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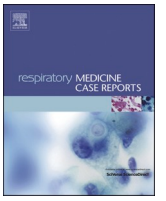

Case Report

# Bronchoscopic lung volume reduction complicated by ipsilateral pleural effusion

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ABSTRACT

Chronic obstructive lung disease is the third leading cause of death worldwide. It affects the airways and lung parenchyma leading to emphysema. Bronchoscopic lung volume reduction is another strategy that aims to reduce air trapping and hyperinflation, leading to improvement in symptoms and pulmonary function. Several techniques have been employed, one of them is the blocking method using Zephyr or Spiration valves. The use of both valves is approved by the Food and Drug Administration view their established efficacy in improving lung functions, quality of life and survival. Although they have a relatively safe profile, several adverse events have been reported, pneumothorax being the most common and pleural effusion being the least reported. We show herein, a case of 74-year-old female presenting with pleural effusion secondary to bronchoscopic lung volume reduction. Although uncommon, highlighting this potential outcome is crucial.

## 1. Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogenous disease resulting from environmental exposures, smoking being the most common, along with genetic predispositions [1]. COPD is the third leading cause of death worldwide and the burden is expected to increase along with aging and ongoing exposures [1,2]. Pulmonary symptoms include shortness of breath, chronic cough with or without phlegm, wheezing, and fatigue. These manifestations result from the irreversible remodeling of the airways (bronchitis/bronchiolitis) and or alveoli. The destruction of the alveoli and lung parenchyma will lead to emphysema, and gas exchange impairment [1]. This parenchymal destruction will cause an increase in lung elasticity reducing by then the elastic recoil of the lung resulting in hyperinflation [3]. Treatment of COPD consists of bronchodilators, anti-inflammatory, adequate vaccination, oxygenation, and pulmonary rehabilitation when indicated [1]. However, hyperinflation and air trapping, arising from the underlying expiratory airway collapse, play a major role in dyspnea and both do not respond well to bronchodilator [4].

Lung volume reduction surgery in certain population has showed improvement in quality of life, dyspnea, exercise capacity, and mortality benefit [1], [5]. Bronchoscopic lung volume reduction (BLVR) is a less invasive technique which was first described in 2003 [6], [7], and has been an alternative option for patients who are not surgical candidates [6]. BLVR consists of blocking techniques using endobronchial valve (EBV) or intrabronchial valve (IBV) and non-blocking techniques such as thermal vapor ablation or coiling [6]. Candidates who might benefit from BLVR are those who have total lung capacity (TLC) $>$ 100 L and residual volume (RV) $>$ 175 L, reflecting hyperinflation and air trapping respectively, and exercise limitation: 6 minutes walking test (6MWT) $>$ 100 m [6], [8].

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Additional criteria exist: symptomatic COPD, emphysema phenotype, destruction score >15 %, controlled COPD (no more than 2 exacerbations per year), severe airflow limitation, smoke cessation for 4–6 months, no collateral ventilation to the targeted lobe, and modified medical research council dyspnea scale (mMRC) > 1 [5], [8].

Certain absolute and relative contraindications for BLVR exist: presence of allergy to device material, active or recurrent lung infections, active smoking, uncontrolled or severe heart failure, inability to hold antiplatelets/anticoagulant, prior thoracic surgery/pleurodesis to targeted lobe, chronic immunosuppression, severe resting hypoxemia (arterial pressure of oxygen (PaO2) < 45 mmHg), severe resting hypercapnia (arterial pressure of carbon dioxide (PaCo2) > 50 mmHg) and pulmonary hypertension [6], [9].

There are two types of valves used in blocking techniques, both are approved by the Food and Drug Administration (FDA) [6,9] and both function as one way valve: they prevent the inspired air from entering but they allow expired air and mucus to exit [4] which will lead to atelectasis with subsequent decrease in hyperinflation, improvement in lung function, gas exchange and mortality [10,11]. The first one serves as EBV: Zephyr® (*Pulmonx Corporation, Red Wood City, California, United States of America*), its core is composed of nitinol covered by a silicone layer [6], comes in two sizes 4 mm (mm) that serves up to 7 mm bronchial lumen diameter and 5.5 mm that serves up to 8.5 mm bronchial lumen [12]. The other one is an IBV, umbrella shaped, 5–9 mm [13], has a core of nitinol covered by a polyurethane membrane and is called the Spiration® valve (*Olympus, Tokyo, Japan*) [6], [11]. The choice between the two is based on airway anatomy rather than efficacy [11]. The Zephyr valve was the first to be approved by FDA and its efficacy has been studied by several trials: VENT, STELVIO, BeLieVer-HiFi, TRANSFORM and LIBERATE [7,8]. The Spiration valve was approved by the European Union first, studied by Stermann et al., then approved by the FDA [13].

The success of endobronchial valve placement is predicted by the outlined conditions: the absence of collateral ventilation, the presence of an intact fissure and the presence of heterogenous emphysema [4], [6], [10], [14], [15]. The presence of collateral ventilation will contradict the presence of the valve allowing airflow to the targeted lobe preventing atelectasis. To exclude the presence of collateral ventilation, the Chartis measurement during bronchoscopy is obtained [16]. Another method would be calculating the fissure completeness score using imaging [17].

Although BLVR efficacy is approved, its safety is affected by several reported adverse events. We show herein a case of 74-year-old female presenting with pleural effusion secondary to BLVR. Although uncommon, highlighting this potential outcome is crucial.

## 2. Case report

74-year-old female known to have severe chronic obstructive pulmonary disease (COPD) with chronic hypoxic respiratory failure on 3 L per minute (l/min) continuous oxygen at baseline presents early September 2023 to our institution for worsening shortness of breath and increased oxygen requirements (5–7 l/min) secondary to new onset left pleural effusion. To understand better her current hospital admission, a comprehensive history of her progressive illness is detailed below.

The patient has a remote smoking history estimated as 80 pack year and has quit 4 years prior to this admission. She has been diagnosed with COPD for the past 10 years. Her history is also relevant for occupational exposure as she used to work in metal welding for 20 years. Hypertension and low body mass index (BMI) of 16 kg/meter$^2$ (kg/m$^2$), were also noted as additional comorbidities. Echocardiography one year earlier demonstrated a moderate reduction in ejection fraction (EF) 45 % along with grade I diastolic dysfunction. Prior computed tomography of the chest (CT) was significant for severe emphysema, mainly upper lobe, and multiple bilateral small pulmonary nodules.

Pulmonary function test (PFT) was obtained during prior outpatient clinic visits and did show evidence of severe obstruction with severely reduced diffusion capacity of the lungs for carbon monoxide (DLCO). Her Forced expiratory volume in 1 s (FEV1) was 0.6 L (29 % predicted) and her (DLCO) was 35 mL/minute/millimeter of mercury ml/min/mmHg. Lung volumes indicated hyperinflation with TLC of 170 L (L) and air trapping with RV of 292 L. The patient was maximized on medical therapy following the guidelines of COPD management. She was receiving a daily fixed dose of triple therapy. This treatment was coupled with as needed nebulizer and inhaler short acting therapy and daily azithromycin. The patient was also receiving pulmonary rehabilitation sessions which helped improve slightly her symptoms and exercise capacity: her 6MWT improved from 300 to 349 m and her COPD Assessment Test (CAT) improved from 24 to 16 points. Her symptoms consisted mainly of shortness of breath on exertion without reported wheezing, cough, sputum production or hemoptysis.

The patient has been evaluated for bronchoscopic lung volume reduction (BLVR) therapy, aiming at the improvement of her exercise capacity, quality of life and survival. At that time her mMRC dyspnea scale was 3 and her BODE index was 7. In February 2022 she underwent the placement of six endobronchial 4.0 mm Zephyr valves (EBV) for the left upper lobe (LUL): in the superior segment of the lingula 3 sub-segments were visualized LB4a/LB4b/LB4c and 3 EBVs were placed, similarly another 3 were placed in the upper division sub-segments (anterior and apico-posterior) LB1 LB2 and LB3. Post-operatively, the patient was discharged home after adequate monitoring without adverse events.

After lung volume reduction, her total lung volume was reduced 590 ml equivalent to 32.4 % reduction from her initial volume. On subsequent clinic visits, the patient reported using less oxygen 1–2 l/min. She also reported gradual improvement in her breathing. Her post operative CT chest emphysema protocol showed some volume loss which was expected and desired. Sixteen months later, the patient was back to her preoperative clinical state in terms of shortness of breath and exercise capacity. The patient was scheduled for revision of her EBVs.

The patient underwent removal of her Zephyr valves which were replaced with two spiration valves, 9 mm each, one at the upper division of LUL and one at the opening of the lingula. The patient was discharged home after adequate monitoring without developing pneumothorax. Eight days later the patient reports to the hospital with worsening shortness of breath, dyspnea on minimal exertion and increase in oxygen requirements 5–7 l/min. She denied fever, chills, productive cough, or sick contact.

The initial white blood cell (WBC) count was normal without evidence of an infection. Her initial chest x-ray (CXR) did show moderate sized left pleural effusion along (Fig. 1). There was an upper lobe consolidation deemed secondary to atelectatic lobes. Left pleural pigtail catheter was placed with removal of straw-colored fluid. CT chest post pigtail insertion demonstrated large dense consolidation in the left upper lobe along with bronchial stents (Fig. 2). Pleural fluid studies revealed transudative effusion: pleural fluid protein <2 g/deciliter (g/dl) (versus serum protein 4.7 g/dl) and lactate dehydrogenase (LDH) level of 89 units/liter (U/L) (versus serum LDH 217 U/L). Both fluid cytology and cultures were negative for malignancy or infection respectively. Fluid WBC count was 301 with lymphocytic predominance (lymphocyte 71 %, neutrophils 17 %, eosinophils 5 %, and 7 % mononuclear cells), fluid glucose was 202 mg/deciliter (mg/dl) and fluid albumin was 1.1 g/dl. Initial blood cultures were negative. The pleural effusion was deemed secondary to atelectasis from BLVR. Other causes of transudative effusion such as heart failure exacerbation were ruled out.

The pigtail catheter demonstrated an active drainage over 12 days of hospital stay before decline in daily output and subsequent removal. The chest tube was successfully removed with stabilization in her oxygen requirements prior to discharge. The patient was instructed to repeat a CXR after a week from discharge to monitor for effusion recurrence.

## 3. Discussion

The efficacy of BLVR has been widely studied throughout the years with an exponential increase in available data as BLVR has been more commonly used. A metanalysis has shown, after 12 months follow up from Zephyr valve placement, an increase in FEV1 up to 26 % in both homogenous and heterogeneous emphysema [10]. Xiao et al. have reported similar improvement in FEV1 (26 %) and a reduction in lung volume more than 350 ml [18]. Similar findings were reported by other metanalysis [2,19] which proved a statistical significant difference in lung functions and 6MWT. Similar data were illustrated by Kontogianni et al. along with an improvement in RV on PFT results [13]. The VENT and BeLieVer-HiFi studies documented a statistically significant improvement in FEV1 and 6MWT after EBV placement (Zephyr) [20]. The EMPROVE and the LIBERATE trial showed improvement in FEV1, 6MWT and quality of life with Zephyr and Spiration valve placement [21]. The safety profile of BLVR is also well reported in the literature. As the employment of BLVR has increased throughout the years, more complications have been highlighted, and experts have learned along the way to predict these incidents. We illustrate in our case, a simple pleural effusion occurring within a week from BLVR. This complication is sparsely reported in literature.

The complications secondary to BLVR are randomly listed: pneumothorax, hemoptysis, COPD exacerbation, post obstructive, valve dislocation, infection, respiratory failure, pleural effusion and death [6], [10], [13], [14], [15], [22]. There is one reported case of pulmonary edema occurring after EBV placement [23]. Granulation tissue formation is another potential outcome. According to Roodenburg et al., revision bronchoscopy was performed secondary to loss of initial treatment effect in 43 % of cases, similar to our patient, among which 53 % had granulation tissue causing valve dysfunction [24].

Pneumothorax is by far the most common complication occurring after BLVR and is reported to be as high as 26 % [13,15]. The risk is higher with decreased collateral ventilation, complete fissure, and successful atelectasis of the desired lobe [4,6]. Hypothetically, it results from the pulling of adjacent lobe by the atelectatic one, while trying to expand and fill the resultant void [22]. The highest

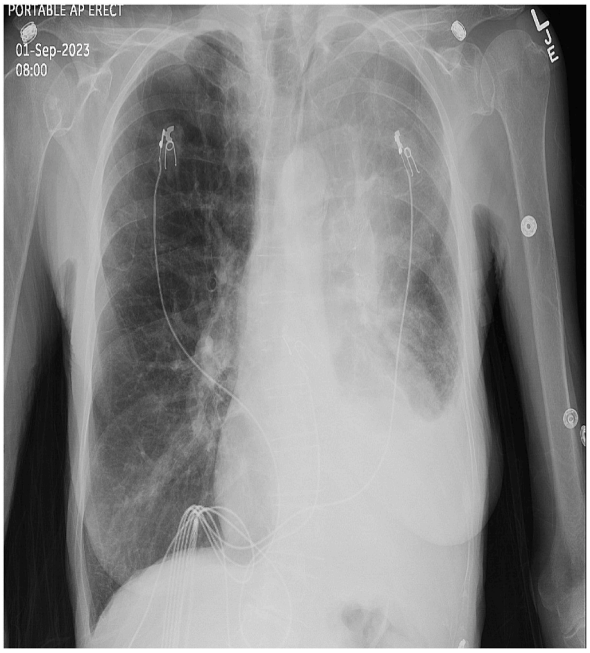


**Fig. 1.** Chest x-ray on admission showing moderate left pleural effusion with associated atelectasis.

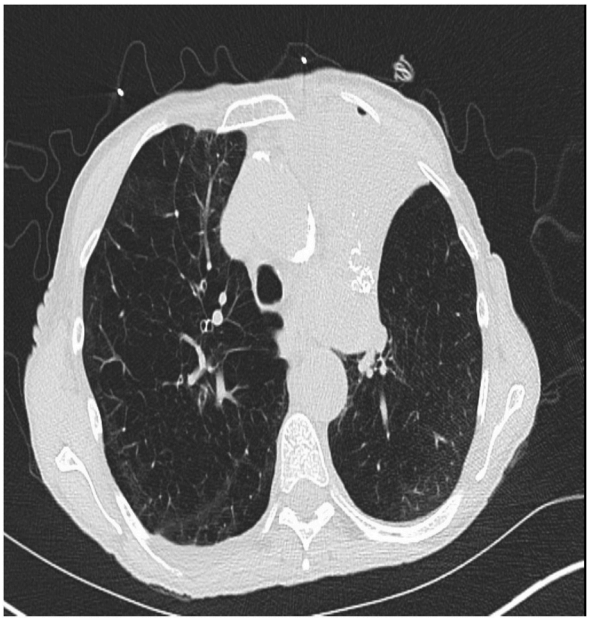

**Fig. 2.** Computed tomography of the chest showing left upper lobe endobronchial valves along with adjacent consolidation/atelectasis.

incidence of pneumothorax occurs within 3 days [13] and it gradually declines but persists up to 45 days [9]. Valve migration is reported in 24 % of the cases, and it mainly occurs in the lower lobes view their higher length [13].

COPD exacerbation with or without hospitalization is another reported complication. Some advocate the use of prophylactic steroid and antibiotic therapy as a preventative strategy, although there is no clear consensus [9,21].

The occurrence of pleural effusion secondary to BLVR is barely reported. Among 124 outlined patients post EBV placement, only one developed pleural effusion [22]. Another paper delineates the development of pleural effusion in one case, in a review of 98 patients post BLVR [25]. The increase in negative pleural pressure secondary to atelectasis is a potential cause of effusion in these cases. Ruling out other etiologies or infection is crucial, thus pleural fluid analysis is mandatory, however the best practice for the management of EBV related pleural effusion and whether a chest tube should be placed, remain uncertain due to its rarity.

## 4. Conclusion

Bronchoscopic lung volume reduction is an effective therapy to treat hyperinflation in symptomatic patients with emphysema. However, interventional pulmonologist should be aware of all its associated adverse events even the rare ones. Although uncommon, simple pleural effusions can occur and sometimes are hard to treat. View the rarity of pleural effusions associated with BLVR, identifying the population at risk, and outlining preventive measures remain challenging.

## CRediT authorship contribution statement

**Marc Assaad:** Writing – review & editing, Writing – original draft. **Wasif Shamsi:** Writing – review & editing, Supervision. **Anthony Loschner:** Writing – review & editing, Supervision. **Maria Del Mar Cirino-Marcano:** Writing – review & editing, Validation, Supervision, Resources, Conceptualization.

## Availability of data and materials

All used data is available within the manuscript.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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