Bronchoscopic Treatment of Emphysema

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KEYWORDS

• Advanced emphysema • Bronchoscopic lung volume reduction • Zephyr valve • Spiration valve

KEY POINTS

- Bronchoscopic lung volume reduction (BLVR) is a less invasive treatment option for patients with advanced emphysema and hyperinflation.
- Following intervention, patients can anticipate improved quality of life, exercise tolerance, survival, and potentially reduced exacerbation frequency.
- The most common complication of BLVR is pneumothorax, requiring inpatient admission for monitoring following the procedure.
- Pneumothorax risk can be reduced by anesthesia strategies.

BACKGROUND

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of death worldwide with an increasing prevalence.[1] COPD refers to a group of diseases that cause airway obstruction and breathing problems and includes bronchitis and emphysema. The changes seen in emphysema lead to impaired elastic recoil, dynamic hyperinflation, and compromised pulmonary mechanics that are associated with dyspnea and exercise limitations.[2]

The management of advanced emphysema involves medical and surgical interventions. Medications include inhaled therapies such as bronchodilators and inhaled steroids, oral therapies such as oral steroids, phosphodiesterase-4 inhibitors, and theophylline. Patients with moderate to severe COPD may also be prescribed supplemental oxygen or pulmonary rehabilitation. When symptoms persist despite these therapies more invasive options such as lung volume reduction surgery (LVRS), bronchoscopic lung volume reduction (BLVR), and lung transplantation are explored. Lung volume reduction therapy has emerged as a treatment option to address hyperinflation in advanced forms of emphysema. BLVR[3–6] and LVRS[7] are well-studied interventions and carefully selected patients can improve their lung function, quality of life, and increase exercise capacity through this therapy.

BRONCHOSCOPIC LUNG VOLUME REDUCTION PHYSIOLOGY

In advanced emphysema, impaired elastic recoil and parenchymal loss presents as hyperinflation and airway obstruction. To overcome the reduced elastic recoil, large intrathoracic pressure changes occur and these swings in pressure cause compression of the pulmonary vascular bed. In addition, the vascular bed reduction due to the parenchymal loss causes an increase in pulmonary vascular resistance, a driving force in the development of pulmonary hypertension in COPD.[8] The increased intrathoracic pressures also lead to a reduced venous return (cardiac preload) and smaller size of the right and left ventricles.[9,10] To assess whether BLVR improves cardiac preload or further reduces pulmonary vascular bed, cardiac MRI was performed at baseline and at 8-week postintervention. A cohort of 24 patients underwent

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Abbreviations	
AECOPD	acute exacerbations of COPD
BLVR	bronchoscopic lung volume reduction
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CV	collateral ventilation
CV−	CV-negative
CV+	CV-positive
EBV	endobronchial valve
FVC	forced vital capacity
LVRS	lung volume reduction surgery
SOC	standard of care
TLVR	target lobe volume reduction

BLVR with significant improvement in hyperinflation. At the 8-week follow-up, improvements in cardiac preload, myocardial contractility, and cardiac output (+0.9 L/min; SD, 1.5; P=.007) were noted, without changes in pulmonary artery pressures.[11]

The main effects of lung volume reduction are improved compliance via target lobe atelectasis and matching of lung size to chest wall size. These result in improved lung elastic recoil at similar thoracic inspiratory volume, better expiratory airflow, and reduced dynamic and static hyperinflation.[12] BLVR has well-established effects on forced expiratory volume (FEV1), vital capacity, total lung capacity, and residual volume, but predicting the impact on gas exchange is less certain, with some patients experiencing small improvements in diffusing capacity of the lungs for carbon monoxide (DLCO) even though there is a reduction in gas-exchange surface. Improved ventilation and perfusion of the ipsilateral and contralateral lung lobe(s) are probably responsible for the observed improvements in DLCO after successful lung volume reduction (LVR) treatment,[13] particularly in cases performed in heterogeneous emphysema.

BRONCHOSCOPIC LUNG VOLUME REDUCTION KEY STUDIES

BLVR studies were initially performed in patients with heterogeneous emphysema, similar to the NETT trial. Over time, the inclusion criteria have broadened and studies have included homogeneous disease, alpha-one antitrypsin deficiency, and individuals with lower FEV1 and DLCO. The criteria used in the trials have varied and lead to small differences in potential valve candidates for the 2 commercially available valves in the United States (**Table 1**).

The TRANSFORM trial[6] was a randomized, prospective, multicenter study conducted at 17 sites across Europe. It compared the effectiveness of Zephyr endobronchial valve (EBV) treatment with standard of care (SOC) in patients with severe heterogeneous emphysema and no collateral ventilation. A total of 97 subjects were enrolled and randomized in a 2:1 ratio to the EBV and SOC groups, respectively.

Three months after the procedure, 55.4% of the EBV group experienced an improvement of more than 12% in FEV1 from baseline, compared to just 6.5% in the SOC group. On average, the EBV group saw an increase of 140 mL (20.7%) in FEV1. The TRANSFORM study also showed statistically significant improvements in exercise capacity and quality of life for the Zephyr EBV group compared to the SOC group. In the EBV group, the 6-min walk distance improved by an average of 36.2 m, while the SOC group saw a decline of 42.5 m. Additionally, the EBV group had changes in the modified Medical Research Council (mMRC) and body-mass index, airflow obstruction, dyspnea, and exercise (BODE) index scores of −0.56 and −0.97, respectively.

Pneumothorax was the most common serious adverse event in the EBV group, occurring at a rate of 21.5%; however, this did not appear to negatively impact the overall clinical outcomes.

STELVIO[14] is a randomized controlled trial that evaluated the effectiveness of EBV in patients with severe heterogeneous emphysema and confirmed absence of collateral ventilation. A total of 68 subjects were randomly assigned to the EBV and SOC groups in a 1:1 ratio. The primary outcome measures were improvements from baseline to 6 months in FEV1, forced vital capacity (FVC), and 6-min walk distance in the EBV group compared to the control group.

Intention-to-treat analyses showed significantly greater improvements in the EBV group compared to the control group over 6 months. FEV1 increased by 140 mL more in the EBV group, FVC by 347 mL more, and the 6-min walk distance improved by an additional 74 m.

By 6 months, the EBV group reported 23 serious adverse events, compared to 5 in the control group. Serious treatment-related adverse events in the EBV group included pneumothorax (18% of patients) and events requiring valve replacement (12%) or removal (15%).

The VENT trial[15] is a randomized, prospective, multicenter study that evaluated the efficacy and safety of Zephyr EBV in patients with advanced emphysema compared to standard care. A total of 321 patients from 31 centers across the United States were enrolled in a 2:1 ratio into the EBV and SOC groups, respectively.

Table 1
Criteria for valve candidacy

	Zephyr	Spiration
Homogenous emphysema	Yes	No
Heterogeneous emphysema	Yes	Yes
Alpha-one antitrypsin deficiency	No	Yes
BMI	<35	<35
Stable on prednisone dose	<20	<15
FEV1	15%–45%	<45%
Residual volume	>175% >200 (if homogeneous)	>150%
Total lung capacity	>100%	>100%
6-min walk distance	100–500 m 150–500 m (if homogeneous)	>140 m
Quit smoking	> 4 mo ago	>4 mo ago
Fissure integrity	>80% and no CV by Chartis	>90%

The coprimary effectiveness endpoints were the percent change in FEV1 and the distance on the 6-min walk test in the EBV group compared to the control group, measured 6 months after randomization. In the EBV group, the confidence interval (CI) ranged from 1.4 to 7.2, representing an absolute increase of 1.0% point (95% CI, 0.2–1.8) of the predicted value. In contrast, the control group saw a decrease of 2.5% (95% CI, −5.4–0.4), equivalent to a drop of 0.9% points (95% CI, −1.7 to −0.1) in the percent of the predicted value. Consequently, the mean between-group difference in FEV1 was 6.8% (95% CI, 2.1–11.5; *P*=.005).

At 6 months, the distance covered in the 6-min walk test increased by 2.5% (95% CI, −1.1–6.1) in the EBV group and decreased by 3.2% (95% CI, −8.9–2.4) in the control group, resulting in a mean between-group difference of 5.8% (95% CI, 0.5–11.2; *P*=.04). This corresponded to an increase of 9.3 m (95% CI, −0.5–19.1) in the EBV group compared to a decrease of 10.7 m (95% CI, −29.6–8.1) in the control group (*P*=.02).

Post hoc analysis showed that patients in the EBV group with complete fissures had incremental improvements in FEV1 of 16.2% at 6 months and 17.9% at 12 months (*P*<.001 for both comparisons), compared to insignificant changes of 2.0% and 2.8%, respectively, in those with incomplete fissures. However, the between-group differences in the 6-min walk test were not significant at either 6 or 12 months in either group.

In the EBV group, the volume of the adjacent nontargeted lobes expanded compared to the control group, with this effect being more pronounced in patients with complete fissures. Although the overall effect of EBV was modest, patients with high values for disease heterogeneity and fissure integrity on CT imaging were more likely to have a clinically significant response.

The study titled "Radiological and clinical outcomes of using ChartisTM to plan endobronchial valve treatment"[16] was a nonrandomized, multicenter, prospective study conducted at 5 clinical sites across 3 countries in Europe. The study aimed to investigate whether Chartis assessment of collateral ventilation (CV) could predict significant target lobe volume reduction (TLVR) following EBV placement.

Among the 80 patients who received Zephyr EBV and underwent CV assessment with the Chartis system, 51 were classified as CV-negative (CV-) and 29 as CV-positive (CV+). The CV-all group achieved a median TLVR of 752.7 mL, surpassing the threshold previously identified for significant clinical improvement (350 mL). In contrast, the CV + all group achieved a TLVR of 98.6 mL, falling short of this threshold. A significant difference in TLVR was observed between the 2 groups. Chartis demonstrated positive predictive and negative predictive values of 71% and 83%, respectively, resulting in an overall accuracy rate of 75%.

The IMPACT study[3] was a randomized, prospective, multicenter trial that compared EBV plus SOC to SOC alone. The primary outcome measured the percentage change in FEV1 at 3 months relative to baseline in the EBV group versus the SOC group. A total of 93 subjects with heterogeneous emphysema and no collateral ventilation (CV-negative) in the primary or secondary target lobe were randomized in a 1:1 ratio, with 50 subjects in the SOC group and 43 subjects in the EBV group.

At 3 months postprocedure, there was an average improvement from baseline in FEV1 of 13.7% in the EBV group, while the SOC group experienced a decline of 3.2%, resulting in a mean between-groups difference of 17.0%. The study demonstrated statistically and clinically significant improvements in lung function, exercise capacity, and quality of life associated with EBV therapy compared to usual SOC.

PROCEDURE OVERVIEW

Two different types of valves—EBV (Zephyr, Pulmonx Corp., Redwood City, CA, USA) and intrabronchial valves (IBV, Spiration, Olympus, Tokyo, Japan)—are approved for bronchoscopic lung volume reduction, and they differ in shape but have a similar mechanism of action. The eligibility criteria were determined by the clinical trials outline above. The Spiration Valve (Fig. 1) is an umbrella-shaped self-expanding device with a Nitinol (nickel-titanium) frame with 5 distal anchors and a polyurethane membrane held by 6 proximal struts. The membrane is apposed to the bronchial wall, thereby allowing the unidirectional valve to block air from traveling distally, while allowing secretions and air to drain.[17] The Zephyr EBV (Fig. 2) is a silicone-based, 1-way valve affixed in a self-expanding nitinol retainer. The retainer stabilizes the valve in the airway and provides an airtight seal against the bronchial wall.[17] The spiration valve is available in a 5 mm, 6 mm, 7 mm, and 9 mm valve. The Zephry valve is available in a 4.0 EBV, 4.0-LP EBV, 5.5 EBV, and 5.5-LP EBV. The low-profile sizes are for deployment in shorter airways.

Each valve uses similar steps for placement. The procedure is typically performed via a flexible bronchoscopy using a bronchoscope with a working channel 2.6 mm or greater. After analysis for fissural integrity, via imaging or Chartis (Figs. 3 and 4), sequential sizing of the airway and valve deployment in the target lobe occurs. The procedure duration is typically less than 1 hour. The spiration valve is sized with the accompanying sizing balloon and calibration kit to determine which size valve to deploy. The appropriately sized valve is loaded into the catheter and then deployed under direct (bronchoscopic) visualization. The Zephyr valve is sized using a catheter that measures depth and diameter. The endobronchial delivery catheter is used for sizing and placement and the catheter size is equivalent to the valve size. The catheter is available in a *J* configuration to improve access to angulated airways.

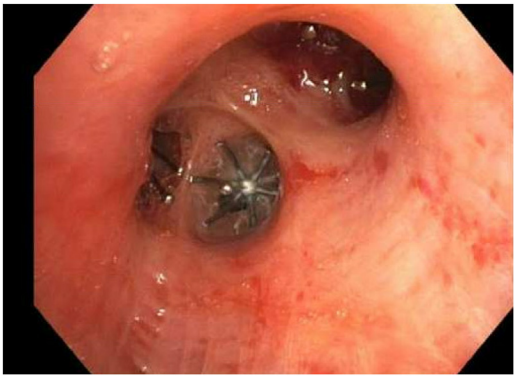

Fig. 1. Spiration valves with umbrella-like shape in the right upper lobe.

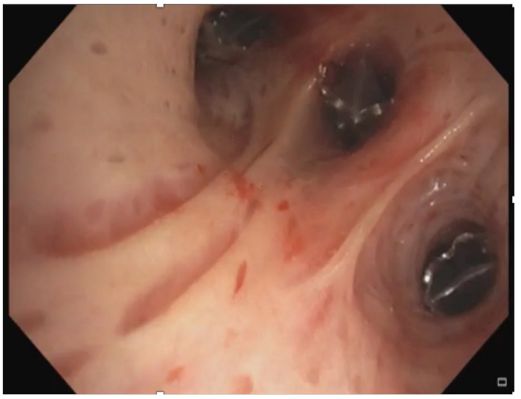

Fig. 2. Zephyr valves with duckbill-like shape in the left upper lobe.

ANESTHESIA APPROACH

BLVR may be performed using general anesthesia with an endotracheal tube or laryngeal mask airway or be performed in the spontaneously breathing patient under moderate sedation with airway topicalization using monitored anesthesia care.[18] Procedures performed using an endotracheal tube may be shorter, related to patient tolerance, and for the proceduralist provides increased ease of collateral ventilation assessment, valve sizing, and placement. In 1 study,[19] the average procedure duration was similar between the monitored anesthesia care (MAC) (24.90 min) and general anesthesia (GA) via ETT (20.70 min) group, but the total anesthetic time was much longer for the MAC group (61 min vs 37 min). An additional benefit of performing the procedure using total intravenous anesthesia and an endotracheal tube is improving the speed and accuracy of the Chartis assessment. This is particularly important given the low ventilation rates of 8 to 10/min and prolonged expiration (I/E ratio 1:3–1:4) seen intraprocedurally.

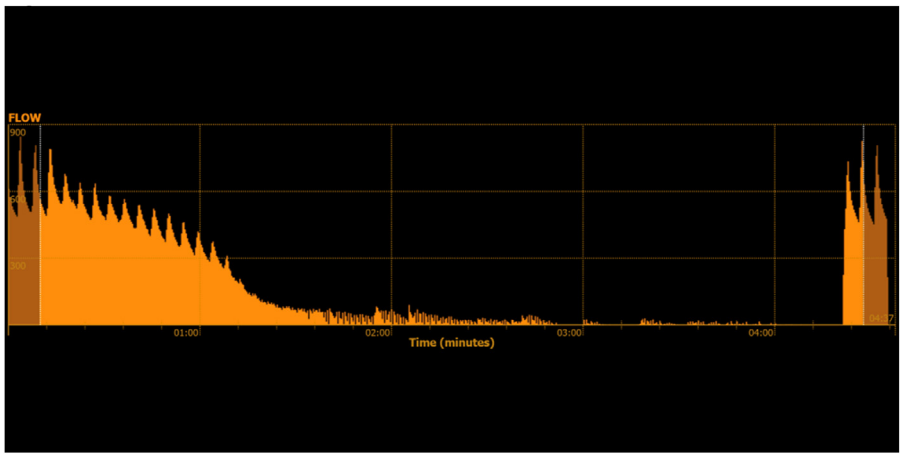

Fig. 3. Absence of collateral ventilation.

The intraoperative management of mechanical ventilation via an artificial airway may also be used to minimize postprocedural complications. Based on the hypothesis that a low intraprocedural fraction of inspired oxygen (Fio_2) might slow absorption atelectasis by preventing nitrogen washout of the treated lung and reduce the incidence of pneumothorax, 2 institutions adopted a low Fio_2 protocol.[20] Before protocol development, Fio_2 was per anesthesia preference, usually 1.0. Under protocolized low Fio_2, inspired oxygen was reduced to the lowest possible concentration needed to maintain and oxygen saturation of greater than 89%. Valves were not placed until exhaled O2 concentration approximated Fio_2, suggesting adequate alveolar partial pressure of oxygen equilibration with delivered low inspired oxygen. Minimized Fio_2 during BLVR procedures to the minimal concentration tolerated was associated with marked reduction in the incidence of postprocedural pneumothorax, from an incidence of 31% of cases in high Fio_2 to 7% in the protocolized low Fio_2. Pneumothoraces occurred later in the low group, likely due to pleural tears as atelectasis progresses.

BRONCHOSCOPIC LUNG VOLUME REDUCTION BENEFITS

Improvements in quality of life, lung function, and exercise capacity have been noted by various randomized controlled trials. More recent data has suggested that BLVR has an impact on exacerbation frequency, cardiac hemodynamic, and survival.

Hartman and colleagues developed a study to explore survival benefit.[21] The study goal was to investigate survival rates among patients evaluated for BLVR treatment and to compare the survival outcomes between those who underwent BLVR treatment and those who did not. A total of 1471 patients were included in the study, with 483 patients (33%) undergoing BLVR treatment. Patients treated with BLVR had a significantly longer median survival time compared to those not treated with BLVR (3133 days (95% CI 2777–3489) versus 2503 days (95%CI 2281–2725), $P<.001$), reflecting a difference of 630 days, approximately equivalent to 1.7 years. Additionally, undergoing BLVR treatment independently predicted survival when adjusted for other factors

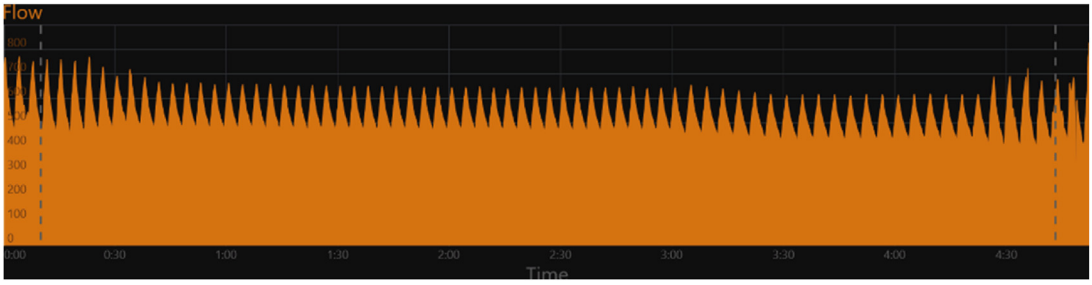

Fig. 4. Presence of collateral ventilation.

influencing survival such as age, gender, and disease severity.

In a study of 129 patients undergoing BLVR, a reduction in exacerbation was noted with the largest decrease noted in those with complete lobar atelectasis.[22] Patients experienced a mean of 2.5 ± 2.2 moderate and severe exacerbations in the year before BLVR. The number of exacerbations decreased significantly to 1.8 ± 2.2 exacerbations in the first year after intervention (P=.009). The decrease in exacerbation rate was associated with the development of complete lobar atelectasis, from 2.8 ± 2.0 to 1.4 ± 1.8 exacerbations (P<.001).

In a smaller study of only 24 patients,[23] improvement in cardiac function was also noted. In this study, cardiac magnetic resonance imaging was obtained 1 day before treatment and at 8-week follow-up. At follow-up imaging, right ventricle end-diastolic volume index was significantly improved (+7.9 mL/m^2; SD, 10.0; P = .001). Patients also had significantly higher ejection fractions and strain measurements. Although cardiac output was significantly increased (+0.9 L/min; SD, 1.5; P = .007), there were no changes in pulmonary artery pressures demonstrating that BLVR could improve cardiac preload, myocardial contractility, and cardiac output without changing pulmonary pressures.

BRONCHOSCOPIC LUNG VOLUME REDUCTION COMPLICATIONS

BLVR is a valuable new option in the treatment of patients with advanced emphysema. Despite careful patient selection, following the procedure individuals are at risk of complications including pneumothorax, exacerbation of COPD, postobstructive pneumonia, and hemoptysis as well as failure to achieve TLVR. After valve treatment, it is recommended to monitor the patient for clinical, radiological, and lung functional improvement (or deterioration). Valve revision should be considered if there is no improvement after initial treatment, or if there is loss of the initially observed benefit during the follow-up.

Acute exacerbations of COPD (AECOPD) are common following BLVR and the practices of prescribing prophylactic corticosteroids or antibiotics is variable and often center specific. Though small, a 6-center retrospective review evaluated the management of 170 patients who underwent BLVR.[24] The rate of exacerbations was 21.2% for the full cohort. Prophylaxis was antibiotics, steroids, antibiotics plus steroids, or no prophylaxis. Patients who received prophylaxis had a significantly lower rate of AECOPD compared with those who did not (16.7% vs 46.2%; P=.001). The rate was lowest in patients who received antibiotics alone (9.2%). The antibiotics prescribed included levofloxacin, azithromycin, ceftriaxone, or a beta lactam.

After treatment with valves, TLVR occurs (Fig. 5). Part of this volume reduction is compensated for by the expansion of the untreated ipsilateral lobe and as the volume loss occurs, the negative pressure drop may cause rupture of bullae or blebs in the expanding lung tissue.[25] Symptomatic pneumothoraces require intervention with the placement of a tube thoracostomy. Not all pneumothoraces require intervention as pneumothorax ex vacuo is another presentation seen due to TLVR but is not associated with an air leak and does not require drainage. A *wait-and-see* approach is recommended in these cases as the pneumothorax will slowly resolve.

Pneumothorax is the most common complication of BLVR and whether to proceed with tube thoracostomy, to remove a valve, or remove all of the valves is guided by expert consensus. The greatest risk of this complication is in patients in whom the second-best target was chosen and the emphysema destruction in the contralateral lung was greater than 60% (measured at −910 Hounsfield Units), the patient would be at a higher risk of death or require removal of all valves.[5] In symptomatic pneumothorax, a chest drain is recommended without the use of wall suction. In the unstable patient, suction should be used and early removal of 1 to 2 valves considered. In stable patients with no air leak, the chest tube can be removed when lung expansion is noted or if partial expansion and stable. In stable patients with an air leak after 3 days or with incomplete lung expansion despite tube placement, suction should be considered and 1 to 2 valves removed.[26] If the leak resolves, the chest tube can be removed and replacement of the removed valves can be considered 5 to 6 weeks postprocedure. If the leak persists, chest computed tomography (CT) should be performed to identify potential etiologies of the leak and a Heimlich may be placed for discharge or additional valves may be removed.

Additional complications are related to the valves themselves and include valve migration, incomplete airway occlusion, granulation tissue, and hemoptysis related to the placement of the valves or to the development of granulation tissue.[25] When these complications occur, this can lead to the loss of target lobe volume loss. Granulation tissue is a common cause for loss of effect requiring revision bronchoscopy. In a prospective analysis of patients undergoing BLVR in one center, 74 (41%) patients underwent at least one revision bronchoscopy for an indication related to the

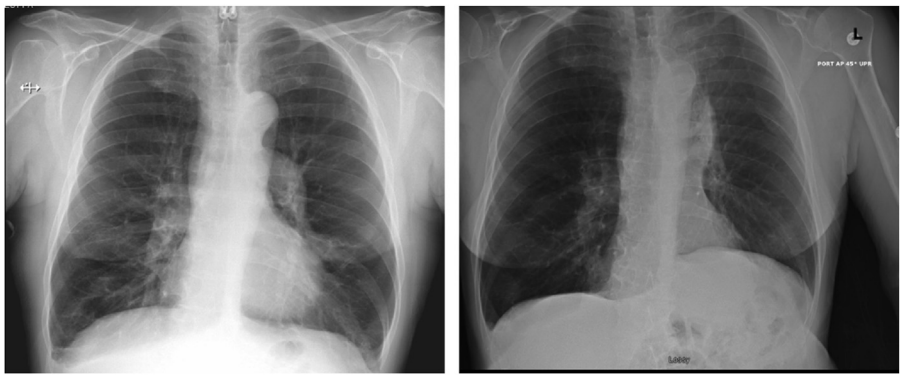

Fig. 5. Pre-procedure chest x-ray versus post-procedure chest x-ray with volume loss and elevated hemidiaphragm.

valves. A second revision bronchoscopy was indicated in 24 patients and a third revision bronchoscopy in 6 patients. Revision bronchoscopy was performed for the lack of desire effect or for the loss of an initial effect.[27] Granulation tissue causing valve dislocation or air leakage was noted in 53% of patients. In 63% of the patients, the revision bronchoscopy led to an improvement in FEV1 and in 64% there was a reduction in the RV.

BRONCHOSCOPIC LUNG VOLUME REDUCTION IN MARGINAL CANDIDATES

BLVR can achieve a significant increase in lung function, exercise capacity, and quality of life and a decrease in hyperinflation and dyspnea on exertion. The impact in patients with low FEV1 (<20%), low DLCO (<20%), and group 3 pulmonary hypertension is less clear as a limited number of patients meeting these criteria were included in the existing clinical trials.

In the NETT trial, patients with an FEV1 lesser than 20% undergoing LVRS had increased mortality and as a result, few patients with very severe airway obstruction were included in the studies of BLVR. In a small study published in 2016, they evaluated the safety and outcomes of procedures performed in patients with an FEV1 lesser than 20% and FEV1 greater than 20%.[28] Twenty patients with FEV 1 $\leq$ 20% predicted underwent valve placement. Complete or partial atelectasis was achieved in 65% of the cases. Pneumothorax occurred in 4 cases (20%), a rate similar to patients with a higher FEV1. Both lung function and exercise tolerance were improved at 1 and 3 months.

Based on the NETT trial, patients with low DLCO (<20%), were also excluded from clinical trials on BLVR. Recognizing the limited data in the area, van Dijk and colleagues evaluated the impact of BLVR in 20 patients with a diffusion capacity less than 20%.[29] There were no other significant differences between the low diffusion capacity and control group. The most common serious adverse event was pneumothorax, occurring in 15% of patients. They also demonstrated statistically significant and clinically relevant improvements in lung function, exercise capacity, and quality of life in the low DLCO group compared to the control group and these similarities were seen up to the 6-month follow-up period.

Patients with severe COPD often have concomitant low FEV1 and low DLCO and whether bronchoscopic lung volume reduction is safe, feasible, and yields clinically meaningful benefit was evaluated via a retrospective cohort in Germany.[30] In 20 patients, there was an overall improvement in lung function with an increase in FEV1, a decrease in residual volume, total lung capacity, and 6-min walk distance, with greatest improvement in walk distance seen with complete lobar atelectasis. There was not significant increase in complications but pneumothorax with air leak was more likely to be prolonged in this group.

Another group frequently excluding from clinical trials are those patients with established pulmonary hypertension. A small feasibility study of 6 patients with group 3 pulmonary hypertension evaluated the safety and clinical impact of BLVR in patients with severe heterogeneous emphysema.[31] Lung volume reduction was documented radiologically in 5 patients. At 90-day follow-up, an improvement was seen in mean pulmonary arterial pressure, wedge pressure, cardiac index, and 6-min walk distance. There were no pulmonary hypertension related complications.

BLVR is intended for patients with hyperinflation and symptoms despite optimal medical therapy and conditioning via pulmonary rehabilitation and is of utmost importance in marginal candidates. The small number of pulmonary rehabilitation

centers is insufficient to meet the need and are often inaccessible to those in rural areas. Home pulmonary rehabilitation and telerehabilitation are options that increase access but whether the home-based options perform at the same level is an area of concern. In candidates with marginal walk distances, hospital-based pulmonary rehabilitation should be encouraged, based on data from a prospective study by Pehlivan and colleagues.[32] In their study of 67 patients, home-based and hospital-based pulmonary rehabilitation provided significant and similar improvements in the mMRC and CAT scores but 6MWD was only significantly increased in the hospital-based programs.

BRONCHOSCOPIC LUNG VOLUME REDUCTION STAGED AND BILATERAL PROCEDURES

To minimize the risk of pneumothorax, a 2-step valve-implantation in staged procedures was hypothesized to allow for progressive TLVR and ipsilateral lung expansion.[33] In the staged protocol, during the first procedure, valves were placed in all but the most proximal segment or subsegment (1 segment or subsegment left untreated in both right middle lobe (RML) and right upper lobe (RUL) lobe for RUL/RML treatments). Four weeks later, patients underwent a second procedure with valve-implantation in the remaining segment(s) or subsegment(s). In the 58 patients, only 4 pneumothoraxes (7%) occurred. Two pneumothoraces occurred after the first procedure. One patient was treated for RUL and RML resulting in complete atelectasis of the RML and a 31% TLVR of the RUL. In the other case, valves were implanted in the RUL resulting in its complete atelectasis. Two patients suffered from pneumothorax immediately after the second procedure. There was similar radiological and pulmonary function improvement as well as symptom improvement when compared to the conventional single-step procedure.

The functional improvement obtained with unilateral BLVR may progressively decline to the pre-BLVR level and whether bilateral procedures yield the same benefit as bilateral LVRS was a question to be answered once the safety and efficacy of conventional BLVR was known. Via retrospective analysis, a total of 49 patients were evaluated.[34] In this cohort, 14 (28%) received a repeated BLVR after a median interval of 18 months from the initial procedure. Significant improvements in FEV1 ($P<.05$), FVC ($P<.05$), RV($P<.05$), 6-min walking test ($P<.05$), and St. George respiratory questionnaire ($P<.02$) were achieved after the second procedure demonstrating efficacy in improving pulmonary function in patients with emphysema who have lost the benefit from their first procedure.

BRONCHOSCOPIC LUNG VOLUME REDUCTION AS A BRIDGE TO LUNG TRANSPLANT OR LUNG VOLUME REDUCTION SURGERY

Lung transplantation and surgical LVRS are both well-studied interventions for individuals with end-stage COPD with strict criteria to qualify for each intervention. In patients who qualify for lung volume reduction, the selection of BLVR over LVRS is related to concerns that LVRS leads to increased pleural adhesions and an increased surgical time and bleeding risk at the time of lung transplantation. While not statistically significant in the analysis performed by Backhus and colleagues,[35] the impact of prior LVRS on the development of adhesions and the difficulty of explant should be considered, particularly in individuals who are also candidates for BLVR.

BLVR is a successful tool to bridge potential transplant candidates. Lung transplantation for end-stage COPD is often associated with a longer period of time on the transplant waitlist and the 5-year survival after transplantation for COPD is only 70.4%,[36] BLVR can be used as a bridge to delay transplant evaluation and listing. A concern with this strategy is that this potentially leads to older transplant recipients with increased comorbidities undergoing lung transplantation. A recent European cohort evaluated the outcomes of 82 patients undergoing lung transplant for COPD. 28 of the 82 patients had undergone prior BLVR.[37] The BLVR patients spent comparable time on the waitlist; however, they were older at the time of transplant. Both groups showed comparable 90-day (92%) and long-term survival (BLVR 1-/5-/10-year survival: 92/88/77%, vs control: 89/77/67%, $P=.5$). The odds for postoperative pulmonary complications were similar in both groups. This adds to the growing data to support the use of BLVR as a bridge to lung transplant without an increase in complications or reduced posttransplant survival.

Whether LVRS can be used in patients who failed to achieve atelectasis after their procedure (primary failure) or in patients who have declining benefit after BLVR (secondary failure) has been evaluated in small cohort studies. One such cohort of 38 patients evaluated 19 patients who had primary failure, 15 secondary failure, and 4 were treated as an emergency due to severe air leak after BLVR.[38] Primary failure was defined as no improvement at 3 months and despite valve

revision in cases without lobar atelectasis. Secondary failure was the loss of subjective or objective improvement after initial gains. 3 patients had loss of effect despite persistent atelectasis after initially successful treatment, and 12 patients had both loss of effect and atelectasis. At 3 months post-LVRS, there was a significant improvement in FEV1 but considering subgroups, patients with primary failure after BLVR seem to profit more than those with secondary failure and how to manage the existing valves in those with secondary failure remains unclear.

BRONCHOSCOPIC LUNG VOLUME REDUCTION SUMMARY

BLVR is an option for patients with advanced emphysema with hyperinflation when symptomatic on maximal medical therapy including inhaled therapies, oxygen as indicated, and conditioned with pulmonary rehabilitation. The procedure is complicated by pneumothoraces requiring close observation as an inpatient following the procedure. This risk can be reduced by close attention to procedural technique. Patients experience improved exercise tolerance, survival, and potentially a reduced frequency of exacerbations. Patients undergoing BLVR may be successfully bridged to lung transplantation or LVRS when procedural impact wanes but BLVR postpones or prevents the need for these invasive procedures.

CLINICS CARE POINTS

- Bronchoscopic lung volume reduction (BLVR) is a minimally invasive therapeutic intervention for patients with advanced emphysema.
- Following BLVR, patients can expect an improved quality of life and survival.
- Patients should be counseled on the pneumothorax risk.
- The proceduralist should know procedural techniques to reduce the risk and how to manage complications when they occur.

DISCLOSURES

Dr M. Irandost has nothing to disclose. Dr L.K. Frye is a consultant for Olympus.

REFERENCES

1. Stolz D, Mkorombindo T, Schumann DM, et al. Towards the elimination of chronic obstructive pulmonary disease: a Lancet Commission. Lancet 2022; 400(10356):921–72.
2. Agustí A, Hogg JC. Update on the pathogenesis of chronic obstructive pulmonary disease. N Engl J Med 2019;381(13):1248–56.
3. Valipour A, Slebos DJ, Herth F, et al. Endobronchial valve therapy in patients with homogeneous emphysema. Results from the IMPACT study. Am J Respir Crit Care Med 2016;194(9):1073–82.
4. Criner GJ, Delage A, Voelker K, et al. Improving lung function in severe heterogenous emphysema with the spiration valve system (EMPROVE). A multicenter, open-label randomized controlled clinical trial. Am J Respir Crit Care Med 2019;200(11):1354–62.
5. Criner GJ, Sue R, Wright S, et al. A multicenter randomized controlled trial of Zephyr endobronchial valve treatment in heterogeneous emphysema (LIBERATE). Am J Respir Crit Care Med 2018;198(9):1151–64.
6. Kemp SV, Slebos DJ, Kirk A, et al. A multicenter randomized controlled trial of Zephyr endobronchial valve treatment in heterogeneous emphysema (TRANSFORM). Am J Respir Crit Care Med 2017;196(12):1535–43.
7. Fishman A, Martinez F, Naunheim K, et al. A randomized trial comparing lung volume-reduction surgery with medical therapy for severe emphysema. N Engl J Med 2003;348(21):2059–73.
8. Seeger W, Adir Y, Barber JA, et al. Pulmonary hypertension in chronic lung diseases. J Am Coll Cardiol 2013;62(25 Suppl):D109–16.
9. Nakhjavan FK, Palmer WH, McGregor M. Influence of respiration on venous return in pulmonary emphysema. Circulation 1966;33:8–16.
10. Watz H, Waschki B, Meyer T, et al. Decreasing cardiac chamber sizes and associated heart dysfunction in COPD: role of hyperinflation. Chest 2010; 138:32–8.
11. van der Molen MC, Hartman JE, Vanfleteren LE, et al. Reduction of lung hyperinflation improves cardiac preload, contractility, and output in emphysema: a clinical trial in patients who received endobronchial valves. Am J Respir Crit Care Med 2022;206(6):704–11.
12. Fessler HE, Scharf SM, Ingenito EP, et al. Physiologic basis for improved pulmonary function after lung volume reduction. Proc Am Thorac Soc 2008; 5:416–20.
13. van Dijk M, Klooster K, Ten Hacken NHT, et al. The effects of lung volume reduction treatment on diffusing capacity and gas exchange. Eur Respir Rev 2020; 29(158):190171.
14. Klooster K, Hacken N, et al. Endobronchial valves for emphysema without interlobar collateral ventilation. N Engl J Med 2015;373:2325–35.
15. Sciurba F, Ernst A, et al. A randomized study of endobronchial valves for advanced emphysema. N Engl J Med 2010;363:1233–44.
16. Herth F, Eberhardt R, et al. Radiological and clinical outcomes of using ChartisTM to plan endobronchial valve treatment. Eur Respir J 2013;41:302–8.

17. Toth JW, Reed MF. Endobronchial valves. In: Goldfarb S, Piccione J, editors. Diagnostic and interventional bronchoscopy in children. Respiratory medicine. Cham: Humana; 2021.
18. Slebos DJ, Shah PL, Herth FJ, Valipour A. Endobronchial valves for endoscopic lung volume reduction: best practice recommendations from expert panel on endoscopic lung volume reduction. Respiration 2017;93(2):138–50.
19. Thiruvenkatarajan V, et al. Anaesthetic management for endobronchial valve insertion: lessons learned from a single centre retrospective series and a literature review. BMC Anesthesiol 2018;18:1–8.
20. Lentz RJ, Low SW, Saettele T, et al. Association between inspired oxygen fraction and pneumothorax after endobronchial valve placement for emphysema. Annals of the American Thoracic Society 2023;20(6):926–9.
21. Hartman J, Welling J, et al. Survival in COPD patients treated with bronchoscopic lung volume reduction. Respir Med 2022;196:106825.
22. Brock JM, Böhmker F, Schuster PU, et al. Endobronchial lung volume reduction with valves reduces exacerbations in severe emphysema patients. Respir Med 2023;218:107399.
23. van der Molen MC, Hartman JE, Vanfleteren LEGW, et al. Reduction of lung hyperinflation improves cardiac preload, contractility, and output in emphysema: a clinical trial in patients who received endobronchial valves. Am J Respir Crit Care Med 2022;206(6):704–11.
24. Abia-Trujillo D, Yu Lee-Mateus A, Garcia-Saucedo JC, et al. Prevention of acute exacerbation of chronic obstructive pulmonary disease after bronchoscopic lung volume reduction with endobronchial valves. Clin Respir J 2022;16(1):43–8.
25. Koster TD, Klooster K, Ten Hacken NH, van Dijk M, Slebos DJ. Endobronchial valve therapy for severe emphysema: an overview of valve-related complications and its management. Expet Rev Respir Med 2020;14(12):1235–47.
26. van Dijk M, Sue R, Criner GJ, et al. Expert statement: pneumothorax associated with one-way valve therapy for emphysema: 2020 update. Respiration 2021;100(10):969–78.
27. Roodenburg SA, Klooster K, Hartman JE, et al. Revision bronchoscopy after endobronchial valve treatment for emphysema: indications, findings and outcomes. Int J Chronic Obstr Pulm Dis 2021;21:1127–36.
28. Darwiche K, Karpf-Wissel R, Eisenmann S, et al. Bronchoscopic lung volume reduction with endobronchial valves in low-FEV1 patients. Respiration 2016;92(6):414–9.
29. van Dijk M, Hartman JE, Klooster K, et al. Endobronchial valve treatment in emphysema patients with a very low DLCO. Respiration 2020;99(2):163–70.
30. Trudzinski FC, Höink AJ, Leppert D, et al. Endoscopic lung volume reduction using endobronchial valves in patients with severe emphysema and very low FEV1. Respiration 2016;92(4):258–65.
31. Eberhardt R, Gerovasili V, Kontogianni K, et al. Endoscopic lung volume reduction with endobronchial valves in patients with severe emphysema and established pulmonary hypertension. Respiration 2015;89(1):41–8.
32. Pehlivan E, Yazar E, Balcı A, et al. A comparative study of the effectiveness of hospital-based versus home-based pulmonary rehabilitation in candidates for bronchoscopic lung volume reduction. Heart Lung 2020;49(6):959–64.
33. Egenod T, Tricard J, Fumat R, et al. Two-stage bronchoscopic endobronchial valve treatment can lead to progressive lung volume reduction and may decrease pneumothorax risk. Int J Chronic Obstr Pulm Dis 2021;28:1957–65.
34. Fiorelli A, D'Andrilli A, Anile M, et al. Sequential bilateral bronchoscopic lung volume reduction with one-way valves for heterogeneous emphysema. Ann Thorac Surg 2016;102(1):287–94.
35. Backhus L, Sargent J, Cheng A, et al. Outcomes in lung transplantation after previous lung volume reduction surgery in a contemporary cohort. J Thorac Cardiovasc Surg 2014;147(5):1678–83.e1.
36. Verleden GM, Gottlieb J. Lung transplantation for COPD/pulmonary emphysema. Eur Respir Rev 2023;32(167):220116.
37. Kornyeva A, Semmelmann A, Ogutur ED, et al. Endoscopic lung volume reduction prior to lung transplantation does not increase postoperative pulmonary complications. Respiration 2023;102(12):978–85.
38. Caviezel C, Guglielmetti LC, Ladan M, et al. Lung volume reduction surgery as salvage procedure after previous use of endobronchial valves. Interact Cardiovasc Thorac Surg 2021;32(2):263–9.