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Endoscopic Lung Volume Reduction: An Expert Panel Recommendation – Update 2019

Felix J.F. Herth[a, b] Dirk-Jan Slebos[c] Gerard J. Criner[d] Arschang Valipour[e] Frank Sciurba[f] Pallav L. Shah[f, g, h]

[a]Department of Pneumology and Critical Care Medicine, Thoraxklinik, Heidelberg, Germany; [b]Translational Lung Research Center Heidelberg, German Lung Research Foundation, University of Heidelberg, Heidelberg, Germany; [c]Department of Pulmonary Diseases, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [d]Department of Thoracic Medicine and Surgery, Lewis Katz School of Medicine at Temple University, Philadelphia, PA, USA; [e]Department of Respiratory and Critical Care Medicine, Ludwig Boltzmann Institute for COPD and Respiratory Epidemiology, Otto Wagner Hospital, Vienna, Austria; [f]Division of Pulmonary and Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [g]Royal Brompton, Harefield NHS Foundation Trust, London, UK; [h]Imperial College, Chelsea and Westminster Hospital, London, UK

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Abstract
Endoscopic lung volume reduction (ELVR) therapies are gaining prominence as a treatment option with guideline recommendations by COPD GOLD and NICE and the recent FDA approval for endobronchial valves. The transition from an experiment-based therapy only to clinical care comes with new challenges. A significant volume of evidence-based data has been published; all data demonstrate consistent improvements in several aspects of patient outcomes. Patients suffering from severe air trapping and thoracic hyperinflation seem to benefit the most from ELVR. In addition to lung function, baseline assessment should ideally include cardiopulmonary exercise testing, high-resolution computer tomography scan, perfusion scintigraphy, and echocardiography. This expert ELVR statement updates best practice recommendations from 2017 regarding patient selection and utilization of these various techniques for treating patients with advanced emphysema.

Introduction

The number of patients suffering from chronic obstructive pulmonary disease (COPD) worldwide is growing, and it is now the third leading cause of mortality in the world [1].

The national and international guidelines recommend [2] that all patients should be treated stage dependently with medical therapy that comprises short- and long-acting bronchodilators including anti-muscarinic drugs and beta agonists, inhaled corticosteroids, pulmonary rehabilitation, and smoking cessation. Selected cases may require prophylactic antibiotics, phosphodiesterase inhibi-

E-Mail karger@karger.com
www.karger.com/res

Felix J.F. Herth
Department of Pneumology and Critical Care Medicine, Thoraxklinik
Röntgenstr. 1
DE—69126 Heidelberg (Germany)
E-Mail felix.herth@med.uni-heidelberg.de

tors, oral corticosteroids, domiciliary and ambulatory oxygen support, and, in the context of respiratory failure, non-invasive nasal ventilation.

COPD is progressive and characterized by symptoms such as cough, shortness of breath, and limited exercise capacity, with some patients developing emphysematous parenchymal destruction [3]. Emphysema is a progressive, irreversible, and debilitating disease resulting from inflammation caused by the prolonged exposure to noxious inhaled agents. The most commonly accepted cause of emphysema is cigarette smoking, but genetic, occupational, and other environmental causes also account for up to 10% of the cases [2]. The alveolar destruction leads to impairment in gas exchange and in air trapping with an increase in residual volume (RV) and hyperinflation. Hyperinflation leads to a mechanical disadvantage of the respiratory muscles and decreased compliance of the chest wall [4], ending in an increase of the work of breathing.

For emphysema, only a few treatment options exist. Lung volume reduction surgery (LVRS) seems to be such an option [5], but due to perceived risks and costs it is not commonly offered [6].

Endoscopic lung volume reduction (ELVR) is a minimally invasive procedure that has been demonstrated to improve outcomes in patients with severe hyperinflation.

In 2016, the first expert panel report [7] published a suggested treatment algorithm. The update was published in 2017 [8]. Since then, additional randomized controlled trials (RCTs) have been published that alter the treatment decisions previously outlined in the original 2016 Expert Panel Report. Based on this increasing level of evidence, the use of ELVR techniques has been adopted and incorporated into the 2017 COPD GOLD [2], updated in the GOLD Report 2019 [9], and the use of one-way endobronchial valves (EBVs) has been recommended by the UK/NICE as a standard-of-care therapy [10]. EBVs have recently obtained US/FDA approval. More recently, a meta-analysis has demonstrated the relationship between lung volume reduction and clinical benefit [11].

Patient Selection

The recommendation for the selection of patients for further evaluation remains unchanged [8]. Potential patients who are candidates for intervention are those who remain highly symptomatic despite receiving optimal medical treatment; i.e., maximal pharmacological therapy with bronchodilators, inhaled corticosteroids in selected candidates, and maintenance with systemic therapies in selected patients. Patients should also have completed pulmonary rehabilitation and/or are participating in a structured physical therapy program; nutrition support should be instituted (cachexia/obesity), and patients should have been counseled about smoking cessation. The key evaluations include a full medical assessment, complete lung function measurements, high-resolution computed tomography (CT) scan of the thorax, and a 6-min walk test (6MWT). Based on the available data, in patients with severe and very severe airflow obstruction (i.e., GOLD stages 3 and 4 [forced expiratory volume in 1 s, FEV_1 20–50%]) who are highly symptomatic (Grades C and D; CAT scores ≥10, Medical Research Council scores ≥2; hyperinflation [RV ≥175% or RV/total lung capacity, TLC ≥0.58]), a reduced 6MWD (100–450 m) may be considered for lung volume reduction therapies (Table 1, 2). When an elevated right ventricular systolic pressure measured by echocardiography (>50 mm Hg) is identified, a right heart catheterization should be undertaken to rule out pulmonary hypertension (PH). In the case of severe PH, ELVR with coils, vapor, and sealants should be avoided. In selected cases with PH, EBV placement may be considered following multidisciplinary discussion [12]. Additionally, limited evidence has been published for successful valve treatment in emphysema patients with a FEV_1 <20% pred. [13, 14].

Radiological Assessment

Recommendations for radiological assessment are more or less unchanged. Standardized non-contrast volumetric CT scans are required to characterize the emphysema, degree of destruction on a lobar basis, evaluate distribution of the emphysema destruction, and determine the integrity of the lobar fissures. The CT protocol should be a standardized non-contrast volume acquisition on a multi-detector scanner platform with thin (0.6–1.25 mm) series with some overlap. The CT scan should come with smooth kernel reconstructions for quantitative CT analysis. The primary assessment should also ensure the absence of significant co-morbidity or abnormalities that require further assessment [15]. If there are unexpected findings such as bronchiectasis, pulmonary nodules, suspected lung cancer, interstitial fibrosis, or severe tracheobronchomalacia that are identified on the screening high-resolution computer tomography, patients should be

Table 1. Baseline characteristics of the recently published valve RCTs

	STELVIO	IMPACT	REACH	LIBERATE	EMPROVE	Transform
Device	EBV	EBV	IBV	EBV	SVS	EBV
Age, years	59	63.7	63.7	64.0	67.2	64
FEV_1 (% pred.)	30	29.4	27.2	28.0	30	30.8
RV (% pred.)	217	275	261	225	210	245
6MWT	367	308	335	311	305	291
Emphysema location	UL/LL	UL/LL	UL/LL	UL/LL	UL/LL	UL/LL
Emphysema distribution	Homo/Hetero	Homo	Hetero	Hetero	Hetero	Hetero

Table 2. Results of the trials

Author [ref.], year	Patients treated, *n*	Device	Follow-up duration, months	ΔFEV_1, mL	ΔRV, mL	Δ6MWT distance, m	ΔSGRQ, points
Klooster [35], 2017 (STELVIO)	40	EBV	12	147	–672	61	–11
Li [50], 2016 (REACH)	58	SVS	6	108	n.a.	42	–12.8
Criner [27], 2018 (LIBERATE)	128	EBV	1	106	–490	39	–7.1
Criner [29], 2018 (EMPROVE)	113	SVS	6	101	–361	15	–8.5
Valipour [22], 2016 (IMPACT)	43	EBV	3	120	–480	40	–9.6
Slebos [41], 2017 (IMPACT)	43	EBV	6	120	–430	28	–7.6
Deslee [51], 2015 (REVELONS)	50	Coils	12	80	–360	36% improvement ≥54	–10.6
Sciurba [43], 2016 (RENEW)	158	Coils	12	50	n.a.	15	–8.9
Herth [44], 2016 (STEP-UP)	44	Steam	6	131	–303	31	–11.1
Shah [45], 2016 (STEP-UP)	44	Steam	1	103	–240	4	–12.1
Kemp [23], 2017 (TRANSFORM)	65	EBV	6	230	–670	79	–6.5

evaluated and treated based on the abnormality detected if considered clinically important [8].

Focal areas of destruction of the alveolar tissue with the preservation of other areas is best described as localized emphysema. Emphysema quantification on CT is usually expressed as the proportion of pixels less than –910 or –950 Hounsfield Units (HU) [16]. The -910 HU density threshold is commonly used for thick-slice (>3 mm) CT scans. This threshold yields the best correlation between emphysema as determined from resected lung tissue and 10-mm-thick slice CT measurements [16]. With the advent of multi-slice scanners, also using volumetric reconstructions, the density thresholds for emphysema for different scan settings have been reinvestigated [17]. The strongest correlation between pathology of macroscopic and microscopic emphysema and CT measurements has been reported at a threshold of –950 HU in 1-mm non-contrast chest CT scans [16]. Several density thresholds have since been proposed for emphysema quantification, but for thin-slice volumetric chest CT scans, –950 HU is currently the most commonly used threshold.

Using emphysema quantification scores, a relative lobar difference of this measure is regarded as heterogeneity. This can be done by simple visual analysis, but more accurate results are produced using CT processing software. Heterogeneity is the relative or percentage difference in the emphysema scores between ipsilateral lobes. To date, no clear definition exists for heterogeneity. In most trials reported, a >10–20% difference in the proportion of pixels of less than −910 HUs or a >10% difference in the proportion of pixels of less than –950 HU has been used.

A complete fissure or intact fissure, as determined via qualitative assessment of CT (QCT) scans, is thought to correspond to lack of inter-lobar collateral ventilation (CV)(Fig. 1).

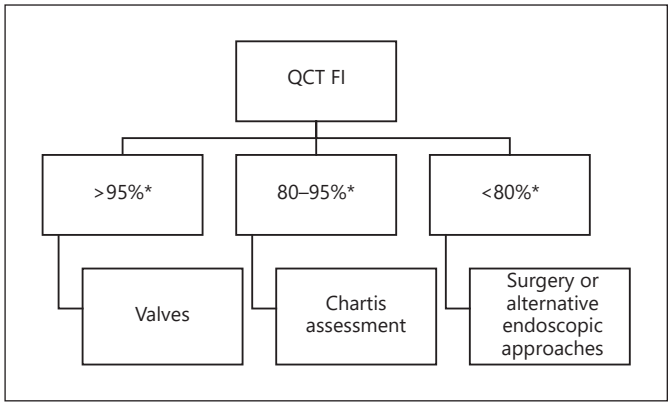

Fig. 1. Assessment to evaluate the collateral flow. * Degree is depending on the used QCT software.

High-resolution CT fissure analysis has been performed for several years; however, only a few trials have focused on patients with emphysema. These studies demonstrate the difficulty of the fissure analysis that presupposes a high degree of experience. One of the major limitations of evaluating fissures on CT scans by the human eyes is its subjective nature and inconsistency in quantifying the degree of integrity. Semi-automated analysis evaluating the integrity of the fissure on a thin-slice CT scan has been developed by several companies. In a recently published paper by Koster et al. [18], CT data from four prospective studies were pooled and analyzed using semi-automated software to quantify the completeness of interlobar fissures. These fissure completeness scores (FCSs) were compared to a reference standard of achieving ≥350 mL of target lobe volume reduction after EBV treatment. A subgroup of patients with partially complete fissures was identified where software had a lower accuracy, and the complementary value of Chartis was investigated in this group. A fissure was defined complete (FCS >95%), incomplete (FCS <80%), or partially complete (FCS between 80 and 95%). The positive predictive value of complete fissures was 88.1%, and the negative predictive value of incomplete fissures was 92.9%, with an overall accuracy of 89.2%. Chartis was utilized in patients with partially complete fissures, with a positive predictive value of 82.3%, a negative predictive value of 84.6%, and an accuracy of 83.3%.

Where there is partial integrity of the fissure (80–95% complete), a Chartis measurement is recommended by the panel. Above 95%, a Chartis is optional, while below 80% it is not useful to further evaluate a patient for treatment with valves [19]. A recent study by Welling et al. [20], showed no difference in outcomes in Chartis results between performing it under conscious sedation (spontaneous breathing) and general anesthesia, thus allowing easier procedures when performed under general anesthesia and best combined with the actual scheduled valve procedure. A possible algorithm for optimal patient selection is illustrated in Figure 2. The definition of a partially completed fissure is partly influenced by the used QCT software utilized, and hence the actual parameters may need to be adapted.

The Technologies

Update on EBVs

Over the last year, several key papers have been published [21–26]. One of the major publications was the multicenter RCT of Zephyr® Endobronchial Valve Treatment in Heterogeneous Emphysema (LIBERATE) [27]. In the Liberate trial, 190 subjects were enrolled with a 2:1 randomization (EBV: standard-of-care [SoC]) at 24 sites. Primary outcome at 12-months was the ΔEBV–SoC of subjects with a post-bronchodilator FEV_1 improvement from baseline of ≥15%. Secondary endpoints included absolute changes in post-BD FEV_1, 6MWD, and St. George's Respiratory Questionnaire (SGRQ) scores. At 12 months, subjects with 47.7% EBV and 16.8% SoC had a $\Delta FEV_1 \geq 15\%$ ($p < 0.001$). ΔEBV–SoC at 12 months was statistically and clinically significant: FEV_1 (L), 0.106L ($p < 0.001$); 6MWD, +39.31 m ($p = 0.002$); and SGRQ, –7.05 points ($p = 0.004$). Significant ΔEBV–SoC were also observed in hyperinflation (RV, –522ml; $p < 0.001$), modified Medical Research Council, –0.8 points ($p < 0.001$), and the BODE Index (–1.2 points). Pneumothorax was the most common serious adverse event (SAE) during the treatment period (procedure to 45 days) in 34/128 (26.6%) EBV subjects. Four deaths occurred in the EBV group during this phase, and one each in the EBV and SoC groups between 46 days and 12 months.

The study confirmed that the Zephyr EBV provides clinically meaningful benefits in lung function, exercise tolerance, dyspnea, and quality of life (QOL) for up to at least 12 months and with an acceptable safety profile in patients with little or no CV in the target lobe.

Intrabronchial Valve (Called "Spiration® Valve System" – SVS since 2018)

At the ERS meetings in Milan (2017) and Paris (2018), the 12-month results of the SVS RCTs have been presented. In Milan, Wang et al. [28] presented the results of 66

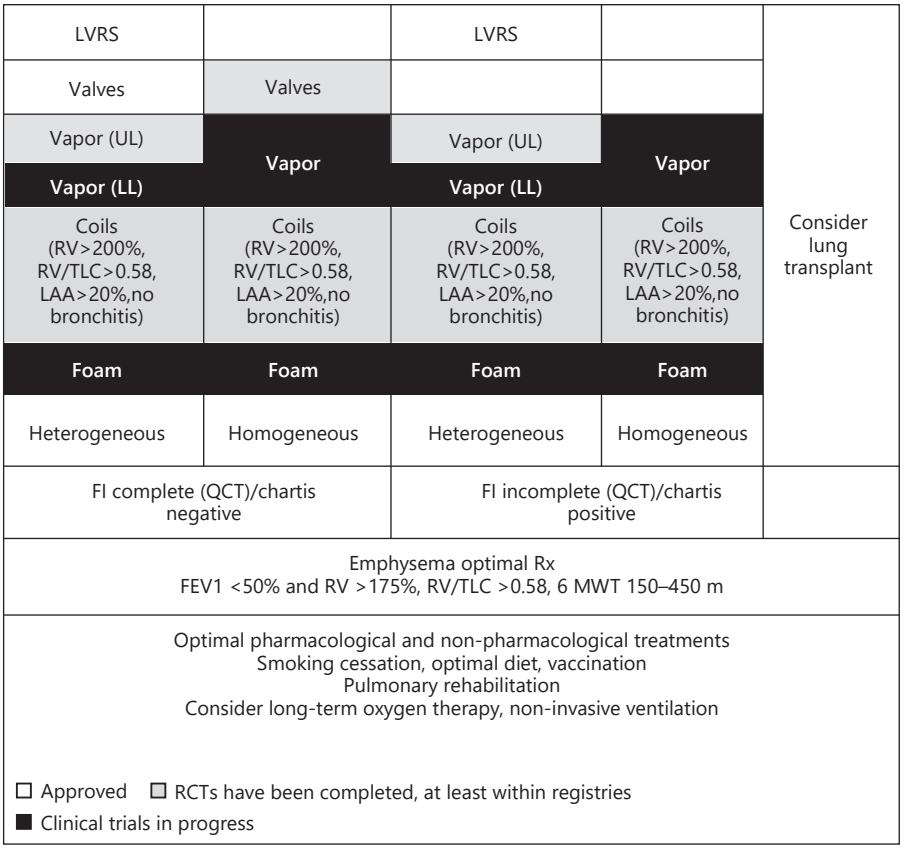

Fig. 2. Recommended algorithm.

patients randomized to active treatment versus 35 patients to the standard-of-care REACH study. In this study, at 12 months, the valve-treated patients showed very modest improvements in FEV_1 (+40 mL), SGRQ (–3.8 points), and 6MWD (+4.5 m). Criner et al. [29] presented the 12-month data of the Emprove trial. This was a multicenter, prospective RCT undertaken at 31 centers in the USA and Canada to assess the safety and effectiveness of the SVS compared to standard medical care. A total of 172 subjects, were randomized in a 2:1 allocation ratio to either the SVS treatment group (n = 113) or the control group (n = 59). The SVS treatment resulted in a mean target lobe volume reduction of 974 mL (52.8%) at 6 months, with the primary endpoint, FEV_1, reaching statistically and clinically meaningful differences between the study groups. At 12 months, the valve group improved in FEV_1 (+99 mL), SGRQ (–9.5 points), and 6MWD (+6.9 m). Pneumothorax and exacerbations of COPD were the most reported complications.

Management of Complications

Pneumothorax is the most frequent complication following insertion of either valve device and is more prevalent in the presence of lobar atelectasis. Hence, to some extent, it is more often associated with technical success. The recent clinical trials have reinforced the finding that the complication is more frequent within the first 3 days after valve insertion [30–33]. Hence, it is important that these patients are admitted to and monitored in a hospital for at least 3 days after valve insertion. Simple intercostal drainage is sufficient in most instances of pneumothorax. If the air leak is moderate with the lung up against the chest wall, simple chest tube drainage or use of an ambulatory drain (with a Heimlich valve) should be considered. In situations where there is a sustained high-flow air leak from the intercostal drain, removal of a single valve should be considered. If this still does not resolve the issue, a further option that may be considered is the removal of all valves. Finally, thoracoscopic intervention may be required. The management of pneumothorax is discussed in more detail by Valipour et al. [34].

ELVR and Survival

In the last months, several retrospective analyses have been published reviewing the previously published evi-

dence [35–37]. The most important review focuses on a survival paper by Gompelmann et al. [36]. She followed 449 emphysema patients who underwent EBV therapy for a mean time of 37.3 ± 21.3 months.

A total of 128 patients (29%) developed complete lobar atelectasis; 34 out of these also experienced a pneumothorax. Fifty patients (11%) developed a pneumothorax without lobar atelectasis and 261 patients (58%) target lobe volume reduction or no volume change. Patients with EBV-induced lobar atelectasis had a significant survival benefit compared to patients without atelectasis ($p = 0.009$; 5-year survival rate 65.3 vs. 43.9%). The advent of pneumothorax in 84 patients did not influence survival ($p = 0.52$). The authors were able to show that lobar atelectasis following endoscopic valve therapy is associated with a survival benefit.

Coils

Besides the existing evidence [38–41], two of the RCTs have published additional data. The multicenter randomized trial performed in France, which recruited 100 patients (Revolens trial [42]), evaluated the efficacy, safety, cost, and cost-effectiveness of nitinol coils in the treatment of severe emphysema compared with usual care. The 2-year data has shown that coil placement is associated with sustained improvements in the QOL, sustained decreases in RV, and an acceptable safety profile with no late-onset or unanticipated events occurring in the post-treatment period. At 2 years, both RV and SGRQ improvements remained significant, whereas the 6MWT, modified Medical Research Council dyspnea scale, and FEV_1 were not statistically different from baseline. This must be considered in the context of severely affected patients with emphysema who are deteriorating over time. There were 45 SAEs in 26 patients within the first year (0.9 SAEs per patient-year), and 27 SAEs in 20 patients over the second year (0.44 SAEs per patient-year). SAEs between the 1- and 2-year follow-up included 18 respiratory events (12 COPD exacerbations, 4 pneumonias, 1 lung transplant, and 1 lung nodule). No unexpected SAEs were observed between 1 and 2 years of follow-up.

The RENEW trial data set has been analyzed in more detail [43]. At the ERS meeting in 2017, Slebos et al. [41] presented a post hoc analysis of the RENEW trial, which was undertaken to identify parameters associated with superior 12-month clinical outcomes. A group of patients with a high baseline RV (>200%), a higher emphysema score (>20%), LAA, and the absence of airways disease was identified that received bilateral treatment of the lobes with greatest ipsilateral emphysematous destruction, as determined by quantitative CT analysis. In that subgroup, greater lobar RV reduction in the treated lobes was achieved, which was associated with a significant improvement in FEV_1 (+15,2%, SE 3.1), SGRQ (–12 points, SE 2), and RV (–0.57L, SE 0.13) from baseline values. The ELEVATE study is a prospective, multicenter, open-label, randomized (2:1), controlled trial designed to evaluate the efficacy of endobronchial coils in patients selected on the basis of the post hoc analysis. The trial aims to enroll 210 patients (140 treatment, 70 control) with severe emphysema with a RV >200% pred. The patients will undergo quantitative CT analysis followed by a formal radiological screen to ensure that only patients with dominant emphysema and minimal airways disease are enrolled. Furthermore, the clinical history, medications, pulmonary function, and CT scans will be scrutinized by at least two members of an eligibility committee prior to randomization. The purpose of this rigorous process is to ensure that only patients who are deemed to be optimal responders are recruited to standardize recruitment. Control patients will be eligible to crossover to coil treatment after 6 months of follow-up. The co-primary effectiveness endpoints are percent change in FEV_1 from baseline to 6 months and QOL measured by the change in SGRQ from baseline to 6 months. All patients (initially treated and cross-over) will be followed for 24 months after initial treatment. Adverse events will be collected on an ongoing basis throughout the study. The first patients have already been enrolled.

The panel expected possible additional predictors as an outcome of this ongoing trial and long-term data information from the initial trials. Therefore, at present, the recommendation is to use the endobronchial coils only in patients with a RV >225%.

Patients need to have significant emphysema (LAA > 20% at 950 HU), be limited by hyperinflation (RV >225% pred. and RV/TLC >58), and show no signs of significant airway wall thickening, bronchiectasis, or clinically significant chronic bronchitis.

Bronchoscopic Thermal Vapor Ablation

Bronchoscopic thermal vapor ablation (BTVA, Uptake Medical Corporation, Seattle, WA, USA) creates a volume reduction by the instillation of heated water in the most destroyed lobe. An inflammatory response is focally induced, which provokes irreversible parenchymal fibrosis and scarring and thus targeted lung reduction in emphysematous tissue.

No addition evidence is available for thermal vapor ablation; hence the evidence is still based on the step-up

trial conducted in upper-lobe-predominant disease [44, 45]. In this trial, the researchers compared thermal vapor ablation with standard medical management and were able to show that targeted thermal vapor ablation of more diseased segments whilst preserving less diseased segments resulted in clinically meaningful and statistically significant improvements in lung function and QOL at 6 and 12 months, with an acceptable safety profile.

The limitation of targeted thermal vapor ablation is the restriction to patients with upper-lobe, heterogeneous disease. At this time, the panel recommends the therapy only for those patients and to be performed only in clinical trials. Trials in patients with homogeneous and lower-lobe disease have already begun, and the results are expected by late 2019.

Biological Lung Volume Reduction

Biological lung volume reduction, using the lung sealant system (AeriSeal), is another irreversible ELVR technique that employs a synthetic polymer to block small airways and collateral channels while promoting atelectasis, remodeling, and scar formation. Since 2017, no new data has been published. All published trials [46–48] confirmed that treatment of up to 3 subsegments during a single session was safe and that bilateral therapy for 4 or more subsegments over 2 separate sessions was associated with therapeutic benefit beyond that achieved with 2- or 3-site therapy, with no emergent safety issues. Based upon these observations, it was hypothesized that an improved risk/benefit could be achieved by performing 4-site therapy during a single session in patients with advanced homogeneous and heterogeneous emphysema. Furthermore, it was noted that patients with baseline DLCO 20–60% pred. benefited the most from the treatment and that outcomes were better following upper-lobe treatment. It was thus hypothesized that limiting the treatment to patients with DLCO 20–60% pred. and acceptable treatment sites in the upper lobes could improve responses to treatment. The technology is currently undergoing further evaluation (NCT02877459) and can only be used in clinical trials in well-selected centers.

What Is Upcoming or To Be Expected?

The field of ELVR is rapidly moving, and new approaches with current devices and new technologies are continuously evaluated. There are some currently ongoing trials in this field, which are worth to be followed. We screened the trial registries clinical trials.gov, NTR, ANZCTR, ISRCTN for COPD, emphysema, volume reduction, endoscopy, and bronchoscopy

Devices

Elevate study (coils) – NCT03360396: a prospective, multicenter, randomized (2:1), controlled study ($n = 210$) comparing outcomes between the endobronchial coil and control groups using best responder criteria for this treatment as inclusion criteria. This trial must finalize the validity of this treatment for our severe emphysema patients.

Reaction study (coils) – NCT02179125: non-randomised, open-label, multi-center intervention study ($n = 48$) focusing on the mechanism of action for coil treatment. Open-label trial exploring the underlying mechanisms of action of endobronchial coil treatment.

Lung Volume Reduction for Severe Emphysema by Stereotactic Ablative Radiation Therapy – NCT03673176: open-label prospective study ($n = 10$).

Next step study (Vapor) – NCT03670121: a pilot study to assess the treatment of patients with homogeneous emphysema using sequential segmental BTVA. Prospective, single-arm pilot study ($n = 15$) following the outcomes at 12 months after initial BTVA treatment

STAGE trial (AeriSeal)- NCT02877459: clinical investigation of a modified staged treatment algorithm using the AeriSeal system ($n = 14$). A multi-center, prospective, single-arm clinical investigation of a modified staged treatment algorithm using the AeriSeal system.

Targeting the Incomplete Fissure

NCT03010449 – LVR in severe emphysema using bronchoscopic autologous blood instillation in combination with intrabronchial valves (blood valves); $n = 20$; single-arm study.

NTR5007 – proactive treatment of CV in CV-positive emphysema patients before EBV treatment; ($n = 20$); single-arm study.

Pneumothorax after ELVR

NCT03034421 – prevention of pneumothorax following endoscopic valve therapy in patients with severe emphysema. RCT (1:1), $n = 130$. Patients will be randomly

assigned in a 1:1 ratio to receive modified medical care including a 48-h bed rest or standard medical care following valve implantation

Chartis Assessment

NCT03205826 – Chartis CV measurement: conscious sedation versus general anesthesia. Prospective study ($n = 50$) comparing outcomes of Chartis under conscious sedation versus general anesthesia.

Rehabilitation and ELVR

Solve trial (NCT03474471): a trial on the effects of bronchoscopic lung volume reduction (BLVR) in severe emphysema. RCT ($n = 135$), rehabilitation before or after ELVR with EBV?

NCT03518177: comparison of the effectiveness of home and supervised pulmonary rehabilitation in candidate patients with BLVR; non-RCT; parallel; ($n = 64$).

Surgery versus Valves

CELEB trial (ISRCTN19684749): lung volume reduction in COPD – surgery versus EBVs; RCT ($n = 76$). Patients will be randomised to either unilateral video-assisted thoracoscopic LVRS or EBVs (BLVR) placed to achieve lobar occlusion.

Expert Algorithm

An initial consensus meeting followed by further panel discussions led to the development of the original algorithm in 2016 [7]. The actual updated algorithm for the advanced treatment of severe emphysema patients, based on the above presented literature, is presented in Figure 2. Following the recent GOLD recommendation, possible patients should be on optimal pharmacological and non-pharmacological treatment. Active smoking is still a clear contraindication in the opinion of the panel members. Following the recommendation from 2016, patients should have significant hyperinflation measured in the lung function by body plethysmography. A non-contrast thin-slice volume CT scan should be performed, and any relevant findings must be reported and co-existent disease identified. All suitable patients should be presented to a multidisciplinary team discussion including radiologists, pulmonologists, thoracic surgeons as well as an interventional pulmonologist.

Unchanged from 2016 for all patients is that lung transplantation should be considered as an option. If so, a connection or easy access to a lung transplantation program is recommended. The option of transplantation is not a contraindication for ELVR [49], and the techniques can be used as a bridging strategy.

Only LVRS and EBVs reached the evidence level to be used outside clinical trials. The current evidence suggests that the degree of volume reduction is directly correlated to the magnitude of benefit, and therefore, the technique most likely to induce volume reduction in a particular patient should be considered [11]. Patients who are not suitable for EBVs or LVRS should be enrolled into the numerous active clinical trials with endobronchial coils, vapor, or sealants. Broader treatment has demonstrated new challenges and unusual complications, and hence clinical experience should be concentrated on the early phase of introduction of these therapies. Therefore, the panel also advises that patients should be treated in expert/high-volume centers, which are participating in clinical trials and registries to capture all treatments when performed outside clinical trials.

Disclosure Statement

All authors treated patients in clinical trials, sponsored by PneumRx/BTG, USA, Pulmonx, Switzerland, and Spiration, USA. F.J.F.H and A.V. treated patients with vapor. All authors advised the supporting companies.

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