



Postoperative Management of Hyperinflated Native Lung in Single-Lung Transplant Recipients with Chronic Obstructive Pulmonary Disease: A Review Article

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ABSTRACT

End-stage chronic obstructive pulmonary disease (COPD) is the most common indication for single- or double-lung transplantation. Acute

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native lung hyperinflation (ANLH) is a unique postoperative complication of single-lung transplantation for COPD patients, with incidence varying in the medical literature from 15 to 30%. The diagnosis is made radiographically by contralateral mediastinal shift and ipsilateral diaphragmatic flattening. ANLH can deteriorate into hemodynamic instability, and respiratory impairment can result from compression of the allograft, which can precipitate atelectasis, hypoxemia, and hypercapnia, necessitating specific ventilatory intervention or volume reduction surgery. Currently, there is consensus for a therapeutic role of noninvasive positive pressure ventilation (NIPPV) in acute respiratory failure after lung transplantation as a well-tolerated measure to avoid re-intubation. This manuscript presents a concise review on the diagnosis and treatment of ANLH following unilateral lung transplant, along with a management algorithm created by the authors.

Keywords: Chronic obstructive pulmonary disease (COPD); Hyperinflated lung; Lung reduction surgery; Lung transplant; Postoperative

Key Summary Points

Acute native lung hyperinflation (ANLH) is a unique postoperative complication of single-lung transplantation for COPD patients.

ANLH can deteriorate into hemodynamic instability, and respiratory impairment can result from compression of the allograft, which can precipitate atelectasis, hypoxemia, and hypercapnia necessitating specific ventilatory intervention or volume reduction surgery.

If the patient develops respiratory failure diagnosed by radiology as ANLH, noninvasive positive pressure ventilation (NIPPV) or high-flow nasal cannula (HFNC) oxygen therapy should be applied as preliminary measures.

If the patient's condition worsens and intubation becomes mandatory, or if extubation was initially impossible, we recommend performing bronchoscopy for good suction and applying a bronchial blocker to prevent ANLH.

DIGITAL FEATURES

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD), specifically emphysema COPD, is defined as a common, preventable and treatable lung disease characterized by persistent respiratory symptoms and airflow limitation causing hyperinflation and reduced gas exchange [1]. End-stage COPD remains the most common

indication for lung transplantation, which can improve quality of life and prolong short-term survival [2]. One of the common postoperative challenges in COPD patients undergoing single-lung transplant is acute native lung hyperinflation (ANLH), a mediastinal shift and diaphragmatic flattening on a chest x-ray, with respiratory or hemodynamic failure requiring cardiac pressor agents or independent lung ventilation. The aim of the present manuscript is to present a review on the diagnosis and treatment of ANLH following unilateral lung transplant, along with a management algorithm created by the authors. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

COPD PATHOPHYSIOLOGY

The anatomic changes in COPD include destruction of the pulmonary parenchyma, with loss of elastic recoil, causing hyperinflation. It is defined as an increase in remaining air volume at the end of spontaneous expiration, resulting in lung hyperinflation. COPD is classified into two types: static (during rest) and dynamic (during exercise). Hyperinflation in the form of reduced functional lung mass is a clinically relevant hallmark of COPD causing the disabling symptoms of dyspnea, resulting in daily life limitations [3].

ACUTE NATIVE LUNG HYPERINFLATION PATHOPHYSIOLOGY

ANLH is a unique postoperative complication of single-lung transplantation for COPD patients, with incidence of 15–30% [4]. It is diagnosed radiographically by contralateral mediastinal shift and ipsilateral diaphragmatic flattening. COPD progression is diagnosed by the evaluation of lung hyperinflation by measuring lung volumes. Body plethysmography is a highly informative, noninvasive technique to obtain information on the airway resistance and the intrathoracic gas volumes, especially functional

residual capacity, residual volume, and total lung capacity [5]. Assessment of lung function by body plethysmography provides a multidimensional evaluation of COPD severity and treatment response [6].

ANLH occurs especially in the setting of positive pressure mechanical ventilation due to the difference in compliance between the highly compliant native lung and the allograft, which can be further worsened by ischemic reperfusion injury, donor lung characteristics, volume during surgery, and ischemic injury. ANLH can deteriorate into hemodynamic instability, requiring cardiac pressor treatment, possibly as a result of reduced right ventricular pre-load and increased left ventricular after-load. Moreover, respiratory impairment can result from compression of the allograft, which can precipitate atelectasis, hypoxemia, and hypercapnia, necessitating specific ventilatory intervention or volume reduction surgery in some cases [7].

LISTING AND CONTRAINDICATIONS FOR SINGLE-LUNG TRANSPLANT IN COPD

The Pulmonary Council of the International Society for Heart and Lung Transplantation formulated specific guidelines for lung transplant listing based on a continuum of expert opinion and available studies [8]. The society recommendations used the BODE index (incorporating body mass index, airflow obstruction severity, level of dyspnea, and exercise capacity) as a tool to guide the listing of candidates for lung transplant. They employed two cutoff values of the BODE index: 5–6 for potential lung transplant evaluation and 7–10 for listing. Active listing has been recommended for patients with moderate to severe pulmonary hypertension, three severe COPD exacerbations in the past year, and a single episode of acute hypercapnic respiratory failure [9]. Regarding the complexity of lung transplant surgery and perioperative mortality, there are absolute and relative contraindications that

should be considered in these futile patients [10]. The common absolute contraindications include recent malignancy, advanced other body system dysfunction, and poorly controlled infection. The relative contraindications include, but are not limited to, significant malnutrition, prior extensive chest surgery, and age over 65 years, with low physiological reserve.

Whether single or bilateral lung transplant is offered remains a complex decision and involves a multidisciplinary approach which evaluates the recipient's overall health, disease state, rehab potential, and anatomy. Improvement in allograft management postoperatively makes this question difficult to answer, especially after consistent findings of similar 5-year survival among single and bilateral transplant recipients in several recent studies [11, 12]. Single-lung transplant may offer a safe choice with a simpler surgical incision, shorter ischemic time, and rare need for cardiopulmonary bypass, with a larger total number of patients transplanted in comparison to bilateral transplant [13].

POSTOPERATIVE MANAGEMENT

Early Extubation, Early Mobility

As mentioned, prolonged positive mechanical ventilation can cause complications. Therefore, extubation either early postoperatively or in the operating room immediately after the surgery is a game-changing technique to minimize hyperinflation and reduce resource utilization and potentially shorten hospital stay [14]. Chest physiotherapy (CPT) with early mobilization should be an integral part of the postoperative standard of care for COPD patients. A recent intervention study that enrolled 319 mechanically ventilated patients indicated that CPT decreased extubation failure and significantly improved the rapid shallow breathing index score [15].

Noninvasive Positive Pressure Ventilation

Noninvasive positive pressure ventilation (NIPPV) is increasingly being used in the post-operative care of lung transplant patients. At present, there is consensus for the therapeutic role of NIPPV in acute respiratory failure after lung transplantation as a well-tolerated measure to avoid re-intubation in a large majority of cases [16]. Questions remain regarding the prophylactic use of NIPPV. In non-transplant patients who are at high risk for failed extubation and have been receiving mechanical ventilation for more than 24 h, the American College of Chest Physicians strongly recommends extubation to preventative NIPPV [17–19].

The rationale for the use of prophylactic NIPPV in the lung transplant population is to prevent alveolar derecruitment and reduce excess lung water which is due to right ventricular overfilling and increased venous return following cessation of positive pressure ventilation [19–21]. This reduction in left ventricular diastolic compliance is by interventricular interdependence. Therefore, prophylactic NIPPV may be an attractive choice to shorten weaning time and reduce the risk of failed extubation by decreasing the respiratory rate and providing resistive and elastic unloading of respiratory muscles which are commonly impaired in COPD patients [22–24].

High-Flow Nasal Cannula

A multicenter randomized clinical study conducted in 830 hypoxic cardiothoracic surgery patients showed that high-flow nasal cannula oxygen therapy (HFNC) was not inferior to NIPPV, with no significant differences in mortality [25].

As regards the safety in COPD patients, a systematic review assessed the effects of HFNC on partial pressure of carbon dioxide (PaCO_2) and found that HFNC was able to keep it unmodified. In addition, HFNC may reduce the expiratory flow limitation and dynamic hyperinflation, decreasing the respiratory rate and prolonging the expiratory time. This effect is

achieved by generating a small amount (up to 8 cmH₂O) of pharyngeal pressure during expiration, which drops to zero during inspiration—the same mechanism as the pursed lip breathing pattern of COPD patients [26].

The effectiveness of HFNC in lung transplant recipients suffering from acute respiratory failure was examined in 37 patients. The authors concluded that HFNC can decrease the need for invasive mechanical ventilation in recipients readmitted to the intensive care unit because of acute respiratory failure [27].

Therefore, implementing HFNC in the clinical management of respiratory failure in lung transplant recipients provides benefits, with ease of implementation, patient tolerance, and reduction in nursing workload.

Pharmacological Treatment

Bronchodilators are the cornerstone of therapy for COPD patients, especially in those patients with significant dynamic flow limitations; therefore, treatment regimens should be maintained in the perioperative period to reduce complications and slow progression [28]. A recent meta-analysis including eight randomized controlled studies which enrolled 1632 COPD patients demonstrated that the combination of muscarinic agent and beta agonist was superior to their mono-components [29]. Heliox (79% helium, 21% oxygen) has also been used effectively in COPD patients by reducing the airflow resistance to improve endurance time and slow the increase in end-expiratory lung volumes (EELV) [30].

INVASIVE VENTILATION

Conventional Ventilation

There are no prospective studies defining the optimal strategy for ventilation of lung transplant patients, but an international survey that enrolled patients from 18 countries showed that the pressure-control/assisted ventilation modality is the most common mode used, followed by the volume type [31]. Limitation of

native lung hyperinflation and its consequences can be achieved by reducing minute ventilation (tidal volume of 4 to 6 mL/kg and respiratory rate) and prolonging expiratory time, which are the main determinants of auto-positive end-expiratory pressure (auto-PEEP). A high inspiratory flow rate (60 to 100 mL/min) is necessary to satisfy the high flow demand and shorten inspiratory time, and is critical to decrease dynamic hyperinflation and auto-PEEP [32]. External PEEP may worsen the dynamic hyperinflation of the native lung, but it has been shown to decrease the work of breathing and improve patient–ventilator synchrony, and to moderate dynamic hyperinflation, so low initial PEEP (5 cm H₂O) should be applied, considered as less than auto-PEEP (intrinsic PEEP), and adjusted according to the patient’s response [33].

Differential Lung Ventilation

Physiological differential lung ventilation (DLV) aims to ventilate each lung as an independent unit to deliver different ventilation settings accommodating the difference in airway resistance and lung compliance. Its implementation in postoperative complications of single-lung transplant is among the recognized indications, with incidence of 12% for COPD patients [34]. A retrospective controlled study on DLV for single-lung transplant COPD patients was conducted by Pilcher and colleagues in 2006 and revealed that the two factors significantly determining the requirement for DLV were preoperative total lung capacity percent predicted ($P = 0.032$) and the postoperative partial pressure of oxygen (PaO₂)/ fraction inspired oxygen (FiO₂) ratio ($P = 0.005$). Surprisingly, the study demonstrated increased duration of mechanical ventilation and ICU stay and increased mortality in the DLV group compared to conventional ventilation [35]. The abovementioned study was conducted between 1990 and 2005, which reflects the effect of the learning curve, and positive impact of the modern evolution of intensive care management and the latest generation of ventilators in

the improvement of alveolar gas exchange by applying DLV in recent case reports [36].

The important consideration with regard to DLV is placement of a double-lumen endotracheal tube (DLT). Problems with the double-lumen tube include inadequate pulmonary hygiene, increased resistance due to the narrow lumen, need for sedation and/or paralysis to improve patient compliance, and malposition of the DLT. In addition, DLT cuffs can generate transmucosal pressures of over 50 mmHg with an inflation of just 2 ml of air, which can cause tracheal erosion. In comparison, a randomized, prospective, controlled trial showed that endobronchial blockers have no added complexity to intubation and were associated with less incidence of vocal cord injuries, hoarseness of voice, and sore throat [37].

Another dilemma is the use of synchronous versus asynchronous ventilation. Asynchronous ventilation offers flexibility and is less complicated in setup than synchronized ventilation, which necessitates that the two ventilators keep the same respiratory rate for both lungs, with no proven advantage compared to asynchronous DLV. Moreover, asynchronous ventilation allows for greater flexibility with the difference in respiratory rate, variable modes, and pressures/PEEP which should be applied to the hyperinflated native lung and the transplanted lung [36].

With regard to ventilation of the native lung, we should apply the strategy mentioned earlier to avoid hyperinflation, with intermittent disconnection of the endotracheal tube to allow lung emptying. As far as ventilation modes are concerned, pressure support ventilation (PSV) may be a poor choice due to variable minute ventilation and ventilator asynchrony, especially in the case of full ventilatory support; also, there is little effect on decreasing auto-PEEP, which may worsen respiratory muscle fatigue [38]. Lung protective ventilation should be applied to the transplanted lung. The lung protective strategy includes low tidal volume (6 ml/kg of recipient ideal body weight), PEEP (5 cm H₂O and adjustment according to the patient course), and limited FIO₂ [39].

Bronchial Suction

Flexible bronchoscopy is indicated for diagnostic or therapeutic purposes. Therapeutic indications include removal of excess mucus, which increases the airway resistance and impedes exhalation of air. It is also important to visualize the position of the DLT (side of the bronchial lumen should be positioned to lie in the main bronchus of the native lung to avoid injury to the bronchial anastomosis) or bronchial blocker.

Endoscopic Treatment

A retrospective study conducted on single-lung transplant recipients 3 months after transplantation showed that the contribution of the native lung was minimal, accounting for less than 30% of the ventilation and perfusion. It is therefore imperative to understand that native lung volume reduction would have a negligible impact on the pulmonary function test (PFT) values; moreover, reducing the hyperinflation and release of the compression on the transplanted lung will improve the PFT [40]. The one-way endobronchial valve (EBV) is designed to prevent air from entering the lobe while allowing it to exit, thus creating a resorption atelectasis of the target lobe causing volume reduction simulating the physiology of lung volume reduction surgery (LVRS).

EBV is a less invasive alternative to LVRS, and is a valid alternative in selected patients with heterogeneous disease with intact lobar fissures or absent collateral ventilation, offering the advantage of removal in the case of no benefit from treatment [41].

A multinational retrospective study that enrolled 14 single-lung transplant patients with ANLH treated with EBV showed successful improvement of symptoms in 11 of 14 (79%) patients and significantly improved lung function ($P = 0.013$) in 9 of 12 (75%) patients [42]. The most common complication after EBV is pneumothorax, so close observation is essential in the postoperative care of these patients. Pneumothorax is ascribable to targeted lobar collapse in the presence of adhesions causing surrounding parenchymal rupture, but a

retrospective analysis of three prospective multicenter trials indicated that this complication may not have a negative impact on outcome in terms of health-related quality of life, and to some extent it improves the clinical outcome [43]. Another complication is an increased risk of bacterial colonization rates after EBV insertion, which was discussed in a retrospective, single-center analysis of lung transplant waitlist candidates [38].

Lung Volume Reduction Surgery

It is crucial to understand that post-transplant LVRS is a high-risk operation because of concerns regarding the frailty of patients receiving immunosuppressive drugs and the possibility of thoracic cavity adhesions and friable tissues, and the potential for prolonged air leaks [44]. Patient selection for LVRS is critical and should be preceded by a CT scan and perfusion scan [45]. Many published studies encourage the use of LVRS by demonstrating its feasibility and efficacy in improving forced expiratory volume in 1 s (FEV1), although the mean time from transplant to LVRS was approximately 50 months, which may exclude LVRS as an immediate postoperative strategy to treat ANLH (46, 47).

ALGORITHM

Given the complexity of management of ANLH following unilateral lung transplant, we propose a management algorithm (Fig. 1) as a stepwise approach to management.

Initially, on admission to the ICU, the patient is either intubated or extubated. If intubated, we recommend early extubation. After extubation, we encourage the use of inhaled bronchodilators and early mobility. If the patient develops respiratory failure diagnosed by radiology as ANLH, NIPPV or HFNC should be applied as preliminary measures. If the patient's condition worsens and intubation becomes mandatory, or if extubation was initially impossible, we recommend performing bronchoscopy for good suction and applying a bronchial blocker to prevent ANLH. If there is

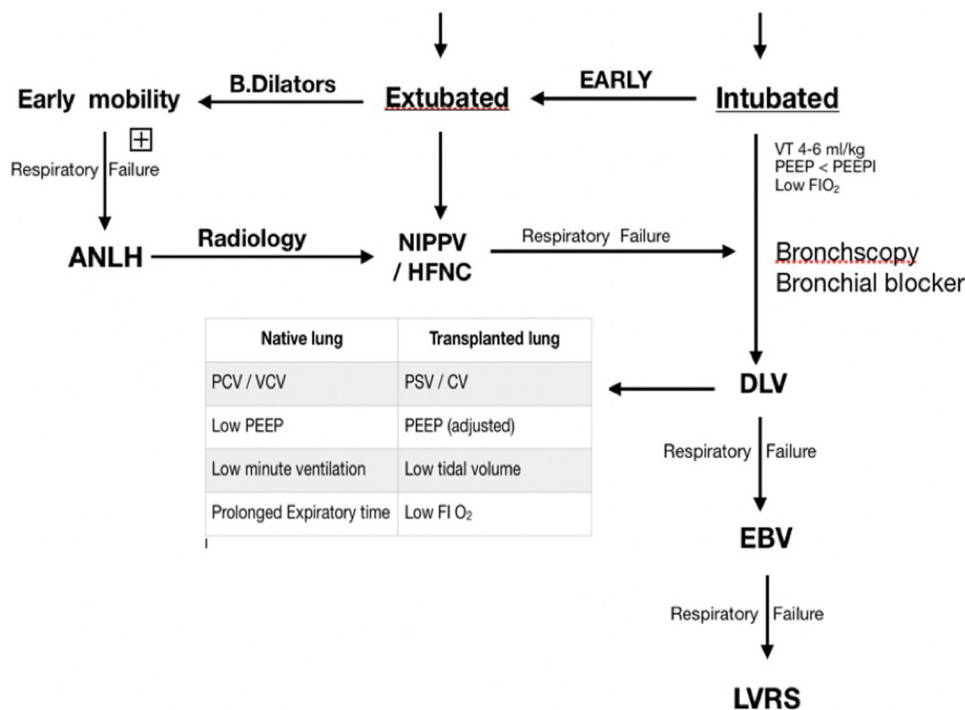


Fig. 1 Algorithm for the management of acute native lung hyperinflation (ANLH) following unilateral lung transplant

no obvious improvement, move on to DLV. If the ANLH is still progressing, we encourage insertion of the EBV. The last resort is LVRS.

CONCLUSION

Acute native lung hyperinflation is a serious postoperative complication of single-lung transplantation for COPD patients. ANLH can deteriorate into hemodynamic instability and respiratory impairment, necessitating careful diagnosis and focused management that includes specific ventilatory intervention or volume reduction surgery. This manuscript presented a detailed review along with a management algorithm for the treatment of ANLH following unilateral lung transplant.

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