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Bronchoscopic interventions for severe emphysema: Where are we now?

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ABSTRACT

Patients with severe emphysema have limited treatment options and only derive a small benefit from optimal medical treatment. The only other therapy to have significant clinical beneficial effect in emphysema is LVRS but the perceived risk and invasiveness of surgery has fuelled bronchoscopic approaches to induce lung volume reduction. There are multiple bronchoscopic methods for achieving volume reduction in severe emphysema: EBV, airway bypass procedure, endobronchial coils, thermal (vapour) sclerosis and chemical sclerosis (sealants). Optimal patient selection is key to successful patient outcomes. This review discusses bronchoscopic approaches for emphysema treatment which has progressed through clinical trials to clinical practice.

Key words: bronchoscopy, chronic obstructive pulmonary disease, emphysema, lung volume reduction.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic, progressive, complex inflammatory lung condition characterized by airflow limitation, sputum production and a decline in exercise tolerance. It is irreversible and ultimately leads to disabling breathlessness and reduced life expectancy. It is a heterogeneous disease predominantly caused by cigarette smoking and, in some developing economies, by the indoor use of biomass fuels for cooking in poorly ventilated homes. The condition consists of chronic bronchitis, airflow obstruction and alveolar destruction.[1] This latter component is known as emphysema, and is defined as the abnormal, permanent enlargement of air spaces distal to the terminal bronchioles, accompanied by the destruction of their walls and without obvious fibrosis. The damage to the elastin and collagen tissue reduces the tethering of the bronchioles and in expiration the airways collapse leading to air trapping. Furthermore, loss of the elastic recoil also leads to an increase in lung volumes.[2] Hyperinflation mechanically disadvantages the diaphragm and intercostal muscles generating an increased work of breathing. Patients with advanced emphysema are breathless despite optimal medical treatment (anticholinergic drugs, beta-2 agonists, long-acting bronchodilators, inhaled steroids and mucolytics), and whilst oxygen has some role in palliation, it barely alters the disability and breathlessness experienced by these patients.[2,3]

Lung volume reduction surgery (LVRS) was proposed by Brantigan and Mueller in 1957 on the premise that resection of up to 30% of the worst effected lung of an emphysematous patient in multiple wedge excisions would permit re-expansion of the remaining healthier tissue, normalize ventilatory mechanics and restore elastic recoil and airflow.[4] Cooper revised the surgical approach and published his experience demonstrating a lower mortality and significant improvements in quality of life and pulmonary function.[5,6] However, the first report from the large NETT study stating a higher mortality with LVRS had the greatest impact and has hampered the progress and impact of LVRS.[7] The subsequent report demonstrating improvements in mortality in a subgroup with upper lobe predominant disease and low baseline exercise tolerance never quite redressed the negative view around LVRS that had ensued.[8] Despite convincing efficacy evidence, this perception of high morbidity and mortality had fuelled the development of bronchoscopic approaches to achieve lung volume reduction.[9,10]

Several approaches have been developed from the initial development of artificial airways placed both endobronchially[11] and even transthoracic.[12,13] These implants allow air to escape and bypasses the airways which are susceptible to expiratory airway collapse in emphysema. Both therapies showed initial promising

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results with even doubling of pulmonary function within 24 h of the procedure. However, occlusion of these artificial airways has limited their development as a viable therapy.[14,15] Hence, the focus of this article is limited to bronchoscopic approaches for emphysema treatment which has progressed through clinical trials to clinical practice. Endobronchial valves (EBV), endobronchial coils and sclerosant treatments are discussed (see Table 1 for randomized controlled trials (RCT) results).

ENDOBRONCHIAL VALVES

The principle of EBV is that if a lobe can be isolated by placing valves or devices that allow air (and secretions) to be expelled from that lobe but preventing any ingress of air into that lobe then that lobe should deflate. Providing the most damaged air-trapped area is targeted, this deflation would effectively lead to lung volume reduction and hence improve chest wall mechanics and diaphragmatic function.[9,16–18] The two main devices that have been extensively investigated are the Zephyr EBV by Pulmonx (Redwood City, CA, USA) and the Spiration Valve System (SVS, previously referred to as the intrabronchial valve or IBV) by Olympus (Center Valley, Pennsylvania, USA). Two other devices with only limited clinical evaluation are the MedLung EBV (MedLung, Barnaul, Russia) and the Endobronchial Miyazawa Valve (Novatech, La Ciotat, France).

ZEPHYR EBV

The Zephyr valve is a silicone skin duckbill valve with a nitinol frame. The nitinol frame allows it to be

Table 1 Change in outcomes following bronchoscopic lung volume reduction treatment options compared to control groups for emphysema of the published RCT's

RCT	Sample size and follow-up period	Difference in treatment vs control groups: Lung function (FEV_1, %)	Exercise capacity (6MWD, m)	Quality of life (SGRQ, points)
Valves				
VENT/US&OUS subset[19]	*n* = 122 6 months	24.8	28	−8.4
STELVIO[24]	*n* = 68 6 months	17.8	74	−14.7
BeLieVeR HIFi[23]	*n* = 50 3 months	20.9	33	−5.1
IMPACT[25]	*n* = 93 6 months	16.3	28	−7.5
TRANSFORM[26]	*n* = 97 6 months	29.3	79	−6.5
LIBERATE[27]	*n* = 190 12 months	18	39	−7.1
REACH[43]	*n* = 107 6 months	†	36	−10.5
EMPROVE[44]	*n* = 172 12 months	†	6.9	−9.5
Coils				
RESET[56]	*n* = 46 3 months	14.2	51	−8.1
REVOLENS[57]	*n* = 100 12 months	8	2	−9.1
RENEW[50]	*n* = 315 12 months	3.8	10.3	−8.
Vapour				
STEP-UP[63]	*n* = 70 6 months	14.7	30.5	−9.7
Aeriseal				
ASPIRE‡[67]	*n* = 57 3 months	11.4	31§	−11

†Data not available.
‡Treatment versus baseline.
§Six months data (*n* = 21).
6MWD, 6-min walk distance; FEV_1, forced expiratory volume in 1 s; RCT, randomized controlled trial; SGRQ, St George's Respiratory Questionnaire.

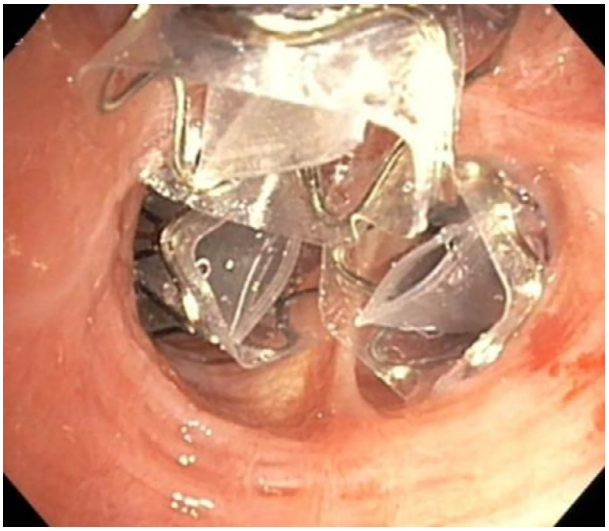

Figure 1 Bronchoscopic image of three Zephyr endobronchial valves (Pulmonx) placed in the right upper lobe segmental ostia (courtesy of Dirk-Jan Slebos).

compressed and delivered through the instrument channel of a flexible bronchoscope. The nitinol frame then expands securing the valve within the airway (Fig. 1). The zephyr valve is available in two airway sizes: size 4 (suitable for airway diameters of 4.0–7.0 mm) and size 5 (airway diameter size of 5.5–8.5 mm). Both valve sizes are also available in standard and low profile lengths. The latter has a shorter landing zone and allows secure valve placements in segments with short airways such as the apical segment of the lower lobe.[19,20]

There have been six randomized controlled studies performed with the Zephyr valves in a total of 970 patients (610 were randomized to treatment with Zephyr valves and 310 to standard of care (SoC)).[21–27] The US arm of the VENT study randomized 321 patients in a 2:1 ratio: 220 EBV and 101 to SoC.[21] The study demonstrated only modest clinical improvements in forced expiratory volume in 1 s (FEV_1) of 6.8% (95% CI: 2.1 to 11.5; $P = 0.005$), 6-min walk distance (6MWD) of 5.8% (95% CI: 0.5 to 11.2; $P = 0.04$) equivalent to 19.1 m and St George's Respiratory Questionnaire (SGRQ) total score improvement of −3.4 (95% CI: −6.7 to 0.2; $P = 0.04$) in the treatment group over SoC. The European arm of the VENT study enrolled 171 patients and hence did not have sufficient power to achieve statistical significance.[22] It was at this stage that the impact of collateral ventilation on outcomes was realized especially as patients treated in the left upper lobe had much better outcomes than those that received right upper lobe therapy.[19,28,29] Post hoc data analysis highlighted that individuals with computed tomography (CT) evidence of fissure integrity (determined by visualization as 90% or more complete), a surrogate for absent interlobar collateral ventilation, experience much better clinical outcomes. In a subgroup of 122 patients (61 treated and 61 matched control patients), the changes compared to control were: FEV_1 of 24.7%, 6-min walk test (6MWT) of 28 m and SGRQ of −8.4 points. It also emphasized that correct placement of the valves to completely occlude the lobe was essential. In the VENT study, approximately one or more valves was not placed in the optimal position in 40% of patients.[19,21] The BeLieVeR HIFi study[23] was a single-centre randomized double-blind sham-controlled study to evaluate the post hoc findings of the VENT study. Patients were required to have intact fissure of the target lobe (proxy for the absence of collateral ventilation) to be eligible. The Chartis system[19] was utilized to determine the status of collateral ventilation. However, patient inclusion was based on fissure integrity. The primary endpoint, percentage change in FEV_1 at 3 months, was improved by 24.8% for EBV recipients compared with 3.9% for subjects in the sham group (between-group difference of 20.9%; $P = 0.033$). Exclusion of six patients who were collateral ventilation positive or indeterminate following Chartis evaluation improved the responder rates to EBV treatment (FEV_1% change of 31% at 3 months).

Klooster *et al.*[24] confirmed these findings in a further, single-centre RCT (the STELVIO trial) of patients with no collateral ventilation confirmed using the Chartis system. They recruited 68 patients who had heterogeneous emphysema and intact fissures (visually assessed on CT) and randomized them to treatment or control in a 1:1 assignment. They excluded patients who were collateral ventilation positive using the Chartis system or those patients where the anatomy was not suitable for complete lobar exclusion with Zephyr valves. The co-primary endpoints, improvements in FEV_1, forced vital capacity (FVC) and 6MWD at 6 months, were significantly greater in the EBV group compared to controls: FEV_1 20.9% versus 3.1%, FVC 18.3% versus 4.0% and 19.6 versus −3.6 m (all <0.01), respectively. This was accompanied by clinically meaningful improvement in RV of −856 mL, target lobar volume reduction (TLVR) of 1366 mL and SGRQ of −14.7 points. The IMPACT study[25] was performed in patients with more homogeneous disease (i.e. less than 10% difference in the degree of destruction on HRCT between ipsilateral lobes) and confirmed that this group of patients also benefit albeit to a lesser degree. Improvements in the treatment group compared to control were: FEV_1 17.1% and 6MWT 40 versus −9.6 m (all <0.01). The TRANSFORM study,[26] was a multicentre study where heterogeneous emphysema patients were randomized 2:1 to either valve treatment or SoC. This study was also important as over half of the centres involved in this study were centres starting valve treatment. Hence, this study is close to real clinical practice as possible and demonstrates that new centres have very similar outcomes to the experienced centres. At 3 months 55.4% of EBV versus 6.5% of SoC subjects reached the primary endpoint of ≥12% improvement in FEV_1 ($P < 0.001$). Improvements in the treatment group compared to control were: FEV_1 29.3% and 6MWT 78.7 versus −6.5 m. These results also confirmed the previous reported single-centre results from the BeLieVeR HIFi and STELVIO trials.[23,24] The LIBERATE study[27] combined all the learning from the previous clinical studies to determine whether these improvements could be reproduced in a large multicentre study involving a majority of US centres and to determine the degree of

benefit that was evident at 12 months in this group of patients with severe emphysema. Furthermore, in this trial, there was the opportunity to revise the procedure at 45 days if there was inadequate volume reduction with evidence of valve mis-placement on a follow-up HRCT scan. At 12 months, 47.7% of EBV versus 16.8% of SoC subjects reached the primary endpoint of ≥15% improvement in FEV_1 ($P < 0.001$). Improvements in the treatment group compared to control were: FEV_1 18% and 6MWT 39 versus −7.1 m.

A retrospective analysis of 547 patients collected from four prospective clinical trials was performed by Koster *et al.*[28] The CT scans were analysed to determine the fissure integrity score and the Chartis procedure to determine whether the patients were considered collateral ventilation positive or negative. A positive outcome was determined as a reduction in the lobar volume of >350 mL. This allowed thresholds to be determined and >95% fissure integrity was associated with a positive outcome in 88% of cases, whereas a fissure that was less than 80% complete had a negative predictive value of 93%. The key finding from this study is that all patients being considered for EBV therapy should have quantitative CT analysis (Fig. 2) and only those with fissure integrity of 80% or greater should be considered for a Chartis procedure and subsequent EBV therapy. Those with fissure that were less than 80% intact should be considered for alternative modes of lung volume reduction.

To facilitate fissure status functionality, the Chartis procedure (Pulmonx) has been developed and is a catheter-based measurement of expiratory flow originating from the treatment target or ipsilateral lobe to assess the functional status of the interlobar fissure.[19] Decline of the measured flow pattern (so-called 'collateral flow negative') has been shown to qualify patients for valve treatment. Especially with fissure completeness scores between 80% and 95%, Chartis is of important additional value and should be performed to get solid treatment outcomes.[30,31] Performing Chartis can be challenging during a bronchoscopy under conscious sedation and spontaneous breathing, but can be as effectively been performed under general anaesthesia with positive pressure ventilation as well, greatly facilitating ease of use.[32] Currently, a new technique to identify the best suitable lobe to be treated using lobar oxygen uptake as perfusion surrogate is also under investigation.[33]

Improved patient selection has significantly improved patient outcomes but it is also evident that the main adverse event as a result of inducing lobar atelectasis or volume reduction is a secondary pneumothorax.[19,34,35] This is presumably due to the remodelling that occurs with volume loss, further decreasing pleural pressures and any areas where the lung is adherent to the pleura may lead to a tear and cause a pneumothorax. This risk ranges from 20% to 25% in the clinical trials and is reflective in clinical

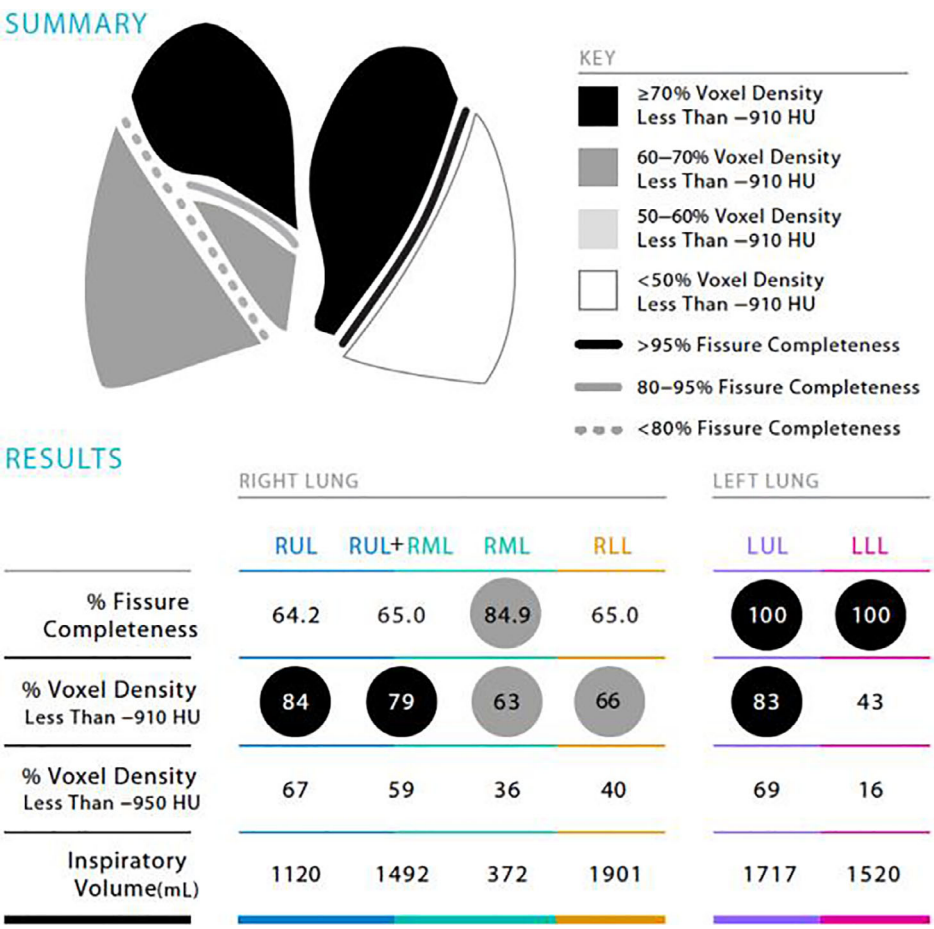

Figure 2 Example image of a quantitative HRCT analysis used for endobronchial valve treatment (StratX analysis; Pulmonx). The image shows the degree of destruction in the different lobes and fissure integrity. The numerical values provide fissure completeness scores, voxel densities at both −910 an d-95 Hounsfield units (HU) and volumes for all the lobes (used with permission). LLL, Left Lower Lobe; LUL, left Upper Lobe; RLL, Right Lower Lobe; RML, Right Middle Lobe; RUL, Right Upper Lobe.

practice. The risk is greatest in the first 4 days with over 89% of the pneumothoraces occurring in this period.[19,27] Late pneumothoraces, which are less likely to be acute tension pneumothoraces, have been observed and are more likely to be secondary to the underlying emphysema than the treatment. The most important aspect in patient care is that the patients are admitted to hospital for at least 3–4 days after valve insertion and the medical teams all are aware of the pneumothorax risk and should be both prepared and able to manage the event. Less than 5% of treated patients develop infectious complications, with some of these involving the treated lobe. Antibiotic treatment is the SoC but in some situations valve removal may be required. Valve expectoration is 2–5% in the clinical trials but should be lower with the introduction of low profile valves with a shorter landing zone.[20] Granulation tissue has been observed in some patients and more unusual adverse events that have been observed include airway torsion especially with left upper lobe treatment.[19,36] In the longer term a significant survival benefit has also been shown in those who achieve EBV-induced lobar atelectasis.[37] This was validated in a larger cohort where 5-year survival was 65.3% with lobar atelectasis (43.9%, no atelectasis; P = 0.009) among 449 patients and even out to 10 years in a smaller retrospective cohort.[38] These potential survival benefits are strengthened by improved predictors of survival, such as Body-mass index, airflow Obstruction, Dyspnoea, and Exercise (BODE) and inspiratory capacity (IC)/total lung capacity (TLC) ratio after EBV treatment,[39] and the large series reported form the Heidelberg group.[40]

SPIRATION VALVE SYSTEM

The SVS is not a true valve and utilized a flexible umbrella device to function as a blocker that is also supposed to allow secretions out from the edge of the device (Fig. 3). The original strategy with this device was to use it as bilateral treatment but without completely occluding the lobe. This strategy was based on airflow re-diversion rather than volume reduction and failed to show clinical benefit.[41,42] The strategy was then aligned with the Zephyr valve to induce unilateral lobar atelectasis, which was investigated in two RCT. The first study (the REACH study) was a multicentre RCT of 99 patients with severe heterogeneous emphysema (≥15% difference between the target and ipsilateral lobes), intact interlobar fissures (≥90%) and hyperinflation comparing the SVS (n = 66) to SoC (n = 33).[43] The primary endpoint, the between-group difference of absolute FEV_1 changes at 3 months, was statistically significant favouring the treatment arm (0.104 ± 0.178 vs 0.003 ± 0.147 L; P = 0.001), although at 6 months the responder rate for $FEV_1 \geq 15\%$ between the two groups was less marked (41% with SVS vs 21% with SoC) The pneumothorax rate in this trial was lower at 7.6%. Longer term data from this trial are not available. The EMPROVE trial was a similar but larger US multicentre RCT of 172 patients with severe heterogeneous emphysema (≥10% difference between the target and ipsilateral lobes), intact interlobar fissures (≥90%) and hyperinflation comparing the SVS (n = 113) to SoC (n = 59).[44] The primary efficacy endpoint, the difference in the groups' FEV_1 changes at 6 months, was statistically significant favouring the treatment arm (0.101 L, 95% CI: 0.060 to 0.141), and a responder rate for $FEV_1 \geq 15\%$ of 36.8% (10.0%, SoC). The primary safety endpoint, a composite score of respiratory-related serious adverse events (SAE), was 31.0% in the treatment arm (11.9%, SoC) largely influenced by a 12.4% incidence of pneumothorax. There were six deaths (5.3%) in the EBV group and one (1.7%) in the control arm. Also for this trial, longer follow-up data have not yet been published, but are expected to become available looking at its investigators and Food and Drug Administration (FDA) guidance.

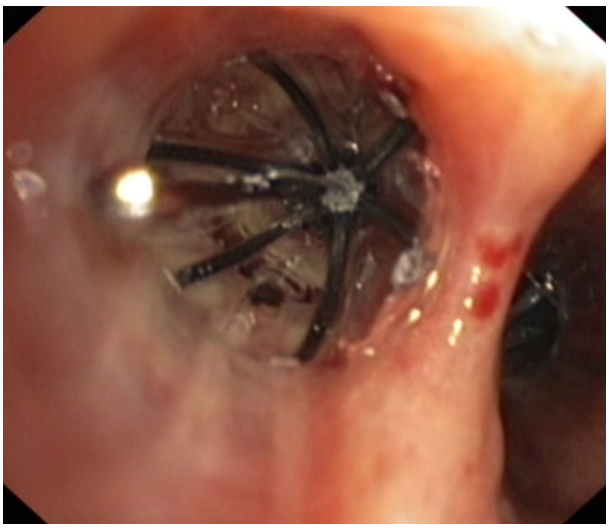

Figure 3 Bronchoscopic image of one SVS (Spiration Valve System; Olympus/Spiration) (courtesy of Pallav Shah).

ENDOBRONCHIAL COILS

The RePneu endobronchial coil treatment (PneumRx/BTG, CA, USA) is a nitinol wire coil-based bronchoscopic therapy for the treatment of patients with severe emphysema, being mostly not eligible for LVRS or EBV treatment.[45–47] About 10–14 memory-shaped coils are placed in the two most diseased emphysematous lobes under fluoroscopic guidance in two sequential procedures (Fig. 4). Post-procedural pneumothoraces are very rare in experienced hands (<5%),[48] but the treatment can be complicated by an increase in infectious complications and coil tension-induced 'coil-associated opacity'.[47–50] The coil treatment exerts its effects through a dual mechanism of re-tensioning the lung tissue, resulting in improved airway tethering, decrease in airway resistance with a reduction in hyperinflation as a consequence, as well as lung volume reduction secondary to the coil-associated opacity phenomenon.[45,46,51,52]

After having established treatment safety, procedural feasibility and a solid efficacy signal on pulmonary function, exercise and quality of life in a number of open label single and multicentre studies,[52–55] the coil treatment was intensively investigated in three RCT (Table 1). In the UK

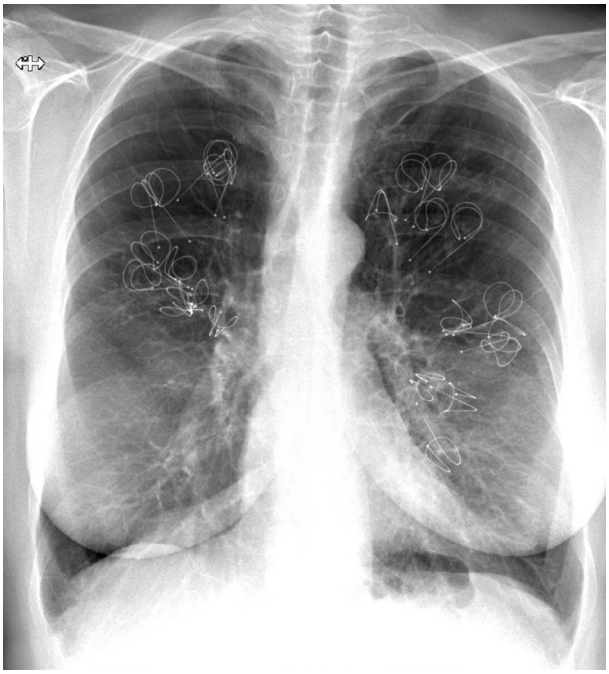

Figure 4 Chest X-ray showing the result after a bilateral endobronchial coil treatment in both the right (11 coils) and left (12 coils) upper lobes (courtesy of Dirk-Jan Slebos).

multicentre RESET trial, 46 emphysema patients were randomized to bilateral coil treatment or best medical care. The primary endpoint, the change from baseline in SGRQ at 3 months post treatment, showed an of improvement of −8.4 points (P = 0.04), with subsequent improvements in both 6MWD (+63.6 m; $P < 0.001$) and FEV_1 (+10.6%; $P < 0.05$).[56,57] In the French multicentre REVOLENS trial, 100 severe emphysema patients were 1:1 randomized to bilateral endobronchial coil treatment or regular care.[58] The primary endpoint, the rate of responders having an improvement in 6MWD of >54 m, showed a significant benefit for the coil treated group (36%) versus the controls (18%) (P = 0.03). Secondary outcomes showed improvements in FEV_1 (+0.09 L; P = 0.001) and SGRQ (−13.4 points). In the combined USA/EU FDA-IDE randomized controlled RENEW trial, the largest of all, 315 severe emphysema patients were studied.[50] In this trial, where over 70% of the included patients had a homogeneous emphysema distribution, the 6MWD primary endpoint at 12 months post treatment showed a +14.6 m difference (P = 0.02) between treatment and control. Also, secondary endpoints significantly improved, with a −8.9 points improvement in SGRQ ($P < 0.001$), a decrease in RV of −0.31 L (P = 0.01) and a 7% increase ($P < 0.01$) in FEV_1. Post hoc analysis showed the best improvements when the RV was >200%, if there was absence of significant cardiac comorbidity and chronic bronchitis.[48] Similar as with the valve treatments, the post hoc analysis indicates the importance of using quantitative CT analysis to plan the treatment.[49]

A few studies did show up to 2- and 3-year treatment benefit,[59,60] with also one study showing the safety and feasibility of retreating these patients at least 3 years out.[61] Longer term follow-up of the RESET study cohort has shown that subjects who had a greater than 105 reduction in residual volume also had a survival benefit at 5 years.[62] Future prospective studies, focusing on better patient selection, mechanism of action and maybe even updated coil design, will show the potential of this interesting treatment approach for our non-valve candidates.

THERMAL VAPOUR ABLATION

Bronchoscopic thermal vapour ablation (BTVA; Uptake Medical Corporation, Seattle, WA, USA) utilizes thermal energy to induce a localized inflammatory response which in turn leads to fibrotic remodelling of the treated region and lung volume reduction.[63,64] Thin slice non-contrast inspiratory CT scans are first evaluated to identify potential treatment targets and an established algorithm allows an estimate of the weight of the tissue to be treated and hence the thermal energy required to treat the target area of the lung. A steam generator delivers the required calorific energy via a catheter introduced through the working channel of the bronchoscope. The catheter has a distal balloon allowing the target segment of the lung to be isolated whilst the vapour is being delivered. The procedure is very quick but the use of general anaesthesia is encouraged as instillation of steam induces a strong cough reflex and it is possible for the catheter to become displaced into a different segmental airway. As the energy calculations are based on specific lung subsegments, it is essential that only the selected target area is treated.[63]

The only multicentre randomized controlled study (STEP-UP) randomized 70 patients with segmental vapour ablation (n = 46) to SoC (n = 24).[65] The patients had severe upper lobe-predominant emphysema (defined as >15% difference between the target and ipsilateral lobes using quantitative CT analysis). One segment was targeted during the first treatment session and up to two segments of a single contralateral lobe in the second session 13 weeks later. The co-primary endpoints, changes in FEV_1 and SGRQ-C scores between the treatment and control groups at 6 months, were statistically significant favouring vapour ablation: FEV_1 of 14.7% (7.8 to 21.5; $P < 0.0001$) and SGRQ-C of −9.7 (−15.7 to −3.7; P = 0.0021). Results were greater at 6 months and treated effects persisted through at 12 months.[66]

The main complication from BTVA is the inflammatory process triggered by the thermal energy. The response is variable between individuals and in some patients there is an exaggerated response leading to fevers and breathlessness secondary to pneumonitis. In some cases, there was dense consolidation resembling pneumonia. In the short term, this may be complicated by bacterial infections. They may also develop exacerbations of their underlying COPD. Hence, one option is to send the patients home with a reserve course of steroids and antibiotics and advice to contact the treating physician if symptomatic. In the longer term, a few patients have developed cavities in the treated areas which can then be colonized with Aspergillus.

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SEALANT

Bronchoscopic biological lung volume reduction, formerly known as emphysematous lung sealant, and now Aeriseal polymeric foam treatment (Pulmonx) is a synthetic crosslink containing glutaraldehyde and polyvinyl alcohol causing a local inflammatory response thereby inducing lung volume reduction. The two components are immediately, before installation into the desired segment, premixed to a foam and then instilled through a dedicated single lumen catheter. The early studies using Aeriseal showed a solid efficacy signal,[67,68] thereby driving a larger RCT (ASPIRE),[69] which was terminated prematurely due to lack of financing. The remaining data from this trial have been published, and repeated increased response rate in FEV_1, quality of life and 6MWD. However, two patients died in the treatment group, and there was an SAE hospitalization rate of over 40%. Sclerosing techniques do however have potential in emphysema treatment, and therefor ongoing efforts are underway to test this application (STAGE trial, NCT02877459). Attempts are also underway to elegantly use this sclerosis agent to close small interlobar fissures,[70] thus to be able thereafter treat the patient with valves (NL4905; NCT04256408).

CONCLUSION AND FUTURE PERSPECTIVES

The meta-analysis of all effective lung volume reduction interventions has clearly demonstrated that the driver for clinical benefit is reducing static lung hyperinflation.[9] The clinical studies have demonstrated that for any particular therapy there is an optimal patient group based on clinical characteristics, comorbidity, degree of hyperinflation and CT features.[19,45,47,71] Hence, patients should be carefully evaluated and discussed in a multidisciplinary setting so that the most effective treatment option for the individual patients is offered.[72,73]

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Professor P.L.S. (MD, MBBS, FERS, FRCP) is a respiratory physician at the Royal Brompton Hospital and the Chelsea and Westminster Hospital and professor of respiratory medicine at Imperial College London. His research interests include airways disease and lung cancer, particularly how interventional bronchoscopy can contribute to these areas. Professor Dr D.-J.S. (MD, PhD) is a pulmonary physician and interventional bronchoscopist at the University Medical Center Groningen, The Netherlands. His main clinical and research focus is the development of innovative bronchoscopic treatments for patients with COPD from bench to bed-side in very early first-in-human studies to phase-3 clinical trials.

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Abbreviations: 6MWD, 6-min walk distance; 6MWT, 6-min walk test; BTVA, bronchoscopic thermal vapour ablation; CT, computed tomography; EBV, endobronchial valve; FDA, Food and Drug Administration; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HRCT, high-resolution CT; LVRS, lung volume reduction surgery; RCT, randomized controlled trial; RV, residual volume; SAE, serious adverse event; SGRQ, St George's Respiratory Questionnaire; SGRQ-C, SGRQ for COPD; SoC, standard of care; SVS, Spiration Valve System.

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