Lung volume reduction: surgery *versus* endobronchial valves

Laurens J. Ceulemans[1,2], Dorina Esendagli[3], Giuseppe Cardillo[4,5] and Marcello Migliore[6,7]

[1]Department of Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium. [2]Department of Chronic Diseases and Metabolism Laboratory of Pneumology and Thoracic Surgery (BREATHE), KU Leuven, Leuven, Belgium. [3]Department of Chest Diseases, Baskent University Hospital, Ankara, Turkey. [4]Department of Thoracic Surgery, San Camillo-Forlanini Hospital, Rome, Italy. [5]UniCamillus, University of Health Sciences, Rome, Italy. [6]Program of Minimally Invasive Thoracic Surgery and New Technologies, Policlinic Hospital, Department of Surgery and Medical Specialties, University of Catania, Catania, Italy. [7]Thoracic Surgery and Lung Transplantation, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.

Corresponding author: Marcello Migliore (mmiglior@hotmail.com)

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Lung volume reduction (LVR): surgery or valves? A discussion of the pros and cons of surgery and endobronchial valves as the most used strategies for LVR https://bit.ly/4gZdwzE

Cite this article as: Ceulemans LJ, Esendagli D, Cardillo G, *et al*. Lung volume reduction: surgery *versus* endobronchial valves. *Breathe* 2024; 20: 240107 [DOI: 10.1183/20734735.0107-2024].

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Received: 28 May 2024
Accepted: 3 Oct 2024

Abstract

Volume reduction is a disease-modifying treatment that aims to reshape the diseased lung towards a more normal total lung capacity by removing severely damaged and overinflated lung parenchyma. It is an effective therapeutic strategy in well-selected patients, resulting in improvements in exercise tolerance, lung function, quality of life and survival. The most widespread strategies for volume reduction are either video-assisted thoracoscopic surgery or bronchoscopic lung volume reduction. It is crucial to decide which approach would be more suitable for specific patients, as this is related to the outcome of the procedure. Factors like emphysema distribution on computed tomography, the presence or absence of collateral ventilation, the patient's pulmonary function tests, a history of other comorbidities and previous interventions might all influence the choice of procedure. It is crucial that this decision is taken by a multidisciplinary expert team to have the best outcome and fewer complications.

Educational aims

- To discuss the pros and cons of surgery and endobronchial valves as the most commonly used strategies for lung volume reduction.
- To compare the surgical and endobronchial procedures.

Introduction

COPD is one of the most debilitating lung conditions and is the third leading cause of death worldwide [1]. It is the result of a complex inflammatory reaction and affects both (small) airways and lung parenchyma. The destructive process suffered by the lung alveoli is called emphysema and results in loss of elastic recoil and limits the area available for gas exchange. As a result, the small airways collapse [2], causing chronic irreversible airflow limitation, air entrapment and lung hyperinflation.

This constant state of hyperinflation causes disabling symptoms such as increased dyspnoea, increased work of breathing, restricted exercise tolerance, frequent exacerbations and poor quality of life, resulting in early death [3]. Medical treatment may delay progression and temporarily alleviate the symptoms but cannot reverse the underlying pathophysiology of the disease, or the damage to the parenchyma, so that many patients remain severely symptomatic and evolve towards end-stage emphysema.

Lung volume reduction surgery (LVRS) is one of the few therapies directly targeting hyperinflation in emphysema patients by addressing the excess residual volume [4]. However, due to initial poor selection criteria at the turn of the millennium, it has been one of the most underutilised and controversial topics in

thoracic surgery. Nevertheless, over the past few years, with the wider integration of multidisciplinary patient selection, minimal invasive surgical techniques (thoracoscopy and robot-assisted thoracoscopic surgery (RATS)) and enhanced recovery programmes, outcome has drastically improved, resulting in increasing case numbers in specialised centres.

The history of LVRS

Early surgical approaches to treat lung emphysema were focused on altering the chest wall or diaphragm [5–7]. LVRS was first introduced in 1959 by Otto Brantigan, who described it as a reduction pneumoplasty with the main objective being to improve the respiratory mechanics and the lung's outward traction to keep the small airways open [8]. It consisted of a staged bilateral thoracotomy followed by resection of the most emphysematous parts of the lung and lung denervation by radical hilar stripping. The most affected side was operated on first, followed by the contralateral side 3 months later. Due to the high perioperative mortality rate of 16% and the lack of data demonstrating subjective improvement in survivors, Brantigan's work was not widely accepted. During the following four decades, various groups experimented with versions of his method. Bullae excisions, plications of the air sac, segmentectomies, lobectomies, and pneumonectomies were attempted, resulting in very sporadic success [9].

In the 1995, Joel Cooper hailed the dawn of a new era of LVRS after modifying Brantigan's technique to a bilateral LVRS *via* median sternotomy [10]. In 20 patients with heterogeneous non-bullous emphysema, he reported no perioperative mortality, with forced expiratory volume in 1 s (FEV_1) improvement of 82% at 6 months, which was associated with marked relief of dyspnoea and improvement in quality of life (QoL) [11]. Re-evaluation of Coopers' technique in 150 consecutive patients demonstrated an increase in FEV_1 of 51%, perioperative mortality in six patients (4%) and continuing improvement in QoL [12].

In Zürich (Switzerland), Walter Weder started a bilateral LVRS video-assisted thoracoscopic surgery (VATS) programme in 1993 and reported the initial results of 20 patients from 1994 to 1995 with no perioperative mortality, improvement in FEV_1 of 41%, an increase in walking distance (12 min: 495 m to 688 m, $p<0.001$) and a substantial relief of dyspnoea at 3 months [13]. The same technique was reported in 1996 by Keenan *et al.* [14] from Pittsburgh (USA) who performed a unilateral LVRS by VATS in 57 patients, resulting in one perioperative death and significant improvements in forced vital capacity (2.69 L after *versus* 2.26 L before) and FEV_1 (1.04 L after *versus* 0.82 L before), with 63% of patients showing an improvement of more than 20%.

These promising results provided an impetus for several new LVRS groups to implement their own LVRS programme and led to a randomised National Emphysema Treatment Trial (NETT), performed in North America, evaluating the efficacy of LVRS on QoL and survival benefit in comparison to medical treatment [15]. Out of the 1218 patients included in the NETT, VATS was only used in 30% of cases.

The results were published in 2003 and the trial confirmed a significant improvement in survival, exercise capacity and QoL in non-high-risk emphysema patients. Unfortunately, patients with FEV_1 <20%, diffusing capacity of the lung for carbon monoxide (D_{LCO}) <20% and homogenous morphology on a computed tomography (CT) scan were also included and not surprisingly identified as a high-risk cohort and experienced a mortality of 16% [16]. Based on the latter group, the report led to several misconceptions in medical society, concluding that LVRS was an invasive and risky procedure.

Further analysis of the data showed that for LVRS patients with heterogeneous emphysema (predominantly upper-lobe) and low baseline exercise capacity, a significant improvement was attained in survival (up to 5 years), exercise capacity (up to 3 years) and QoL (up to 5 years) [17]. Although several other studies [11, 18–22] have confirmed the efficacy and safety of LVRS, a supposed high surgical morbidity and mortality, the high cost of the procedure and poorly defined patient selection criteria seem to have influenced both the medical community and patients, as the number of LVRS procedures remained low [12, 23]. In addition, continuing hope for less invasive endoscopic alternatives undoubtedly delayed integration of a surgical procedure in the multidisciplinary treatment armamentarium.

Over the past two decades, with further development of the VATS approach and increased experience at high-volume centres, surgical mortality has steadily improved (ranging from 0% at 6 months to 4% in-hospital) [22, 24–27], with a significant and maximal functional improvement (spirometry, dyspnoea scores and QoL) from 3 months up to 5 years after LVRS. These data, together with appropriate multidisciplinary patient selection, further bolster the general acceptance of LVRS in the field of thoracic surgery.

These solid results inspired expert centres to investigate expanding indications in patients with severe hyperinflation and other morphologies than heterogeneous upper lobe disease. In a retrospective analysis of

prospectively collected, single-centre data from Zürich, 138 out of 250 patients had a homogenous morphology of emphysema with no or very limited target zones for resection. In this subgroup, similar to heterogenous patients, significant improvement of FEV_1 (+35%) and 6-min walking distance (6MWD) (+79 m) at 3 months were shown, with no differences in perioperative and 1-year mortality [18]. Additionally, in experienced centres, LVRS can cautiously be considered in a subgroup of highly selected patients with severely impaired diffusion capacity (D_{LCO} <20%) and presence of major hyperinflation and heterogeneous emphysema. In a retrospective analysis of 33 patients, good results have been achieved for these patients at 3 months with a significant increment of FEV_1 (23% to 29%) and D_{LCO} (15% to 20%) and no mortality at 3 months [28]. Subgroups of patients presenting with mild to moderate pulmonary hypertension (systolic pulmonary artery pressure >35 mmHg, median systolic pulmonary artery pressure: 41 mmHg), with heterogenous emphysema and clear target zones, also have the potential to benefit from LVRS with pulmonary hypertension no longer considered an absolute contraindication [29]. Since endothelial function and blood pressure have been found to improve 3 months after LVRS, the procedure may have a positive impact on cardiovascular outcome as well [30].

"*Volume is the issue, not the tissue*"

The chest wall, lungs and diaphragm normally coordinate mechanically with each other to optimise elastic recoil. In emphysema, lung hyperinflation presses the diaphragm down, inhibiting its full function. The increased distensibility of the emphysematous lung parenchyma results in a lung that is easily inflated but tends to remain pathologically inflated throughout the breathing cycle and especially during an effort. Dynamic hyperinflation during exercise is difficult to assess but can be identified from specific questions addressed to the patient. An important consequence of the defect is that portions of severely emphysematous lung act as non-functional, volume-occupying areas impairing diaphragmatic and chest wall function.

Emphysema is a generalised pulmonary disease, but all areas of the lungs are not equally involved. The areas that are more involved are probably entirely or at least mostly useless as respiratory tissue. Volume reduction aims to reshape the normal lung volume by removal/shaving of severely damaged, poorly ventilated, and expanded lung tissue. It restores the lung to its original form and may cause the diaphragm to return to its former, dome-like shape. This results in increased expiratory flow rates, improved alveolar gas exchange and improved mechanical function of the diaphragm and thoracic cage with a decreased work of breathing.

Surgery provides a unique volume-oriented approach as surgical resection has the inherent benefit of personalised reshaping of the lungs. One or several target zones for resection are identified on CT scans or ventilation/perfusion scintigraphy, leaving the better-preserved lung parenchyma intact.

Patient selection

Patient selection is crucial to the success of the procedure and should be performed at an experienced centre with a multidisciplinary team approach to emphysema treatment. Referrals are based on advanced emphysema which is not adequately responsive to standard medical therapy. Chest CT, ventilation/perfusion scintigraphy, spirometry, plethysmography, 6MWD and echocardiography are conducted to identify eligible LVRS candidates. Cardiac assessment is recommended to evaluate coronary disease, pulmonary artery pressure and right ventricular function. Patients must be highly motivated to undergo surgical treatment and be willing to participate in a pulmonary and physical rehabilitation programme.

Indications

In general, eligible ambulatory emphysema patients are good candidates for LVRS if there is a suitable morphology identified by CT scan (figures 1 and 2); FEV_1 ranges between 15% and 45% predicted (pred); with a residual volume >150% pred; modified Medical Research Council dyspnoea score $\geqslant$2; smoking cessation (confirmed by urinary cotinine test) for $\geqslant$6 months; and mean pulmonary artery pressure <45 mmHg (invasively confirmed if cardiac ultrasound is considered unreliable). However, among all the parameters the most important is severe hyperinflation of the lungs and morphology on CT scans [31].

Contraindications

Patients with a very low functional reserve (FEV_1 <20% and D_{LCO} <20%) should be carefully assessed and only considered if a markedly heterogeneous or bullous-like morphology can be identified and they have a marked hyperinflation (residual volume >250%). Patients with important bronchiectasis, more than two exacerbations in the past year and any comorbid disease rendering them unfit for surgery are considered ineligible.

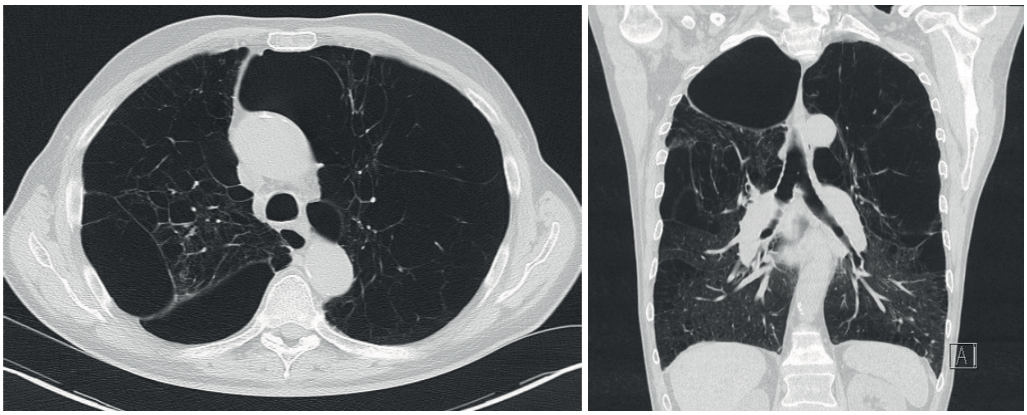

FIGURE 1 Transverse and coronal computed tomography sections from a patient with severe heterogenous emphysema, selected for lung volume reduction surgery. Both apexes show severe emphysematous destruction with some prominent bullae.

Surgery is also considered a higher risk in patients with BODE index of 7 or above (BODE: body mass index (BMI), airflow obstruction, dyspnoea, and exercise capability). Extreme cachexia or obesity (BMI: 32 $kg \cdot m^{-2}$ for women, 31 $kg \cdot m^{-2}$ for men) and patients older than 75 years were formerly listed as an absolute contraindication. However, in general, patients should be fit enough to undergo surgery and therefore, advanced calendar age, BMI or previous thoracic surgery should be considered as relative contraindications and assessed on an individual basis to strike a balance between anticipated benefits and risk of the procedure.

The multidisciplinary emphysema expert team

A multidisciplinary team should consist of pulmonologists experienced in COPD and lung transplantation, thoracic surgeons, chest radiologists and an interventional pulmonologist. A visual assessment of the type and distribution of emphysema (morphology of hyperinflation), any unexpected findings and an estimation of fissure integrity by a dedicated chest radiologist is needed. Software is used to support quantification of emphysema destruction, target lobe selection and fissure integrity measurement (*e.g.* StratX, Coreline soft). The decision making of this multidisciplinary emphysema expert team finally addresses the target area for volume reduction in the context of individual morbidity risk and benefit. As the patient selection and the right treatment approach is crucial for the outcome, multidisciplinary team meetings are strongly recommended [32, 33].

Surgical concept: personalised remodelling of the lungs

Surgery offers a unique volume-oriented strategy since the resection has the intrinsic advantage of resecting several target zones while leaving the better-preserved lung parenchyma unaltered and the shape of the lung intact. The resection of an entire lobe comparable to valve treatment resulting in total atelectasis is almost never indicated.

The history of LVRS has clearly shown that selected emphysematous patients can benefit from a remodelling intervention that aims to restore chest geometry by reshaping the overinflated lung to its normal size [26, 34, 35]. Identifying the target zones for resection is crucial in preparing an LVRS procedure. Every morphology is unique, and can generally be categorised into three types: marked heterogenous, intermediate heterogeneous, and homogeneous [36].

The UK National Institute for Health and Care Excellence has reviewed evidence on the effectiveness and cost-effectiveness of LVRS and further recommends cooperation between specialist interventional respirologists and VATS or robotic surgeons offering LVRS [37]. The standard of surgical care, at the time of writing, is a bilateral minimal invasive VATS approach to tackle all target areas, however intra-operative evaluation of the patient's safety is crucial, sometimes rendering a unilateral or staged bilateral approach more suitable. In a period from October 2017 to November 2022, Lee *et al.* [38] from St Barthlomew's Hospital in London performed 177 consecutive lung volume reduction procedures: 83 patients (54 male, 29 female) with a median age of 66 years (range 57–71 years) underwent RATS LVRS and 94 patients underwent bronchoscopic lung volume reduction (BLVR) (52 male, 42 female), median age 69 years

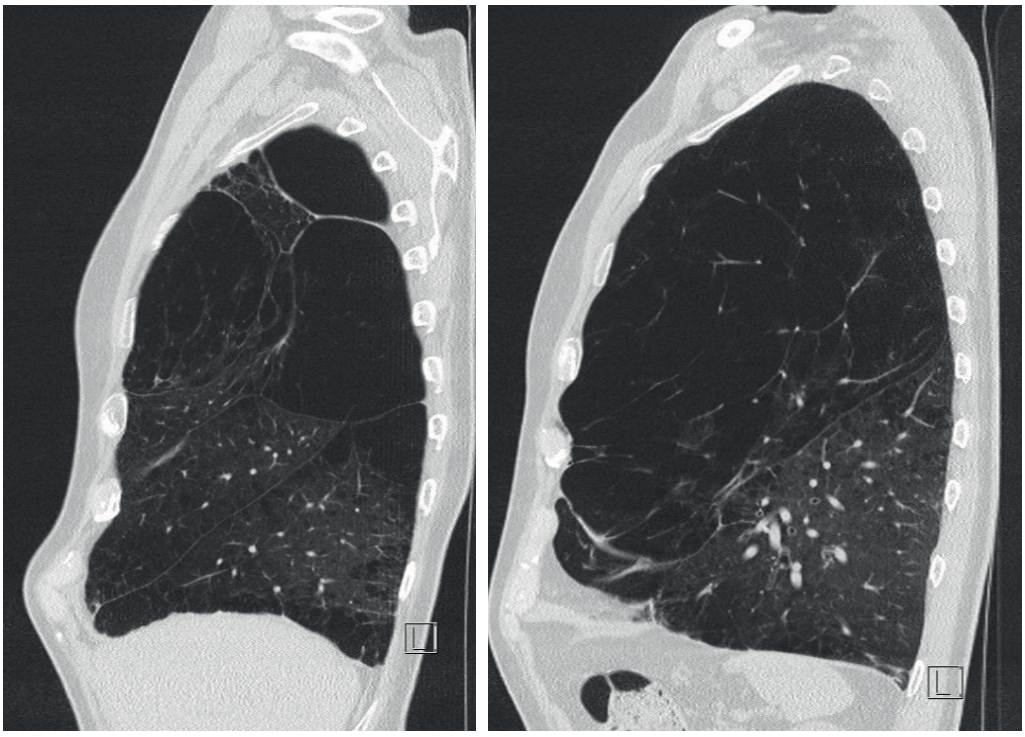

FIGURE 2 Sagittal computed tomography sections from a patient with severe heterogenous emphysema, selected for computed tomography. Target areas are clearly identified in both upper lobes with still well-preserved tissue in the middle and lower lobes.

(range 43–82 years). BLVR does use less hospital resources than RATS LVRS in comparable groups if the recovery is uncomplicated. However, this advantage is lost if one includes the resources needed for the treatment of complications and revisional procedures.

Furthermore, RATS offers at least equal results compared to VATS and in the near future RATS will gain more evidence for LVRS in order to confirm the trend towards a better outcome in many thoracic surgical procedures. The question of whether a bilateral staged approach is better or worse has not been finally solved scientifically and must be decided on an individual level. In general, in patients with bilateral target zones, a bilateral approach is preferred over unilateral LVRS, since the functional benefits achieved are of greater dimension compared to the unilateral procedure [18]. However, a staged bilateral procedure can lower post-operative morbidity and can improve functional results up to 6 years [39–41].

Implementation of an enhanced recovery programme, a clinical pathway to accelerate recovery based on a multimodal programme with optimal pain relief, stress reduction with regional anaesthesia, early extubation, early enteral nutrition and early mobilisation, has shown to improve patient outcomes. At our own institution (UZ Leuven), we recently demonstrated that an enhanced recovery programme for LVRS results in fewer complications and a reduced length of stay related to decreased incidence and duration of air leak.

Surgical technique

Several techniques have been described for LVRS and currently still depend on the experience of the institution and the surgeon. Today the preference is for minimally invasive VATS and consists of unilateral or bilateral LVRS by stapling.

A 10 mm 30-degree camera is preferred. The number of ports depends on the location of the target areas, ranging from one up to four ports (upper and lower lobe targets), with the camera in the sixth intercostal space on the midaxillary line. This first port is placed under direct vision to avoid damage to the lung. The second port is normally placed just anterior to, but one intercostal space higher than, the first incision, on the inframammary line and the third port inferior to the tip of the scapula in the same intercostal space as the first incision. All ports are a minimum of 10 mm wide, a mini-Alexis can be used as well if lubricated.

Lung manipulation should be performed with care, using minimally invasive forceps or a 10 mm cherry dissector (Ethicon Endo-Surgery, Cincinnati, OH, USA). A no-touch policy regarding the lung parenchyma that remains must be followed. Ipsilateral lung ventilation is stopped only at the moment of incision, thereby allowing the most diseased parts to remain inflated [42]. Complete and careful adhesiolysis, if necessary, is the first step (figure 3, step 1), allowing full re-expansion of the lung after the procedure. The phrenic nerve must be protected. Dissection of the pulmonary ligament is recommended in most cases.

A volume-based parenchymal resection/shaving of the more peripheral target areas is performed, according to a pre-operative defined plan based on detailed CT analysis. By minimal touch re-shaping (figure 3, step 2) of the voluminous lung, the most severely destroyed tissues are confirmed and their volume can be assessed. The lack of resorption atelectasis is helpful in identifying target areas for resection. Deflation by cautery should be avoided since the purpose is to resect actual volume. When these target zones are identified, pre-stapling compression of the lung can be performed gently with endoscopic forceps (figure 3, step 3).

Volume reduction is then realised by performing a series of (reinforced) staples (Tri-Staple 2.0, Signia; Medtronic Limited, Watford, UK), starting at 45 mm, since the first stapling will be closest to the thoracic wall. In our practice, we aim at reducing the additional lung volume as calculated from the estimated total lung capacity subtracted from the measured total lung capacity.

To avoid tearing of the fragile lung tissue, it is advised not to force the stapler over the lung, but slide the lung gently between the stapler, which can be lubricated with paraffin. In cases of heterogeneous upper lobe predominant emphysema, the lateral one third of lung parenchyma and the apical part (lung parenchyma superior to the arch of the azygos vein or aorta) are stapled, with avoidance of the fissures, so that the resulting line of resection follows an inverted J-shape (hockey-stick resection). Each consecutive stapler line begins at the last centimetre of the previous stapler line to prevent an air leak at the junction.

If there is concern about air-leak, it is an option to submerge the lung in water while restarting ventilation to exclude an air-leak (figure 3, step 5). When the lung appears fragile, a polyglycolic acid sheet (Neoveil; Gunze, Kyoto, Japan) can be applied along the staple line to reinforce the tissue that is most prone to post-operative tearing during re-expansion [43] or covered with Progel Pleural Air Leak Sealant (Becton Dickinson and Company, Franklin Lakes, NJ, USA) (figure 3, step 6) [44, 45]. Talc pleurodesis is rarely

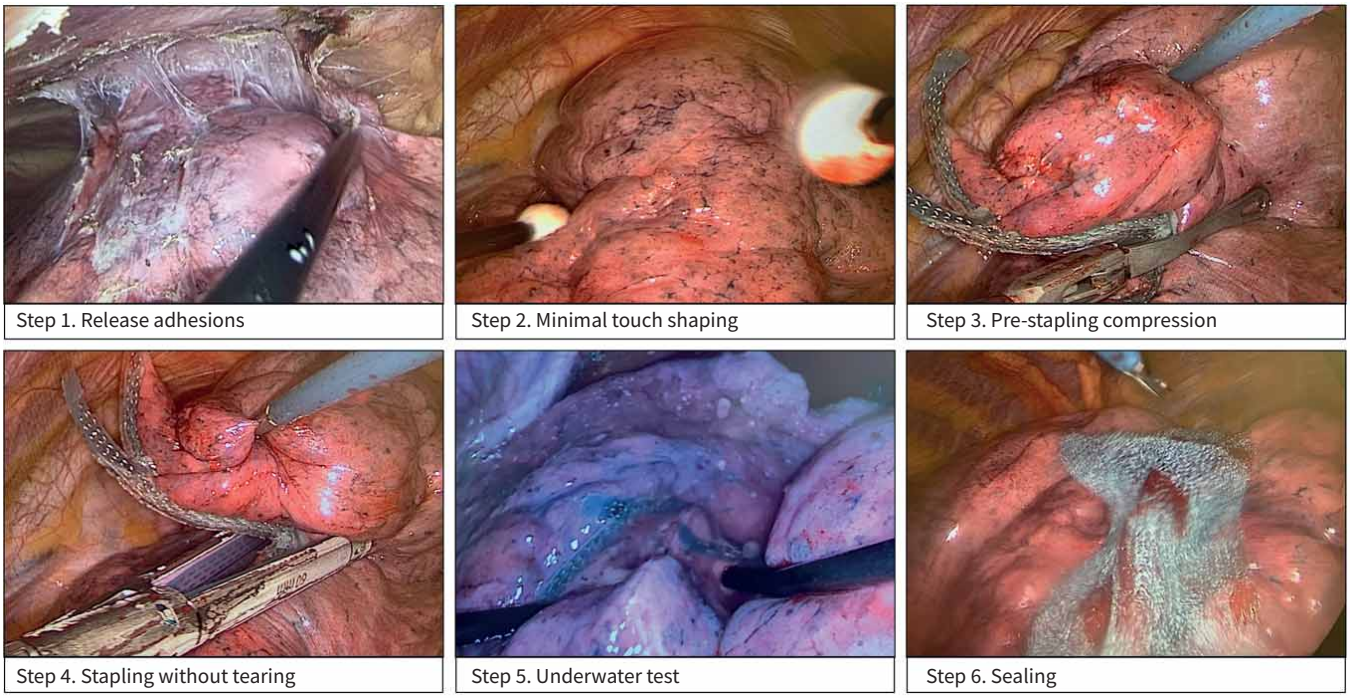

FIGURE 3 Sequence of steps in lung volume reduction surgery.

performed and then only in patients who are no longer eligible for lung transplantation. One curved chest-drain (20–28G) is placed in the chest cavity, pointed with the curve in the posterior sinus and the tip pointed apically. In cases of very fragile tissue or minimal air-leak, a second straight drain can be positioned. Mechanical ventilation is gradually resumed under visual control to assure the remaining lung is expanding completely. Aggressive recruitment should be avoided [46]. No or minor suction (−3–5 cmH_2O) is required. In case of a major air-leak, the suction can temporarily be increased up to −10 cmH_2O. The resected lung tissue is sent for pathological investigation.

Post-operative phase

To prevent coughing or Valsalva and to limit the time that the delicate, surgically repaired lungs are exposed to positive pressure ventilation, early extubation is important. This should be realised slowly, so that the carbon dioxide (CO_2) tension built-up during the operation can be decreased and to prevent bronchospasm or coughing, which pose major risk factors for air-leak. Switching from a double-lumen-tube to a laryngeal mask can prevent coughing. Because a high arterial oxygen tension may be harmful in a patient with pre-operative CO_2 retention, the arterial oxygen tension is kept close to baseline [47]. Use of non-invasive ventilatory support is considered if progressive hypercapnia occurs, with no more than 2 L of oxygen per minute to avoid the risk of additional CO_2 retention. No standard admission to the intensive care unit is planned, unless medically required. Adequate use of non-narcotic analgesics, prophylactic use of antibiotics, chest physiotherapy to manage secretions, and early, pain-free mobilisation (day of surgery) is vital in the prevention of respiratory failure or infection.

Patient-controlled epidural analgesia (PCEA) is removed at day 2 to 3 post-operation. Ranitidine, β_2-adrenergic agonist aerosol, acetylcysteine, prophylactic dose of low-molecular-weight heparin and an oral osmotic laxative are administered according to the protocol.

Vigilant and limited intravenous fluid administration is maintained until PCEA removal. The weight should be monitored daily and in case of volume overload, diuretics should be administered. Daily respiratory and general physiotherapy is mandatory and starts 2–3 h post-operatively when patients are still in the recovery room. Patients receive protein-enriched meals from day 1 post-operation. The urinary catheter is removed on day 1 post-operation. Chest drains are removed early in the absence of an air-leak and drainage of <200 mL. Air-leak is evaluated daily as a function of breathing, talking, Valsalva or coughing.

When prolonged air-leak (>7 days) occurs, or in the case of a major air-leak early on, a re-intervention should be considered to prevent prolonged hospitalisation. It is advised that all patients are included in a 3-month respiratory rehabilitation programme.

Complications

An air-leak (lasting more than 7 days after surgery) is the most common event, occurring in around 20–25% patients [21] and can usually be managed with continued pleural drainage until resolution. The presence and duration are associated with patient characteristics and preexisting disease [48]. The use of buttressed staplers [49] and coverage of the staple line with sealants could potentially reduce the incidence of prolonged air-leak [50]. Failure to implement early extubation in the operating room resulting in prolonged ventilation and pneumonia is extremely rare. In a recent study to decrease the risks of barotrauma during nonintubated thoracoscopic-surgery (NITS) under spontaneous ventilation, Taje *et al.* [51] investigated NITS under spontaneous ventilation with adjuvant transthoracic negative-pressure ventilation in 30 patients. There was no mortality and improved 24 h oxygenation measures and lung expansion with negative pressure ventilation, change in oxygen tension/inspiratory oxygen fraction (9.3±16 *versus* 25.3±30.5, p=0.027) and change in arterial carbon dioxide tension (−2.2±3.15 mmHg *versus* 0.03±0.18 mmHg, p=0.008) [51]. Of the potential cardiac complications, arrhythmias are most frequent; approximately 22% of patients experienced post-operative arrhythmia that required additional medical treatment [15]. Gastrointestinal complications may also occur infrequently [52], although in our experience this is much less commonly seen.

BLVR

Due to the post-operative complications and the strict selection criteria for LVRS, bronchoscopic techniques have also been developed, and employed to achieve lung volume reduction in patients with severe emphysema. Data about endobronchial procedures have only been published for around two decades, and many clinical trials have shared their results.

There are different approaches for endobronchial lung volume reduction including endobronchial valves, sealants, coils, stents or thermal vapour ablation. This review will mainly focus on endobronchial valves,

which are the most commonly employed measure and are also included as a treatment in the Global Initiative for Chronic Obstructive Lung Disease report for COPD patients with advanced emphysema.

Endobronchial valves are unidirectional valves that allow the air to exit the targeted lobe thus causing a collapse and atelectasis of the hyperinflated lobe and also preventing further entrance of air during inspiration [53].

The first randomised clinical trial was the VENT trial, a multicentric study that included 321 patients. 220 patients were assigned to undergo endobronchial valves and were then compared to a control group that received standard medical care [54]. The study showed that there was an increase in FEV_1 of 4.3% and a minimal improvement of the 6MWD and the subgroup with a greater emphysema heterogeneity and fissure completeness were associated with a better response to treatment.

Later the IMPACT study, which included 93 patients from which 43 patients were allocated to the BLVR treatment, showed an improvement in FEV_1, 6MWD, modified Medical Research Council Dyspnoea grade and quality of life in patients with homogenous emphysema without collateral ventilation together with a decrease in residual volume and BODE index score when compared to the control group [55]. 1-year follow-up results also showed that the benefit of this intervention was persistent even after 12 months [56].

The TRANSFORM study also showed an improvement of 12% or more in FEV_1, dyspnoea, exercise tolerance and quality of life in 65 patients with severe heterogenous emphysema without collateral ventilation [57]. The LIBERATE study included patients with hyperinflated emphysema with little or no collateral ventilation and also showed that patients treated with endobronchial valves showed a statistically significant improvement in multidimensional scores for breathlessness, activity and psychosocial parameters for at least 12 months [58].

Studies have also shown improved quality of life and exercise capacity after BLVR treatment are associated with a survival benefit when compared to a control group, and the median survival period after treatment in these studies was 7.4 [59]. and 8.2 years [60]. The cardiac preload, output and the myocardial contraction was shown to be improved significantly after the treatment, but there was no change in the pulmonary artery pressure [61].

All these randomised clinical trials have shown benefits for patients with severe emphysema, whether homogenous or heterogenous, that persist even over a longer-term period when compared to the standard patient care. Yet it is crucial to specify and carefully select the most appropriate patients for this intervention in order to achieve the best results. Welling *et al.* [62] showed that only a small proportion (one out of five) of the patients referred for BLVR were actually suitable for the treatment and met the selection criteria, thus better referral tools should be developed in the future.

Patient selection

It is crucial to define the group of patients that is going to benefit the most, as the proportion of patients that respond to treatment improves from 20% in an unselected group to 75% with appropriate patient selection [63]. Patients should first be investigated by radiological tools if they possess a hyperinflated lung. Then, patients should be selected by following the minimum criteria: residual volume >175% predicted, FEV_1 between 15 and 50% of predicted, little or preferably no collateral ventilation in the targeted lobe and an intact fissure integrity, no evidence of significant coexistent pulmonary pathology, clinically stable prior to the procedure, able to undergo sedation or general anaesthesia, and cessation of smoking. Patients with a 6MWD of 100–500 m can be considered for BLVR, and if severe hypercapnia (>60 mmHg) or severe hypoxaemia (<45 mmHg) is present reassessment can be considered after at least 3 months of positive airway pressure treatment [64, 65]. Patients with prior surgery including bullectomies, lobar or segmental or wedge resections on the contralateral lung can also be considered as candidates for BLVR treatment [64].

An important factor that affects the outcome of the treatment is the composition and the features of the target lobe. Hartman *et al.* [66] compared the responders and non-responders after a 1-year follow-up and characterised the non-responders as patients with less emphysematous destruction and air trapping together with a higher perfusion in the target lobe.

Contraindications

It is important to evaluate the patients not only based on a single criterion but as a whole and a multidisciplinary team approach is crucial to decide if a patient is suitable for either BLVR or alternative

treatment options. Patients with the following conditions should be carefully evaluated and reassessment might only be considered for reversible causes [64, 65]:

- Unstable cardiovascular disease or severe heart failure (ejection fraction <35–40%),
- Presence of myocardial infarction or stroke in the past 6 months,
- Pulmonary hypertension (systolic pulmonary artery pressure >45 mmHg),
- Unstable patients with more than three exacerbations in the past 12 months despite optimum medical treatment,
- Significant symptomatic bronchiectasis and colonisation with *Pseudomonas* or methicillin-resistant *Staphylococcus aureus*,
- Severe hypercapnia or hypoxaemia,
- 6MWD <100 m, and
- A previous history of LVRS, lobectomy or pleurodesis.

Complications

According to the published literature BLVR is a safe procedure and generally well tolerated. Although less invasive when compared to surgery there remain some complications related to this treatment. The rate of complications varies by centre as the experience of the team is also a determinant of both outcome and complication frequency. Even in experienced centres pneumothorax has been reported in approximately 20–34% of the procedures [67, 68]. The majority (up to 80%) of the pneumothoraxes occur within the 48 h after intervention, 10% during days 3–5 and the rest occur after day 6 [69]. This is a common complication due to the conformational changes in the lung with the collapse of the targeted hyperinflated lobe and the expansion of the other, or the rapid change in elastic recoil that might lead to the rupture of bullae and this group of patients have the greatest benefit at long-term follow-up [63]. It is important to have all the necessary equipment for the immediate intervention and patients should be closely followed-up for signs or symptoms of pneumothorax [68].

Other possible complications are acute bronchitis, pneumonia or lung infections within the 3 months after the procedure and COPD exacerbations occur and should be treated accordingly [56, 64]. A rare complication is valve migration which should be suspected if there is an increase in coughing, and usually occurs when the valve has been placed incorrectly or if undersized [64].

Follow-up and management of complications

The close follow-up of patients is important to assess if any complications occur in the long-term, and enables appropriate intervention. Patients should be informed in detail about any possible sign or symptom that is related to a complication after discharge. The patient is examined by radiological techniques and pulmonary function tests after 6 weeks to assess the clinical benefit of the procedure and if there is no lobar atelectasis then bronchoscopy is performed to replace the valve if migration or mispositioning has occurred [70]. If bacterial pneumonia occurs and is not resolved with antibiotics then removal of the valve can be considered and the valve can be replaced later after the pneumonia has been resolved [64]. Patients are followed-up once every 6 months for the first year and then annually up to 5 years [70]. Sometimes there might be an increase in exacerbations in the long-term follow-up and to ensure the patient receives the proper treatment it is important to discriminate between the disease progression or course *versus* any complication related to the BLVR procedure [64]. In some patients granulation tissue formation might be a complication which can present with cough, haemoptysis or loss of volume reduction, and cryoablation is a treatment option for this [64].

Surgery *versus* endobronchial valves

There is a lack of evidence to show whether surgery or endobronchial valve treatment is superior to the other. There is only one randomised controlled trial (the CELEB study) which compared 41 patients that had a LVRS and 47 patients that had a BLVR procedure and at the 12-month follow-up there was no significant difference between them regarding the outcomes [71]. The most common complication was subcutaneous emphysema (29%) in the LVRS group and pneumothorax (30.4%) in the BLVR group [71]. In terms of mortality, there were two deaths; one in each group due to complications [71].

However, previous LVRS history in a patient is a contraindication for BLVR, whereas LVRS has been shown to be safe, feasible and even restores the lung volume reduction effect in emphysema patients that have been previously treated with endobronchial valves [72].

Conclusion

Lung volume reduction either *via* surgery or endobronchial procedures such as the insertion of valves has evolved over the years and has been shown to be safe for treatment of severe emphysema that remains

symptomatic despite optimal medical treatment. The outcome is better if the patient selection is done carefully and if a multidisciplinary approach is implemented.

Key points

- Lung volume reduction improves the lung function, exercise tolerance, quality of life and survival of patients with severe emphysema who remain symptomatic after optimal medical treatment.
- It is crucial that patients are evaluated by a multidisciplinary team in order to choose the best approach.
- Minimally invasive video-assisted thoracoscopic surgery and endobronchial valves are the most commonly used techniques and there is no study to show that one is superior to the other.
- Lung volume reduction is safe but caution is still important to handle any complications and to intervene promptly.
- Patient selection criteria have evolved through time and are crucial to the outcome of the procedures used.

Self-evaluation questions

1. Which of the followings describes the aim of the lung volume reduction treatment?
    a) Removal of severely damaged lung tissue
    b) Increase the ventilation of the lung
    c) Press the diaphragm down to improve ventilation
    d) It is limited to only one lobe
    e) All of the above
2. Which parameters improve with the lung volume reduction intervention?
    a) Forced expiratory volume in 1 s (FEV_1)
    b) 6-min walk distance (6MWD)
    c) Cardiovascular outcome
    d) Quality of life
    e) All of the above
3. Which of the following is an absolute contraindication for lung volume reduction surgery (LVRS)?
    a) Cachexia
    b) Obesity
    c) Bronchiectasis with more than two exacerbations in the past year
    d) Bode index less than seven
    e) Patients older than 65 years
4. Which of the following is the most common complication of endobronchial valves?
    a) Air leak
    b) Pneumothorax
    c) Subcutaneous emphysema
    d) Haemoptysis
    e) Arrhythmias
5. Which of the following criteria makes the patient eligible for BLVR intervention?
    a) FEV_1 more than 50% of predicted
    b) Presence of collateral ventilation
    c) Fissure integrity is intact
    d) A 6MWD less than 100 m
    e) Severe hypoxaemia

Conflict of interest: The authors have nothing to disclose.

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Suggested answers

1. a.
2. e.
3. c.
4. b.
5. c.