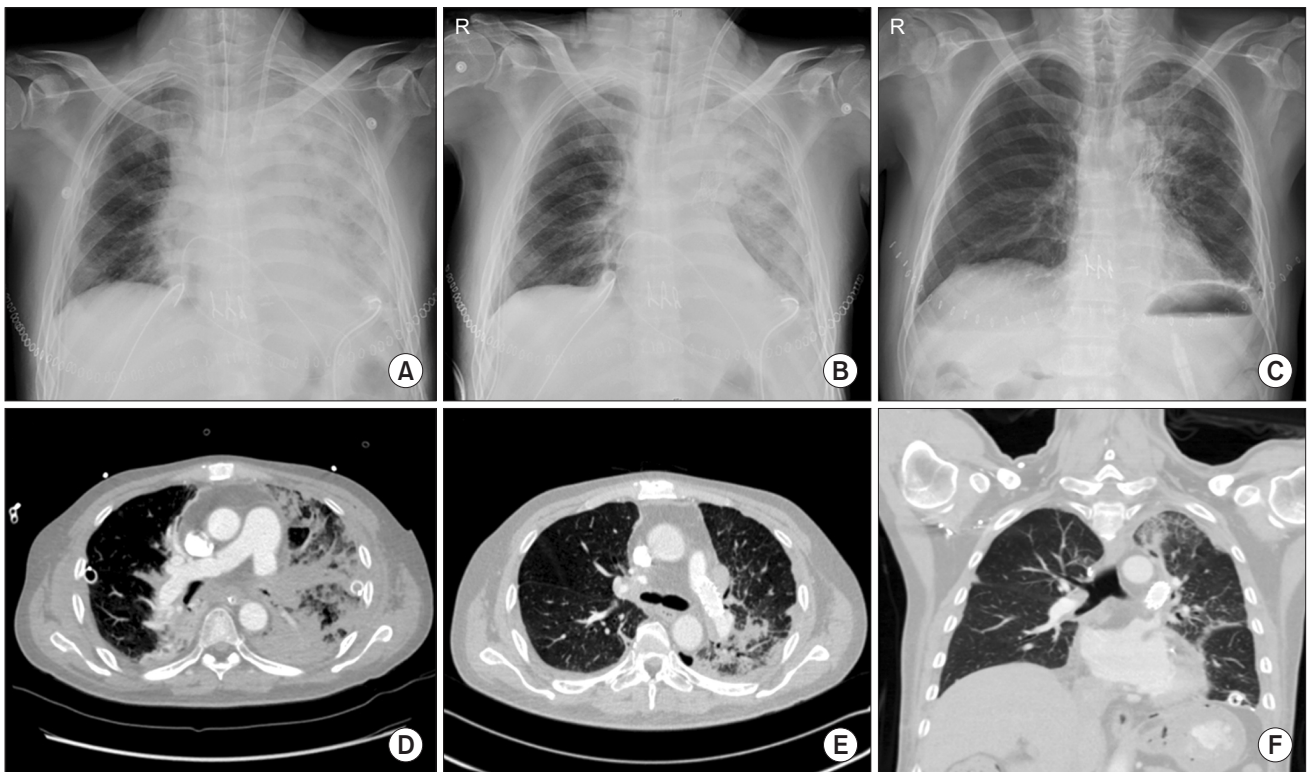


Fig. 1. Left pulmonary artery (LPA) obstruction due to kinking. (A) A chest X-ray showing left side lung haziness. (B) Chest X-ray after LPA stent insertion. (C) Chest X-ray 10 days after a pulmonary artery (PA) stent. The lung parenchyma had recovered to near normal. (D) Contrast computed tomography (CT) showing LPA obstruction and lung parenchymal injury. (E, F) On contrast CT, insertion of the stent into the LPA and lung parenchyma recovery after PA stent insertion can be confirmed.

without treatment [10,11]. In cases limited to the mucosa and without air leakage, antibiotics and bronchoscopic follow-up may be adequate. Meanwhile, extensive necrosis and dehiscence can be treated with self-expanding metallic stent implantation [9,12-14]. This allows uncovered stents to promote neo-epithelialization, and covered stents to aid in sealing against dehiscence. Recovery takes 6–8 weeks, after which the stent is removed [9]. If refractability or stent insertion is not possible for these treatments due to very serious dehiscence, surgical repair or re-anastomosis should be considered (Fig. 2). However, the latter is not easy because re-anastomosis itself is poor and is accompanied by inflammation and ischemia. After re-anastomosis, vascularized flaps, such as pericardium, intercostal muscle, or omental flaps, create favorable conditions for healing and aid in a successful recovery [15-17]. Allograft pneumonectomy can be considered as the last treatment option.

Stenosis is a highly prevalent complication, with an incidence of approximately 8.3%–32% [12,14,18,19], that is associated with a decrease in forced expiratory volume in one second. Treatment methods include balloon dilatation, endobronchial stent replacement (Fig. 3), laser ablative therapy, electrocautery, and argon plasma coagulation, which are used alone or in combination. If stenosis is refractory to these methods, retransplantation may be performed.

Pleural space complications

Pleural space complications, including empyema, pleural effusion, pneumothorax, and chylothorax, require treatment in approximately 22% of cases [20]. Pneumothorax is a source of air leaks in the parenchyma of the lung except for bronchial anastomosis complications, and it can occur when the donor/recipient size mismatch is severe [21]. Most of these complications can be resolved by maintaining and managing the chest tube; however, bronchial complications must be distinguished. A small amount of pleural effusion without evidence of infection can be observed through follow-up, but if there is evidence of lung compression with a large amount of pleural effusion, drainage through a chest tube or percutaneous catheter is required. Complex loculated pleural effusions may require surgical exploration and drainage. Chylothorax, which occurs due to thoracic duct injury during surgery, is uncommon. Most cases of chylothorax can be treated with the treatment generally used for this condition, and patients' diet can be controlled while maintaining chest drainage.

Phrenic nerve palsy

The phrenic, recurrent laryngeal, and vagus nerves may be injured during transplantation. Nerve injury may occur during the dissection of the pulmonary hilum adhesions for anastomosis; therefore, identification and protection of

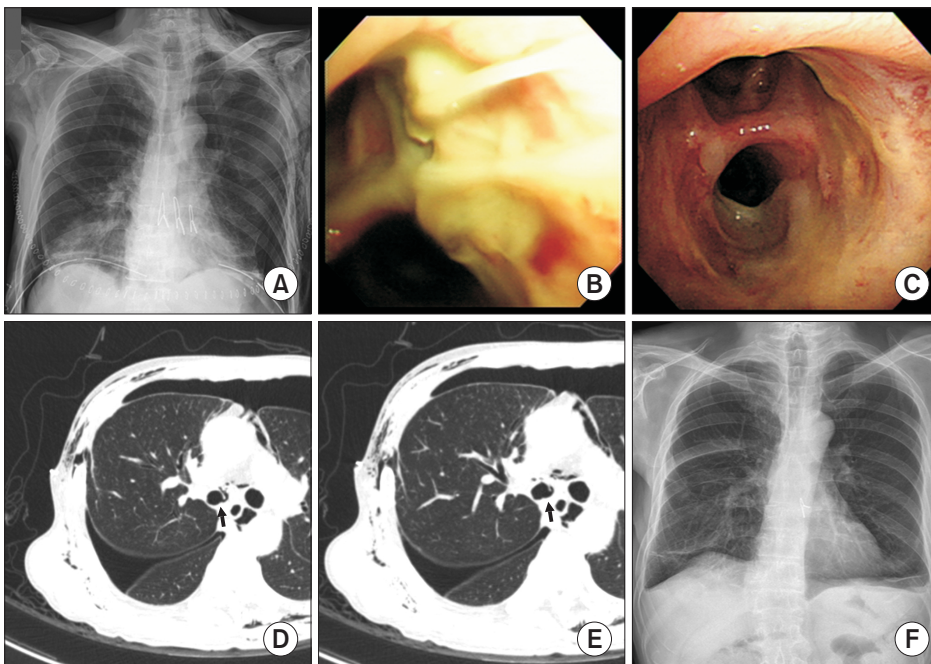


Fig. 2. Radiological and bronchoscopic findings of bronchial dehiscence. (A) Subcutaneous emphysema and pneumothorax were observed on a chest X-ray. (B, D, E) Dehiscence of the right bronchial anastomosis site was confirmed by bronchoscopy and contrast computed tomography (black arrow). (C, F) Bronchoscopy and chest X-ray images after right bronchial dehiscence recovered following surgical repair.

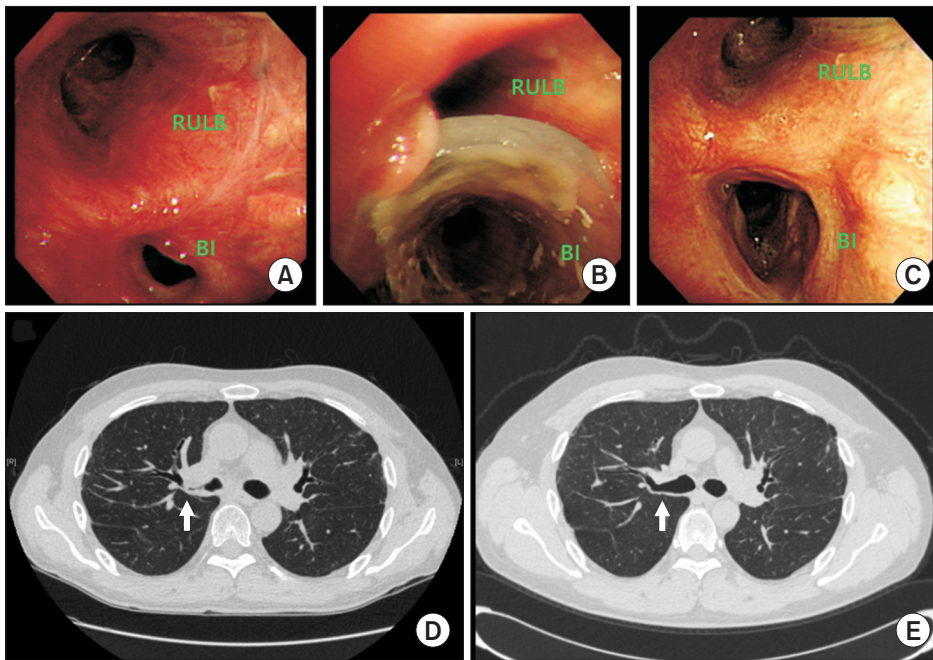


Fig. 3. Bronchus intermedius (BI) stenosis and its management with the insertion of a silicone stent. (A, D) BI stenosis at postoperative 4 months (arrow). (B) A silicone stent was inserted at the BI. (C, E) After silicone stent removal, the BI was well maintained in its expanded state (arrow). RULB, right upper lobe bronchus; BI, bronchus intermedius.

the nerves are important. The phrenic nerve is particularly important because of its key role in the mechanics of breathing. If it is damaged, mechanical ventilation may be required for a longer period [16,22]. Phrenic nerve injury should be suspected if an abnormally elevated diaphragm shadow is observed on chest radiography, which can be confirmed by fluoroscopy. Recurrent laryngeal nerve palsy may occur during dissection of the left hilar region, and this is critical because it increases the risk of incomplete opening and closing of the vocal cords and bronchial aspiration. Vagus nerve paralysis can occur when posterior mediastinal adhesions are dissected, and bilateral paralysis can result in decreased gastrointestinal motility. In cases of diaphragmatic nerve palsy, plication can be considered if the symptoms are severe, but the effect on long-term outcomes is not well known. Injection laryngoplasty can be considered for recurrent laryngeal nerve palsy.

Donor recipient size mismatch

Size mismatch between donors and recipients is common. The current consensus is that a donor's predicted total lung capacity can be 75%–125% of the recipient's [23], with larger donor sizes sometimes requiring resection of a part of the lung. In the case of the right lung, the middle lobe may be considered for resection; while the lingular segment is resected in the left lung. In addition, due to pulmonary edema and graft injury during surgery, closing the

thoracic cavity may interfere with ventilation because of an increase in intrathoracic pressure. In such cases, the thoracic cavity can be closed after a delay, as the condition improves within a few days post-operation while the thoracic cavity is kept open [24,25].

Wound complication

Wound-related complications may include wound dehiscence, infection, hematoma, and fracture of the wire used for sternal closure, which is rare. Wound dehiscence can be caused by obesity, long-term use of high-dose steroids before surgery, and inadequate blood sugar control. Most patients can be treated with wound dressing and re-suturing. In cases of sternal suture wire fractures, follow-up observation is possible, but re-wiring may be required if the sternum is unstable. Wound hematoma is mainly caused by bleeding from the wounded muscle. Hematoma may be delayed due to the use of anticoagulants after surgery, and it can be treated with compression dressing or drainage.

Conclusion

Despite advances in organ procurement and surgical techniques in the field of lung transplantation, surgical complications may occur, which affect patients' survival despite appropriate interventions. A multidisciplinary approach, in addition to skilled surgical technique, can be

helpful for the early detection and appropriate treatment of complications. The information presented herein is expected to assist in the management of complications after lung transplantation and the prevention of mortality and morbidity.

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Author contributions

All work was done by Jee Won Suh.

Conflict of interest

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