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Research Article

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Advanced Solutions for Native Lung Hyperinflation: Endobronchial Valves in Post Transplant Care

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ABSTRACT
Background: Native lung hyperinflation (NLH) is a potential late complication in patients with chronic obstructive pulmonary disease (COPD) following single lung transplantation, characterized by radiologic evidence of native lung expansion, mediastinal shift, and respiratory deterioration. The progressive dynamics of NLH and its detrimental effect on graft function serve as reminders of the imperative to address this condition. Few effective treatments exist for NLH, and the most common option is lung volume reduction surgery (LVRS). Conversely, endobronchial valves (EBV) are a potential treatment option for NLH. This case series describes two post-transplant patients successfully treated with EBVs, highlighting the benefits and limitations of this approach.

Keywords: Bronchoscopic Lung Volume Reduction, Collateral Ventilation, Emphysema, Endobronchial Valves, Hyperinflation

Abbreviations Page

6MWD	-	6-Minute Walk Distance
BLVR	-	Bronchoscopic Lung Volume Reduction
BOS	-	Bronchiolitis Obliterans Syndrome
COPD	-	Chronic Obstructive Pulmonary Disease
CV	-	Collateral Ventilation
EBV	-	Endobronchial Valve
EMPROVE	-	Endobronchial Valve for Emphysema Palliation Trial
FEV1	-	Forced Expiratory Volume in 1 Second
HRCT	-	High-Resolution Computed Tomography
LVRS	-	Lung Volume Reduction Surgery
NLH	-	Native Lung Hyperinflation
PAL	-	Persistent Air Leak
PFTs	-	Pulmonary Function Testing
RV	-	Residual Volume
TLC	-	Total Lung Capacity
VATS	-	Video Assisted Thoracoscopic Surgery

Introduction

Native lung hyperinflation (NLH) affects approximately 5-30% of single-lung transplant recipients with COPD, occurring when the hyperinflated native lung compresses the transplanted allograft [1,2]. Clinically significant NLH is associated with declining forced expiratory volume in 1 second (FEV1), reduced exercise tolerance, and increased oxygen requirements. Patients with severe airway obstruction, air trapping, and relative pulmonary hypertension are at higher risk [3]. Importantly, the contribution of the native lung to overall ventilation and perfusion is minimal, accounting for less than 30% of total function, suggesting that its loss will not significantly impair respiratory capacity [4].

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Surgical options, including LVRS, pneumonectomy, and lobectomy, carry high morbidity and mortality in this population [5-7]. Endobronchial valves (EBVs) have emerged as a less invasive alternative for treating NLH. EBVs are widely utilized in bronchoscopic lung volume reduction (BLVR) to manage advanced emphysema. These one-way valves are placed bronchoscopically and can be removed if not tolerated by the patient, providing a reversible and minimally invasive means to address NLH by redirecting airflow and reducing hyperinflation [8]. BLVR with EBVs has shown to improve pulmonary function, quality of life, and diaphragmatic motion [9]. When placed in diseased target lobes, EBVs induce lobar atelectasis, effectively replicating the results of LVRS [9]. The first reported use of EBVs for NLH was in 2007, and subsequent cases have shown varying degrees of success, further underscoring the potential of this approach [1,9-11].

This case series describes two patients with post-lung transplant NLH treated with EBVs, demonstrating clinical and radiographic improvements.

Patient 1

A 70-year-old female with a history of emphysema underwent a left single-lung transplant five years prior. Her post-transplant course was complicated by primary graft dysfunction, recurrent acute cellular rejection, and bronchiolitis obliterans (BOS). She presented with progressive dyspnea and declining spirometry over two years. CT imaging revealed significant compression of the transplanted lung due to NLH. Figure 1

Figure 1: A coronal CT showing significant compression of transplanted left allograft by the native, hyperinflated lung.

Following BLVR assessment, the right upper lobe was identified as a target for EBV placement. Six Zephyr valves were deployed. The procedure was complicated by pneumothorax, managed with a pigtail catheter. Post-procedurally, complete lobar atelectasis was achieved, with radiographic and spirometric improvements, along with enhanced exercise tolerance.

Patient 2

A 74-year-old female with emphysema underwent a right single-lung transplant six years prior. She experienced progressive dyspnea over 18 months, with imaging confirming left lung hyperinflation.

Baseline pulmonary function tests (PFTs) showed an FEV1 of 1.2L, residual volume (RV) of 180% predicted, and total lung capacity (TLC) of 140% predicted.

The left lower lobe was identified as a target for EBV placement Figure 2. Following BLVR with Spiration valves, radiographic images confirmed lobar atelectasis and reduced NLH Figure 3. Post-procedural PFTs showed improved FEV1 (1.34L0, reduced RV (111% predicted), and increased six-minute walk distance (1,450 feet). The patient reported improved dyspnea and functional capacity.

Figure 2: Endobronchial valves in the left lower lobe

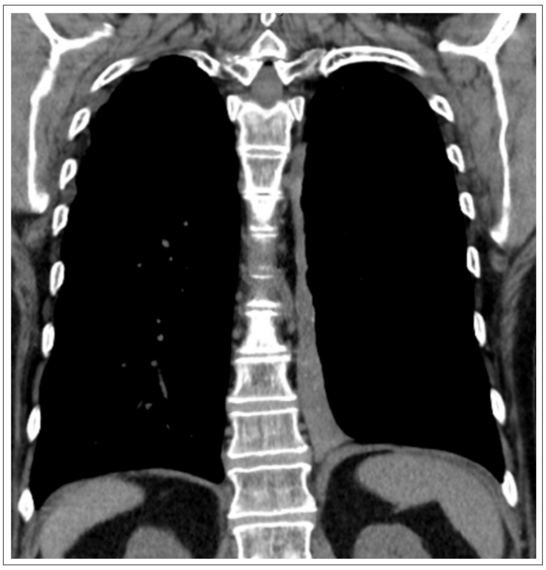

Figure 3: Chest CT showing reduction of NLH with left lobar lobe atelectasis.

Discussion

Traditional treatments for NLH are centered on surgical intervention, with LVRS being a primary approach [1-3,10,12]. LVRS involves surgical excision of the diseased, hyperinflated lungs and has been shown to improve the quality of life and pulmonary function in appropriately selected patients with severe COPD [5-7]. Treatment of NLH by LVRS has been proven to be feasible in various studies, demonstrating post-operative improvements in lung function by reducing hyperinflation and relieving compression on the transplanted lung [1]. However, this treatment is also associated with significant morbidity and mortality [12].

In this case series, EBVs were effective in reducing herniation and the subsequent compression of the transplanted allograft by the native lung. The use of BLVR to treat NLH opens further opportunities for minimally invasive treatments for complex, post-transplantation complications, offering the added advantage of removal if no benefit is derived from the treatment [13]. Notably, the enhanced efficacy observed in these cases may be attributed to the absence of collateral ventilation, a factor that has undergone substantial investigation and is now recognized as a key determinant of successful EBV treatment [14].

EBVs function as one-way devices deployed in the bronchial airways of the native lung, inducing lobar atelectasis by allowing expiratory air escape while preventing inspiratory air entry, thereby simulating the physiology of LVRS [8,9,15,16]. Careful patient selection remains integral to ensuring successful outcomes. Although EBVs offer a minimally invasive option for NLH, not all patients are eligible, and realistic expectations regarding potential risks and benefits are crucial. Comprehensive evaluation includes a full medical assessment, spirometric measurements, computed tomography (CT) imaging, collateral ventilation assessment, ventilation perfusion scanning, and six-minute walk distance (6MWD) testing. Patients should exhibit evidence of hyperinflation, with TLC greater than 100% and residual volume (RV) greater than 175% predicted values [11,17,18]. Although previous studies have proposed higher FEV1/DLCO cutoff values, newer studies have used lower FEV1/DLCO cutoffs; therefore, we are reluctant to conclude that there are absolute contraindications. Individualized assessment is paramount. Additionally, patients with a 6MWD between 100 and 500 meters should be considered for EBV treatment, while those with distances ≤200 meters may benefit from reassessment following pulmonary rehabilitation [13,19].

The goal of EBV in NLH is to induce target lobe atelectasis and reduce native lung hyperinflation. The absence of collateral ventilation (CV) between the treated and ipsilateral adjacent lobes is crucial for success [8,14]. The ongoing CONVERT II trial aims to evaluate the effectiveness of closing collateral ventilation in emphysema, potentially allowing even more patients with NLH to benefit from EBVs. Even when segmental bronchi are occluded, persistent inflation through collateral channels can compromise effectiveness. In both patients presented in this series, the absence of collateral ventilation allowed for successful atelectasis.

The Chartis Diagnostic System is the most extensively studied tool for assessing collateral ventilation, offering precise evaluation of fissure integrity [15,16,20]. Given the variability in determining lobar fissure integrity through visual high-resolution CT (HRCT) assessment, this method alone is not recommended for selecting EBV candidates. However, quantitative CT analysis has demonstrated predictive capabilities comparable to Chartis in smaller datasets, with recent data supporting its role in screening patients based on fissure completeness of ≥80%. In cases with fissure integrity ≥95%, EBV placement may proceed without mandatory Chartis testing [21,22]. When collateral ventilation is present or fissures are incomplete, surgical LVRS may be the only viable treatment option.

HRCT imaging is essential in evaluating the degree and distribution of emphysema, with coronal, sagittal, and axial reconstructions helping identify the most appropriate target lobes. In more homogeneously distributed disease, a perfusion scan may provide additional insights, guiding the selection of target lobes with lower perfusion relative to untreated regions [23].

Physicians should carefully review CT scans for findings such as bullae adjacent to the target lobe, nodules requiring further evaluation, infiltrations suggestive of active infection, or disqualifying features such as severe bronchiectasis, extensive fibrosis, or other impairments that may compromise outcomes. Patients with recurrent infections, severe hypercapnia, unstable cardiovascular conditions, or uncorrectable comorbidities should generally be excluded from EBV treatment for NLH. While specific selection criteria guide decision-making, no single factor should automatically preclude candidacy if other parameters are favorable, necessitating careful clinical judgment [11,17,18].

Numerous studies have demonstrated the efficacy of EBVs in the treatment of NLH, showing significant improvements in lung function, exercise tolerance, and quality of life. In a multinational retrospective study of 14 single-lung transplant recipients with NLH, 79% reported symptomatic improvement, while 75% had significantly improved lung function ($P = 0.013$) [19]. Additionally, radiological assessments confirm reductions in hyperinflation and successful atelectasis following EBV placement.

The procedure may be performed under conscious sedation or general anesthesia using a flexible endotracheal tube or a rigid bronchoscope. Ideally, Chartis assessment and EBV placement should be conducted in a single session. Proper valve placement is critical for ensuring lobar collapse, and if atelectasis does not occur within one month, CT evaluation should be performed to assess valve positioning, with replacement considered for sub optimally positioned valves [2,15].

While EBVs offer a promising therapeutic option, safety considerations remain paramount. Potential complications include valve migration, mucus plugging, infection, and pneumothorax. Pneumothorax occurs in 14–26% of patients following EBV placement, typically within the first two days post-procedure [3,24]. This complication is thought to result from targeted lobar collapse in the presence of adhesions causing parenchymal rupture. However, retrospective analyses suggest that pneumothorax does not necessarily negatively impact long-term outcomes and may, in some cases, be associated with improved clinical responses. In patients on immunosuppressive therapy post-lung transplantation, prolonged pneumothorax healing may increase the risk of persistent air leaks and secondary infections due to extended chest tube placement [25]. Nevertheless, long-term sequelae of EBV therapy are generally manageable [26].

Several challenges remain in optimizing EBV treatment for NLH. The cost-effectiveness of EBV therapy compared to alternative treatments remains an ongoing challenge, particularly in healthcare systems with limited resources. Determining the optimal timing for EBV placement in patients with NLH is still debated, as early intervention may prevent irreversible lung damage, while delaying the procedure could allow for better patient selection. Advances in valve design and delivery techniques aim to enhance procedural precision and minimize complications. Additionally, integrating EBVs with other bronchoscopic interventions, such as thermal vapor ablation, may offer synergistic benefits [27]. Research into the application of EBVs in pediatric NLH patients is also warranted, further expanding the potential of this approach.

Conclusion

NLH is a challenging complication following single lung transplantation in patients with COPD. EBV therapy offers a minimally invasive alternative to LVRS, with its success largely dependent on fissure integrity. The ongoing CONVERT II trial aims to evaluate the effectiveness in closing collateral ventilation in emphysema, potentially allowing even more patients with NLH to benefit from EBVs. While there are risks associated with the use of EBVs in NHL, appropriate patient selection and pre-procedural preparation could allow this treatment to be more common in patients with NLH EBV placement has demonstrated significant improvements in lung function, exercise capacity, and quality of life. Further research is needed to refine the patient selection criteria, enhance safety profiles, and establish the long-term effectiveness of this innovative therapy. With ongoing advancements and growing clinical evidence, EBVs are poised to play an increasingly vital role in NLH management.

Future Directions

The field of NLH treatment using EBVs has continued to evolve. Ongoing research aims to refine patient selection criteria, improve valve design, and optimize post procedural care. Additionally, the use of advanced imaging techniques such as fluoroscopy and three-dimensional mapping may enhance the precision of valve placement.

Some recent studies have explored the combination of EBVs with other modalities, such as bronchoscopic thermal vapor ablation, to further enhance outcomes. These approaches aim to target NLH from multiple perspectives, resulting in synergistic benefits. The use of EBVs in pediatric patients with NLH is an emerging area of research. The initial findings suggest that EBVs can be safely and effectively used in this population, potentially sparing children from more invasive surgical interventions. Continued research is essential to assess the long-term durability of EBV treatments. Understanding the potential for valve-related complications and monitoring patients for late adverse events are crucial.

Ethical Compliance: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Authorship Page

Author Contributions

P.N: participated in writing the paper, editing, and submission of the manuscript.

A.M: Participated in the writing of the paper, reviewing and editing.

A.S: Participated in the writing of the paper, reviewing and editing.

K.H: Participated in the writing of the paper, reviewing and editing.

Conflict of Interest Statement

K. H. has received honoraria and consulting fees from Spiration in the past but has not consulted or received payment since May 2015. He was part of the EMPROVE study (IBV for emphysema) and VAST study (IBV for persistent air leaks). None declared. (P.N., A. M., and A. S.)

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