an observational study

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Endoscopic lung volume reduction coil

treatment in patients with very low FEV<sub>1</sub>:

### Abstract

**Background:** Endoscopic lung volume reduction coil (LVRC) treatment is a therapeutic option for selected patients with advanced emphysema. The effects and the safety of endoscopic lung volume reduction in patients with very low forced expired volume in one second (FEV<sub>1</sub>) remain to be determined. This study was conducted to assess the effects and the safety of LVRC treatment in patients with very low FEV<sub>1</sub>.

**Methods:** The study was performed as a retrospective observational study in the Department of Respiratory Medicine at the University Medical Center Hamburg-Eppendorf on patients with very low  $FEV_1$ , defined as an  $FEV_1 \le 20\%$  of predicted at baseline in whom LVRC treatment was performed between 1 April 2012 and 28 February 2017.

**Results:** LVRC treatment was performed in 33 patients with very low FEV<sub>1</sub>. Of these, 45.5% were female and 54.5% were male. At baseline, mean FEV<sub>1</sub> was 0.46  $\pm$  0.12 liters (15  $\pm$  3% of predicted), mean forced vital capacity (FVC) was 1.61  $\pm$  0.62 liters (42  $\pm$  13% of predicted), mean residual volume (RV) was 6.03  $\pm$  0.81 liters (275  $\pm$  51% of predicted) and 6-minute walk distance was 229  $\pm$  102 m. Bilateral LVRC treatment was completed in 21 of these patients (63.6%). Bilateral LVRC treatment led to significant improvements in functional parameters with an increase in mean FEV<sub>1</sub> from 0.44  $\pm$  0.11 liters to 0.54  $\pm$  0.12 liters (p = 0.001), equivalent to a relative improvement of 24.5  $\pm$  26.9%, an increase in mean FVC from 1.49  $\pm$  0.54 liters to 1.84  $\pm$  0.49 liters (p = 0.001), a decrease in mean RV from 6.27  $\pm$  0.83 liters to 2.63  $\pm$  1.09 liters (p = 0.004) and an improvement in 6-minute walk distance from 218  $\pm$  91 m to 266  $\pm$  96 m (p = 0.01). There were no cases of respiratory failure requiring mechanical ventilation and no deaths.

**Conclusions:** LVRC treatment was effective and safe in patients with very low FEV<sub>1</sub>.

*Keywords:* emphysema, endoscopic lung volume reduction, endoscopic lung volume reduction coil, interventional pulmonology

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#### Introduction

Chronic obstructive pulmonary disease (COPD) constituted of small airway disease and emphysema is a chronic pulmonary condition with high morbidity and mortality.<sup>1</sup> Emphysema is characterized by the destruction of lung parenchyma with consecutive reduction of gas exchange surface, loss of elastic recoil and hyperinflation. Hyperinflation is a key pathophysiological component that is acknowledged to be clinically relevant due to its contribution

to dyspnea, exercise intolerance and reduction in quality of life.<sup>2</sup> Both static characteristics and dynamic processes contribute to hyperinflation. Dynamic hyperinflation is encountered with increasing breathing frequency as progressive amounts of air are being trapped within the lungs. The onset of dynamic hyperinflation is dependent on disease severity and will occur at ever lower minute ventilations as disease severity progresses.<sup>3</sup>

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Therapeutic options for patients with emphysema are limited. An approach targeting hyperinflation is lung volume reduction, which can be considered in selected patients with advanced emphysema.4 Methods for lung volume reduction include lung volume reduction surgery<sup>5</sup> and interventional bronchoscopic procedures including one-way valves,<sup>6</sup> bronchoscopic thermal vapor ablation<sup>7</sup> and coils.8 Careful patient selection is mandatory before lung volume reduction to ensure benefit and safety. The original procedure for lung volume reduction, lung volume reduction surgery, has been investigated in the national emphysema treatment (NET) trial.<sup>5</sup> An interim analysis identified the subgroup of patients with very low forced expired volume in one second (FEV<sub>1</sub>), defined as an  $\text{FEV}_1 \leq 20\%$  of predicted and either a homogeneous distribution of emphysema on computed tomography or a diffusion capacity ≤20% of predicted, to be at high risk of death after lung volume reduction surgery and also to be unlikely to benefit from the surgery.9 Data on endoscopic lung volume reduction in patients with very low  $FEV_1$  are scarce. Recently, two retrospective observational studies on lung volume reduction with valves in patients with very low FEV<sub>1</sub> have been published. Darwiche and colleagues reported on 20 patients with very low FEV1 and concluded that endoscopic lung volume reduction with endobronchial valves could achieve improvements in lung function and exercise capacity and could be performed safely in this group of patients.<sup>10</sup> Trudzinski and colleagues reported on 20 patients with very low FEV1 and concluded that endoscopic lung volume reduction with endobronchial valves was generally feasible and safe.11

To our knowledge, there are no published data on endoscopic lung volume reduction coil (LVRC) treatment in patients with very low  $FEV_1$ . We therefore conducted this observational study on LVRC treatment in patients with very low  $FEV_1$ to assess the effects and the safety of LVRC treatment in this group of patients.

### Materials and methods

### Study design

The study was designed as a retrospective observational study. It was conducted in the Department of Respiratory Medicine at the University Medical Center Hamburg-Eppendorf, Germany. All patients with very low FEV<sub>1</sub>, defined as an  $\text{FEV}_1 \leq 20\%$  of predicted, in whom LVRC treatment was performed were included in the study, provided the availability of complete datasets for analysis. The ethics committee of the Hamburg Chamber of Physicians waived the need for ethics approval and for the need to obtain consent for the collection, analysis and publication of the retrospectively obtained and anonymized data for this non-interventional study.

## Data collection

All cases of LVRC treatment were retrieved from the electronic endoscopic database (Endobase, version 12.0, Olympus, Tokyo, Japan) by searching within a time frame between 1 April 2012 and 28 February 2017. Patient characteristics, details of the LVRC procedure and data collected during initial assessment and follow-up visits, including the results of the assessments of pulmonary function and exercise capacity, were then collected from the electronic patient database, including the electronic patient record (Soarian Clinicals, version 3.00, Cerner Health Services, USA).

## LVRC treatment

The departmental routine in the evaluation, procedural performance and follow up of patients undergoing LVRC treatment was performed as previously described.12 All patients with advanced emphysema are evaluated considering lung volume reduction surgery, different techniques of endoscopic lung volume reduction and lung transplantation. Lung volume reduction is considered in patients with emphysema phenotype, symptoms despite optimal medical therapy and pulmonary rehabilitation, severe or very severe airflow obstruction as defined by the global initiative for chronic obstructive lung disease (GOLD) definition, hyperinflation at the time of this study with a residual volume (RV) of more than 175% of predicted and the absence of active infection. High-resolution computed tomography scans with multiplanar reconstructions are required for evaluation in all patients prior to lung volume reduction. At the time of this study, densitometry software was not routinely used for analysis in our department. The distribution of emphysema was assessed visually on the basis of the computed tomography images. To select the appropriate technique, the distribution of emphysema, the degree of tissue destruction, the evaluation of interlobar collateral ventilation and comorbidities are taken into account. While the importance of the distribution of emphysema for the selection of the appropriate technique is greatly diminished since the publication of the IMPACT trial showing that treatment with one-way valves is also effective in patients with homogeneous emphysema,<sup>13</sup> at the time of this study homogeneous emphysema, the presence of collateral ventilation in patients with heterogeneous emphysema and sufficient tissue to anchor the coils were among the criteria in favor of LVRC treatment.

LVRC treatment is performed bilaterally in two sequential procedures unless complications or contraindications arise or the patient opts for unilateral treatment only. The aim is to complete the second procedure 1–3 months after the first procedure. The targeted lobe and the sequence are selected according to the distribution of emphysema and the degree of tissue destruction, with the upper lobes being preferentially treated in patients with homogeneous emphysema.<sup>12,14,15</sup>

# Assessment of pulmonary function and exercise capacity

In patients with LVRC treatment, pulmonary function and exercise capacity are assessed in a standardized manner at baseline, between the first and second LVRC treatment and at each follow-up visit. Outpatient follow-up visits are routinely scheduled between the first and second treatment approximately 1 month after the first treatment, and 3 months after the second treatment. Pulmonary function tests including spirometry, body plethysmography and carbon monoxide uptake, as well as blood gas analyses, are performed according to the American Thoracic Society and European Respiratory Society guidelines.<sup>16-20</sup> Exercise capacity is assessed using the 6-minute walk test.<sup>21</sup> Improvements in FEV<sub>1</sub>, RV or 6-minute walk distance were defined to be clinically important if FEV1 increased by  $\geq$ 100 ml,<sup>22</sup> RV decreased by  $\geq$ 0.35 L<sup>23</sup> or 6-minute walk distance increased by  $\geq 25 \, \text{m.}^{24}$ Pulmonary function tests and 6-minute walk tests are performed with the patient under optimal pharmacological bronchodilatative therapy.

#### Adverse events

The electronic patient record was systematically reviewed for adverse events. As routine standard

of care, patients after LVRC treatment are questioned about changes in dyspnea and the occurrence of hemoptysis or chest pain on a daily basis during hospitalization and at each outpatient follow-up visit. Any complications encountered during bronchoscopy as well as respiratory failure requiring mechanical ventilation, pneumothoraces, respiratory infections, COPD exacerbations within 3 months of the procedure, pleuritic pain associated with the position of coils and hemoptysis were considered adverse events.

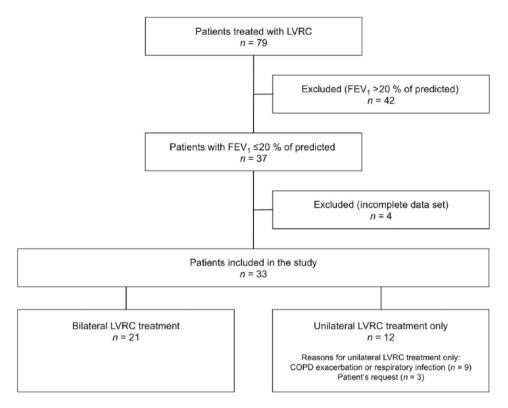
## Data analysis

Categorical variables are presented as absolute numbers and percentages. Continuous variables are presented as mean and standard deviation if normally distributed and as median and range if not normally distributed. Comparisons were performed using the t test for metric data. A twosided p value below 0.05 was considered significant. The software used for statistical analyses was SPSS version 21.0 (SPSS Inc., Chicago, IL, USA).

### Results

### Case selection

A total of 125 LVRC procedures were performed in 79 patients between 1 April 2012 and 28 February 2017. Among these were 37 patients with very low FEV<sub>1</sub>. Complete datasets were available for 33 patients, which were included in this study. Bilateral LVRC treatment was completed in 21 of these patients (63.6%). The process of case selection is illustrated in Figure 1. To determine the fate of the four patients excluded from the study due to incomplete datasets, the referring pulmonologists or general practitioners were contacted and asked to provide information on follow up. It could be determined that one patient, who underwent unilateral LVRC treatment in our department, moved away and successfully completed bilateral LVRC treatment in another hospital. Two other patients were being followed up outside our department. In one of these cases, it could be determined that the patient is alive to date 24 months after LVRC treatment. In the other case, only short-term follow-up data could be obtained stating that the patient was doing well and had experienced improvements in dyspnea and lung function after LVRC treatment. In the one remaining case, the



**Figure 1.** Flow diagram illustrating the process of case selection. COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expired volume in one second; LVRC, endoscopic lung volume reduction coil.

contacted physician declined to provide information. It could, however, be determined that this patient was alive for at least 18 months after LVRC treatment. Data sufficient for detailed analysis of functional parameters or adverse events could not be obtained in any of these cases.

#### Characteristics of patients at baseline

A total of 33 patients were included in the study. Of these, 45.5% were female and 54.5% were male. Mean age was  $60 \pm 8$  years. In addition to optimal pharmacological therapy for their pulmonary disease, which was present in all patients, 51.5% of patients were on long-term oxygen therapy due to chronic hypoxemia and 27.3% were on intermittent non-invasive ventilation. Emphysema was distributed homogeneously in 69.7% and heterogeneously in 30.3% of cases. At baseline, mean  $FEV_1$  was  $0.46 \pm 0.12$  liters  $(15 \pm 3\%$  of predicted), mean RV was 6.03  $\pm$ 0.81 liters  $(275 \pm 51\% \text{ of predicted})$ , mean forced vital capacity (FVC) was  $1.61 \pm 0.62$  liters ( $42 \pm$ 13% of predicted) and mean 6-minute walk distance was 229  $\pm$  102 m. Single-breath diffusion

capacity for carbon monoxide (DLCO) at baseline could be determined in only 20 patients. In the other cases, VC was too low to reliably determine DLCO. For the 20 patients in whom DLCO could be determined at baseline, it was  $1.67 \pm 1.17 \text{ mmol/min/kPa}$  ( $18 \pm 13\%$  of predicted). It has been described above that the interim analysis of the NET trial identified patients with an  $\text{FEV}_1 \leq 20\%$  of predicted and either a homogeneous distribution of emphysema on computed tomography or a DLCO  $\leq 20\%$  of predicted to be at high risk of death after lung volume reduction surgery. In our study, as defined in the inclusion criteria, all 33 patients had an  $\text{FEV}_1 \leq 20\%$  of predicted. The distribution of emphysema was homogeneous in 23 of these patients. Of the 10 patients with heterogeneous emphysema, DLCO could be determined in seven patients. Three of these patients had a DLCO > 20% of predicted, the other four patients had a DLCO  $\leq 20\%$  of predicted. In the remaining three patients with heterogeneous emphysema, VC was too low to reliably determine DLCO. It may therefore be presumed that their DLCO was also  $\leq 20\%$  of predicted. Overall,

#### Characteristics of the LVRC procedure

Bilateral LVRC treatment was completed in two sequential procedures in 21 patients (63.6%). In 12 patients (36.4%), LVRC treatment was performed unilaterally only. Reasons why only unilateral treatment was performed were COPD exacerbations or respiratory infections in nine cases and patient's request in three cases. Characteristics of the 54 LVRC procedures are shown in Table 2.

#### Adverse events

Hemoptysis occurred in the first days after 42 of the 54 LVRC procedures (77.8%). In all but two cases, hemoptysis was mild and self-limiting. In the two remaining cases, hemoptysis required readmission to hospital. In one of these cases bronchial artery embolization was required to terminate the bleeding. This specific patient was on antiplatelet medication with acetyl salicylic acid, but not on any other anticoagulants. Platelet count and international normalized ratio were within the normal range. There were no signs of severe pulmonary hypertension. Exacerbations of COPD were observed within 3 months after 25 of the 54 LVRC procedures (46.3%). Of these cases, eight required readmission to hospital. Pneumonia was observed after 3 of the 54 LVRC procedures (5.6%). Of these cases, two required readmission to hospital. In summary, severe adverse events requiring readmission to hospital occurred after 12 of the 54 LVRC procedures (22.2%). All other adverse events resolved spontaneously or with routine medical care. There were no adverse events during bronchoscopy. There were no cases of respiratory failure requiring mechanical ventilation and no deaths. There were no coil-associated opacities. A summary of adverse events is provided in Table 3.

#### Outcome

After bilateral LVRC treatment there was a significant increase in mean FEV<sub>1</sub> from  $0.44 \pm 0.11$  liters to  $0.54 \pm 0.12$  liters (p = 0.001), equivalent to a relative improvement of  $24.5 \pm 26.9\%$ ; a

significant increase in mean FVC from  $1.49 \pm 0.54$ liters to 1.84  $\pm$  0.49 liters (p=0.001); a significant decrease in mean RV from  $6.27 \pm 0.83$  liters to 5.83  $\pm$  1.09 liters (p = 0.004); and a significant increase in mean 6-minute walk distance from  $218 \pm 91$  m to  $266 \pm 96$  m (p = 0.01) compared to baseline. Improvements defined to be clinically important were seen for FEV<sub>1</sub> in 42.9%, for RV in 57.1% and for 6-minute walk distance in 66.7% of patients. Follow-up values in patients completing bilateral treatment were collected at a median of 84 days after the first procedure and at a median of 49 days after the second procedure. In patients treated unilaterally only, there was a significant increase in FEV<sub>1</sub> from 0.49  $\pm$  0.13 liters to  $0.60 \pm 0.16$  liters (p = 0.02), equivalent to a relative improvement of  $25.7 \pm 26.5\%$ . Changes in mean FVC (from  $1.83 \pm 0.67$  liters to  $2.13 \pm$ 0.72 liters, p = 0.13), mean RV (from 5.61  $\pm$  0.56 liters to 5.78  $\pm$  0.77 liters, p = 0.26) and mean 6-minute walk distance (from  $245 \pm 115$  m to 223  $\pm$  90 m, p = 0.59) were not significant. Follow-up values in patients treated only unilaterally were collected at a median of 70 days after the procedure. Changes in functional parameters are illustrated in Figure 2.

#### Discussion

In this retrospective observational study, we analyzed 33 patients with very low FEV<sub>1</sub>, defined as an FEV<sub>1</sub>  $\leq 20\%$  of predicted in whom LVRC treatment was performed. LVRC treatment was found to be effective and safe in this group of patients.

The degree of airflow limitation, although recognized not to be satisfactory as an isolated parameter,<sup>25,26</sup> has been correlated with mortality in patients with COPD.<sup>27</sup> Therefore, an FEV<sub>1</sub> <25% of predicted has been listed among the criteria for referral to a lung transplant center and an  $FEV_1 < 15-20\%$  of predicted has been suggested as an indication for listing for lung transplantation.<sup>28</sup> However, with the use of the lung allocation score, patients with COPD receive lower priority and hence spend more time on the waiting list.<sup>29</sup> Therefore, therapeutic options to alleviate symptoms and improve or maintain nutritional status and exercise capacity while on the waiting list are needed. As a bridge to lung transplantation, lung volume reduction may help ameliorate or preserve the patient's clinical status and help reach the time of surgery.<sup>30,31</sup> The majority of patients with emphysema will, however, not be

Characteristics	Values
Number of subjects	33
Age (years)	60 ± 8
Gender	
Female	15 (45.5%)
Male	18 (54.5%)
Distribution of emphysema	
Homogeneous	23 (69.7%)
Heterogeneous	10 (30.3%)
Pre-existing treatment for lung disease	
Beta <sub>2</sub> -agonist	33 (100.0%)
Anticholinergic	33 (100.0%)
Inhaled corticosteroid	24 (72.7%)
Systemic corticosteroid	9 (27.3%)
Theophylline	9 (27.3%)
Roflumilast	11 (33.3%)
Acetylcysteine	3 (9.1%)
LTOT	17 (51.5%)
Intermittent non-invasive ventilation	9 (27.3%)
Blood gas analysis	
$PaO_2 < 55 mm Hg or LTOT$	17 (51.5%)
PaCO <sub>2</sub> (mm Hg)	44 ± 7
Base excess (mmol/L)	4.7 ± 2.7
HCO <sub>3</sub> - (mmol/L)	29.6 ± 3.3
рН	$7.43\pm0.03$
Pulmonary function	
FEV <sub>1</sub> /FVC (%)	30 ± 7
FEV <sub>1</sub> (L)	$0.46 \pm 0.12$
$FEV_1$ (% of predicted)	15 ± 3
FVC (L)	$1.61 \pm 0.62$
FVC (% of predicted)	42 ± 13
TLC (L)	$7.78\pm0.91$
TLC (% of predicted)	126 ± 17
RV (L)	$6.03\pm0.81$

(continued)

Table 1. (continued)	
Characteristics	Values
RV (% of predicted)	275 ± 51
RV/TLC (%)	78 ± 7
Raw <sub>tot</sub> (kPa⋅s/L)	$1.60 \pm 0.48$
sRaw <sub>tot</sub> (kPa⋅s)	$10.69\pm3.58$
DLCO (mmol/min/kPa)	$1.67 \pm 1.17^{a}$
DLCO (% of predicted)	$18 \pm 13^{a}$
6-minute walk test (m)	229 ± 102

Values are given as mean and standard deviation or as absolute numbers and percentages. <sup>a</sup>DLCO could be determined in 20 patients only. In the other cases, VC was too low to reliably determine DLCO. DLCO, single-breath diffusion capacity for carbon monoxide; FEV<sub>1</sub>, forced expired volume in 1 s; FVC, forced vital capacity; LTOT, long-term oxygen therapy; PaCO<sub>2</sub>, partial pressure of carbon dioxide in arterial blood; PaO<sub>2</sub>, partial pressure of oxygen in arterial blood; Raw<sub>tot</sub>, total airway resistance; RV, residual volume; sRaw<sub>tot</sub>, specific total airway resistance; TLC, total lung capacity.

suitable candidates for lung transplantation. In this setting, while not being applied as a bridge to lung transplantation, lung volume reduction presents a symptom-modifying treatment approach.

LVRC treatment has been shown to improve lung function, exercise capacity and quality of life in patients with emphysema.14,32-34 The REVOLENS trial and the RENEW trial are the largest randomized trials on LVRC treatment published to date, including 100 and 315 patients respectively. The REVOLENS trial included patients with an RV >220% of predicted and showed improvements in lung function and quality of life in the 50 patients randomized to receive LVRC treatment.<sup>15</sup> The RENEW trial eventually included patients with an RV  $\ge$  175% of predicted and showed that improvements in lung function and quality of life were more pronounced in patients with severe hyperinflation defined as an RV ≥225% of predicted and with a heterogeneous distribution of emphysema.8 It has to be noted that in the REVOLENS trial mean FEV<sub>1</sub> at baseline was 25.7  $\pm$  7.5% of predicted and patients with an  $\text{FEV}_1 < 15\%$  of predicted were excluded from participation, and in the RENEW trial mean  $\text{FEV}_1$  at baseline was 25.7  $\pm$  6.3% of predicted, indicating that FEV<sub>1</sub> was not very low in the majority of patients included in these trials. In our study, mean FEV<sub>1</sub> at baseline was very low, at

Characteristics	First LVRC procedure ( <i>n</i> = 33)	Second LVRC procedure $(n = 21)$	
Treated lobe			
Right upper lobe	21 (63.6%)	4 (19.0%)	
Right lower lobe	3 (9.1%)	1 (4.8%)	
Left upper lobe	6 (18.2%)	14 (66.7%)	
Left lower lobe	3 (9.1%)	2 (9.5%)	
Total number of coils	10 (range 9–13)	10 (range 9–10)	
Values are given as absolute numbers and percentages or as median and range. LVRC, lung volume reduction coil.			

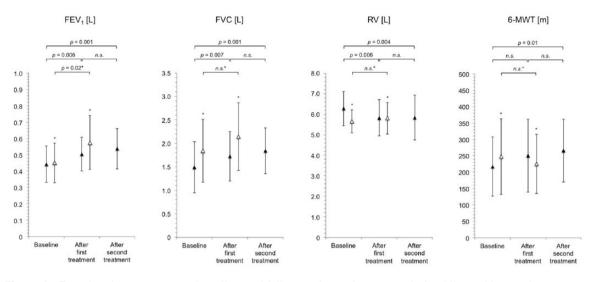
Table 2. Characteristics of the LVRC procedures.

Table 3. Adverse events within 3 months after the LVRC procedures.

Adverse events	First LVRC procedure ( <i>n</i> = 33)	Second LVRC procedure $(n = 21)$
Hemoptysis	27 (81.8%)	15 (71.4%)
Cases of these requiring readmission		2
COPD exacerbation	17 (51.5%)	8 (38.1%)
Cases of these requiring readmission	6	2
Pneumonia	2 (6.1%)	1 (4.8%)
Cases of these requiring readmission	1	1
Pleuritic pain due to position of coil		1 (4.8%)
Values are given as absolute numbers and percent COPD, chronic obstructive pulmonary disease: LVR	5	

 $15 \pm 3\%$  of predicted. After bilateral LVRC treatment in these selected patients with very low FEV<sub>1</sub>, we observed statistically significant and clinically important improvements in FEV<sub>1</sub>, RV and 6-minute walk distance.

Very low FEV<sub>1</sub> puts the patient at an increased periprocedural risk due to limited functional reserves, especially in the event of complications. Indeed, very low FEV<sub>1</sub> in combination with either a homogeneous distribution of emphysema on computed tomography or a very low diffusion capacity has been reported to increase mortality associated with lung volume reduction surgery.<sup>9</sup> LVRC treatment has been shown to have a good safety profile.<sup>35,36</sup> The REVOLENS trial reported 17 severe adverse events within 1 month of the procedure (four COPD exacerbations, three pneumothoraces, one case of hemoptysis, one case of thoracic pain, five cases of pneumonia, one cardiovascular event and two others), as well as one death that was however due to peritonitis.<sup>15</sup> The RENEW trial reported major complications after LVRC treatment including pneumonia requiring hospitalization and other potentially life-threatening or fatal events in 34.8% of cases and other serious adverse events including COPD exacerbations, pneumonia and pneumothorax in 27.7%, 20.0% and 9.7% of cases respectively.8 LVRC in patients with very low FEV<sub>1</sub> in our study was shown to have an acceptable safety profile with severe adverse events requiring readmission to hospital occurring after 12 of the 54 procedures (22.2%). There were no cases of respiratory failure requiring mechanical ventilation and no deaths. For endoscopic lung volume reduction with valves in 20 patients with very low FEV<sub>1</sub>, Darwiche and colleagues reported four



**Figure 2.** Functional parameters at baseline and follow up for patients completing bilateral lung volume reduction coil (LVRC) treatment and for patients with unilateral treatment only. Follow-up values in patients completing bilateral treatment were collected at a median of 84 days after the first procedure and at a median of 49 days after the second procedure. \*Values for patients with unilateral LVRC treatment only. Follow-up values in patients treated unilaterally only were collected at a median of 70 days after the procedure. FEV<sub>1</sub>, forced expired volume in one second; FVC, forced vital capacity; n.s., not statistically significant; RV, residual volume; 6-MWT, 6-minute walk test.

cases of pneumothorax (20%) - of which two were treated with video-assisted thoracoscopic surgery and two with drainage - three cases of pneumonia and two exacerbations of COPD.<sup>10</sup> Trudzinski and colleagues reported five cases of pneumothorax (25%) and three exacerbations of COPD (15%), stating that the greatest risk of the procedure was pneumothorax with prolonged chest tube duration.11 Exacerbations of COPD and pneumonia were equally observed in our study on LVRC treatment. However, bleeding, which was seen after 77.8% of procedures in our study, which was previously reported to occur frequently after LVRC procedures<sup>37</sup> and which led to one procedure-associated death in the RENEW trial,8 is an inherent risk of LVRC treatment. On the other hand, pneumothorax, which was not seen in any patients in our study, is a major risk of endoscopic lung volume reduction with valves. Nevertheless, it has to be noted that there were no cases of respiratory failure requiring mechanical ventilation and no deaths in the patients with very low FEV<sub>1</sub>, neither in the two studies on endoscopic lung volume reduction with valves<sup>10,11</sup> nor in our study on LVRC treatment.

The study has some methodological limitations. The interpretation of the results is limited by potential biases introduced by the retrospective study design and the small number of patients. However, outcome and safety profile of LVRC treatment in this selected and highly vulnerable subgroup of patients with emphysema and very low FEV<sub>1</sub> were comparable with the overall results of previously published studies on LVRC treatment. Hence, further evaluation for LVRC treatment should probably not be withheld from patients otherwise qualified only due to the finding of very low FEV<sub>1</sub>. Prospective studies including more patients are now needed to further assess the value of LVRC treatment in patients with very low FEV<sub>1</sub>.

#### Conclusion

Lung volume reduction coil treatment could be performed safely and effectively in patients with very low FEV<sub>1</sub>. Within 3 months of follow up, it led to statistically significant and clinically relevant improvements in lung function and exercise capacity. There were no cases of respiratory failure requiring mechanical ventilation and no deaths. Hence, further evaluation for LVRC treatment should probably not be withheld from patients otherwise qualified only due to the finding of very low FEV<sub>1</sub>.

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### **Conflict of interest statement**

MS and HK declare that they serve as advisors for PneumRx and have received honoraria for talks and workshops. None of the authors has any financial interest in the company.

#### References

- Vogelmeier CF, Criner GJ, Martinez FJ, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: GOLD executive summary. Am J Respir Crit Care Med 2017; 195: 557–582.
- Gagnon P, Guenette JA, Langer D, et al. Pathogenesis of hyperinflation in chronic obstructive pulmonary disease. Int *J Chron Obstruct Pulmon Dis* 2014; 9: 187–201.
- 3. Ferguson GT. Why does the lung hyperinflate? *Proc Am Thorac Soc* 2006; 3: 176–179.
- Shah PL, Herth FJ, van Geffen WH, et al. Lung volume reduction for emphysema. Lancet Respir Med 2017; 5: 147–156.
- Fishman A, Martinez F, Naunheim K, et al. A randomized trial comparing lung-volumereduction surgery with medical therapy for severe emphysema. N Engl J Med 2003; 348: 2059–2073.
- Klooster K, Hacken Ten NHT, Hartman JE, et al. Endobronchial valves for emphysema without interlobar collateral ventilation. N Engl J Med 2015; 373: 2325–2335.
- 7. Snell GI, Hopkins P, Westall G, *et al.* A feasibility and safety study of bronchoscopic thermal vapor ablation: a novel emphysema therapy. *Ann Thorac Surg* 2009; 88: 1993–1998.
- Sciurba FC, Criner GJ, Strange C, et al. Effect of endobronchial coils vs usual care on exercise tolerance in patients with severe emphysema: the RENEW randomized clinical trial. *JAMA* 2016; 315: 2178–2189.
- National Emphysema Treatment Trial Research Group, Fishman A, Fessler H, et al. Patients at high risk of death after lung-volumereduction surgery. N Engl J Med 2001; 345: 1075–1083.

- Darwiche K, Karpf-Wissel R, Eisenmann S, et al. Bronchoscopic lung volume reduction with endobronchial valves in low-FEV1 patients. *Respiration* 2016; 92: 414–419.
- Trudzinski FC, Höink AJ, Leppert D, et al. Endoscopic lung volume reduction using endobronchial valves in patients with severe emphysema and very low FEV1. *Respiration* 2016; 92: 258–265.
- Simon M, Harbaum L, Oqueka T, et al. Endoscopic lung volume reduction coil treatment in patients with chronic hypercapnic respiratory failure: an observational study. *Ther Adv Respir Dis* 2017; 11: 9–19.
- Valipour A, Slebos D-J, Herth F, et al. Endobronchial valve therapy in patients with homogeneous emphysema: results from the IMPACT study. Am J Respir Crit Care Med 2016; 194: 1073–1082.
- 14. Klooster K, Hacken Ten NHT, Franz I, *et al.* Lung volume reduction coil treatment in chronic obstructive pulmonary disease patients with homogeneous emphysema: a prospective feasibility trial. *Respiration* 2014; 88: 116–125.
- Deslee G, Mal H, Dutau H, *et al.* Lung volume reduction coil treatment vs usual care in patients with severe emphysema: the REVOLENS randomized clinical trial. *JAMA* 2016; 315: 175–184.
- MacIntyre N, Crapo RO, Viegi G, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J* 2005; 26: 720–735.
- Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J 2005; 26: 948–968.
- Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. Eur Respir J 2005; 26: 153–161.
- Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J 2005; 26: 319–338.
- Wanger J, Clausen JL, Coates A, *et al.* Standardisation of the measurement of lung volumes. *Eur Respir J* 2005; 26: 511–522.
- Holland AE, Spruit MA, Troosters T, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. Eur Respir J 2014; 44: 1428–1446.
- Donohue JF. Minimal clinically important differences in COPD lung function. *COPD* 2005; 2: 111–124.

- Hartman JE, Hacken Ten NHT, Klooster K, et al. The minimal important difference for residual volume in patients with severe emphysema. Eur Respir J 2012; 40: 1137–1141.
- Puhan MA, Chandra D, Mosenifar Z, et al. The minimal important difference of exercise tests in severe COPD. Eur Respir J 2011; 37: 784–790.
- Martinez FJ, Foster G, Curtis JL, et al. Predictors of mortality in patients with emphysema and severe airflow obstruction. Am J Respir Crit Care Med 2006; 173: 1326–1334.
- Celli BR. Predictors of mortality in COPD. *Respir* Med 2010; 104: 773–779.
- Anthonisen NR. Prognosis in chronic obstructive pulmonary disease: results from multicenter clinical trials. *Am Rev Respir Dis* 1989; 140: S95–S99.
- Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014. An update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant 2015; 34: 1–15.
- Lane CR and Tonelli AR. Lung transplantation in chronic obstructive pulmonary disease: patient selection and special considerations. *Int J Chron Obstruct Pulmon Dis* 2015; 10: 2137–2146.

 Senbaklavaci O, Wisser W, Ozpeker C, et al. Successful lung volume reduction surgery brings patients into better condition for later lung transplantation. Eur J Cardiothorac Surg 2002; 22: 363–367.

- Venuta F, Diso D, Anile M, et al. Bronchoscopic lung volume reduction as a bridge to lung transplantation in patients with chronic obstructive pulmonary disease. Eur J Cardiothorac Surg 2011; 39: 364–367.
- 32. Deslee G, Klooster K, Hetzel M, *et al.* Lung volume reduction coil treatment for patients with severe emphysema: a European multicentre trial. *Thorax* 2014; 69: 980–986.
- 33. Shah PL, Zoumot Z, Singh S, et al. Endobronchial coils for the treatment of severe emphysema with hyperinflation (RESET): a randomised controlled trial. *Lancet Respir Med* 2013; 1: 233–240.
- Slebos D-J, Klooster K, Ernst A, et al. Bronchoscopic lung volume reduction coil treatment of patients with severe heterogeneous emphysema. *Chest* 2012; 142: 574–582.
- Shah PL and Kemp SV. Springing forward to medium-term results for endobronchial coils for emphysema. *Respirology* 2015; 20: 176– 178.
- Hartman JE, Klooster K, Gortzak K, et al. Longterm follow-up after bronchoscopic lung volume reduction treatment with coils in patients with severe emphysema. *Respirology* 2015; 20: 319– 326.
- Simon M, Ittrich H, Harbaum L, *et al.* Bleeding complications after endoscopic lung volume reduction coil treatment: a retrospective observational study. *Arch Bronconeumol* 2016; 52: 590–595.

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