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COPD

Complete Unilateral vs Partial Bilateral Endoscopic Lung Volume Reduction in Patients With Bilateral Lung Emphysema

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Background: **Intrabronchial valve placement for endoscopic lung volume reduction is used for patients with severe lung emphysema. Different treatment approaches are unilateral valve placement with the goal of complete occlusion and subsequent atelectasis leading to true volume reduction vs bilateral partial closure aiming for redistribution of ventilation but avoiding atelectasis. In this prospective pilot trial, we compared the efficacy of these treatment approaches.**

Methods: **Patients with severe bilateral heterogeneous emphysema were randomized to two groups. In the first group, patients received unilateral valves aiming for total occlusion of one lobe. In the other group, valves were placed in two contralateral lobes with incomplete closure. In all cases, one-way valves were placed via a flexible bronchoscope. Patients were followed at 30 and 90 days, end points being change in pulmonary function tests (PFTs), 6-min walk distance (6MWD), and dyspnea score as measured by the modified Medical Research Council (mMRC) dyspnea score, as well as quality of life as measured by the St. George Respiratory Questionnaire (SGRQ).**

Results: **Twenty-two patients were treated in this study, 11 patients in each arm. At 30 days and 90 days, significant differences were seen in PFT and 6MWD, as well as in mMRC and SGRQ scores, in favor of unilateral treatment. At 90 days, FEV_1 was improved by 21.4% ± 10.7% in this group, but not in the bilateral group (−0.03% ± 13.9%, *P* = .002). One patient in the unilateral group experienced a pneumothorax, and two patients in the bilateral group were treated for transient respiratory failure.**

Conclusions: **Unilateral intrabronchial valve placement with complete occlusion appears superior to bilateral partial occlusion.**

Trial registry: **ClinicalTrials.gov; No.: NCT00995852; URL: www.clinicaltrials.gov**

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Abbreviations: 6MWD = 6-min walk distance; 6MWT = 6-min walk test; ADO = age, dyspnea, and airflow obstruction; BODE = BMI, airflow obstruction, dyspnea, and exercise capacity; ELVR = endoscopic lung volume reduction; HRCT = high-resolution CT; IBV = intrabronchial valve; IVC = inspiratory vital capacity; MCID = minimal clinically important difference; mMRC = modified Medical Research Council; PFT = pulmonary function test; QoL = quality of life; RV = residual volume; SGRQ = St. George Respiratory Questionnaire; TLC = total lung capacity; VENT = Endobronchial Valve for Emphysema Palliation Trial

Static and dynamic hyperinflation of the lung is the main pathophysiologic cause for dyspnea and exercise limitation in patients with severe COPD.[1-3] The assumption that the reduction of lung volumes could improve the elastic recoil of small airways by providing more ergonomic breathing mechanics and diaphragmatic function led to the renaissance of lung volume reduction surgery in the 1990s.[4-7]

Minimally invasive techniques were developed to achieve lung volume reduction, but with lower mortality and morbidity, to improve pulmonary function, patient symptoms, and, ultimately, well-being. The most commonly used of these techniques is the endoscopic placement of intrabronchial valves (IBVs).[8-12] The one-way mechanism of the valves allows air to escape from the distal lung without "fresh" air entering the segment during inspiration. Two different treatment strategies are currently in use. Unilateral treatment occludes the worst lobe completely even in the presence of bilateral emphysema.[8,9,12] Bilateral treatment

targets two contralateral lobes but only occludes them incompletely with the valves. One segment is left open on both sides to avoid atelectasis and risk of pneumothorax.[10,11,13]

Currently it is not clear which technique achieves more improvement in dyspnea and exercise capacity in patients with bilateral heterogeneous emphysema. The aim of this study was to compare the efficacy of these treatment approaches in a prospective randomized fashion.

Materials and Methods

In this single-center study, we prospectively included patients with severe emphysema after obtaining written consent. The study protocol had been approved by the ethics committee of the University of Heidelberg (S-288/2009).

In all patients, endoscopic lung volume reduction (ELVR) with placement of an IBV was indicated because of their severe emphysema. Heterogeneity and bilateral distribution of the emphysema was proven by native thin-slice CT (HRCT) scan and confirmed by perfusion scintigraphy.[14] Furthermore, automated software analysis (Yacta) of the CT scan data was performed, and the distribution of emphysema was visualized.[15] Patients with predominantly unilateral emphysema were excluded, whereas patients with both upper- or lower-lobe-predominant emphysema were included in the study.

Other inclusion criteria were as previously documented for ELVR, with a $FEV_1 < 40\%$ predicted, residual volume (RV) > 150% predicted, and total lung capacity (TLC) > 100% predicted.[8,10,11] Exclusion criteria were walk distance of < 150 m in the 6-min walk test (6MWT) and hypercapnia with $PaCO_2 > 55$ mm Hg.

Patients were recruited into two different study groups according to a stratified (with regard to upper and lower lobe predominance) randomization list with a distribution of 1:1 (Fig 1). Patients in the first group received unilateral IBV placement with complete occlusion of the worst lobe. Patients in the other group had bilateral treatment of either the lower or upper lobes, leaving out one segment on each side.

In all patients, IBVs from one supplier were used (Olympus Medical Co). Details of the valve design, function, and insertion technique have previously been described.[10,11,13] As is our standard protocol, all patients received prophylactic antibiotics and postintervention chest radiograph within 24 h.

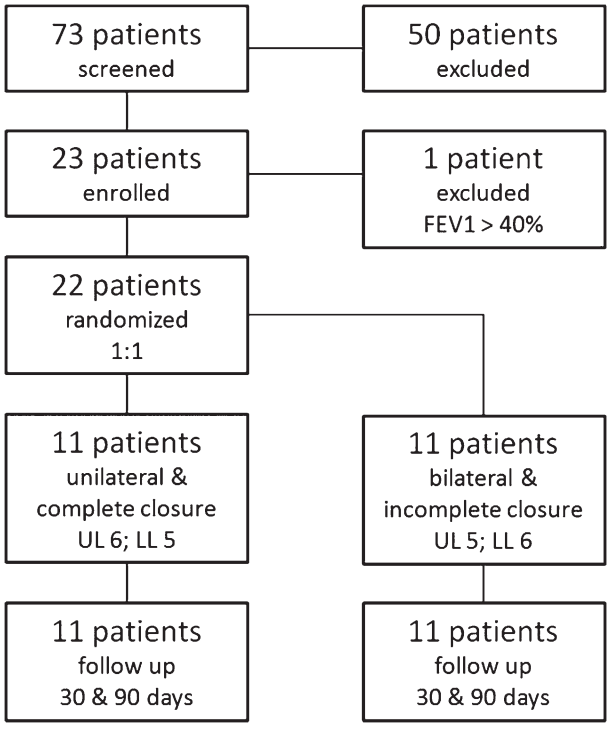

Figure 1. Flow diagram of patients enrolled in the study and procedures performed. LL = lower lobe treatment; UL = upper lobe treatment.

Patients were assessed after 30 and 90 days, and complications were recorded. A pulmonary function test (PFT) and 6MWT as well as questionnaires regarding dyspnea (modified Medical Research Council [mMRC] dyspnea score) and quality of life (QoL) using St. George Respiratory Questionnaire (SGRQ) were repeated.[16,17] Radiologic monitoring was performed with chest radiograph at 30 and 90 days, and a repeat HRCT scan was performed at 3 months. Radiologic definition of atelectasis was total lung parenchymal collapse with the development of a hyperdense tissue area on a lobar, segmental, or subsegmental level. Volume reduction was defined as parenchymal deflation, not necessarily leading to atelectasis.

Primary end points were improvement in FEV_1 and 6-min walk distance (6MWD). Secondary end points were changes in SGRQ as well as in all other lung function parameters (RV, TLC, and inspiratory vital capacity [IVC]). Serious complications (pneumothorax, respiratory failure, or death) and migration of valves were used to assess safety.

Statistical assessment was performed with a software program (SAS8.2; SAS Institute). Descriptive data are expressed as means ± SD or medians; 95% CIs were calculated according to Hodges-Lehmann. To compare both treatment groups, the nonparametric Wilcoxon-Mann-Whitney test was performed ($\alpha = 0.2$). Changes within both groups were tested with the Wilcoxon signed-rank test ($\alpha = 0.05$), and adjustment for multiple tests was not performed.

Results

We enrolled 23 of 73 screened patients between September 2009 and February 2010 (27.4%). One

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patient achieved an FEV_1 of just above the inclusion criteria on the day of the procedure and, hence, had to be excluded from the study. Of the remaining 22 patients (10 women, 12 men, mean age 63.4 years, range 47-78 years) 11 were randomized into the unilateral and 11 into the bilateral group.

Both groups showed no difference in lung function, exercise tolerance, or mMRC and SGRQ score. However, $PaCO_2$ values in the bilateral group and oxygen saturation in the unilateral group were significantly higher, but BMI, airflow obstruction, dyspnea, and exercise capacity (BODE) and age, dyspnea, and airflow obstruction (ADO) indexes to estimate severity of disease showed no significant differences, which leads us to assume an equal distribution of the groups.[18,19] All baseline characteristics are shown in Table 1.

In all patients, endoscopic valve placement according to their randomization was possible without complications. On average, 3.4 IBVs (range 3-4) were required for unilateral treatment and 5.3 IBVs (range 4-11) for bilateral treatment. The distribution of emphysema in both groups was similar. All 22 patients completed the study and were reassessed after 30 and 90 days according to study protocol.

PFT showed significant improvement in FEV_1 and IVC in the unilateral group after 30 days. This improvement was still present after 90 days. Improvement in RV was only significant after 90 days, but the RV/TLC ratio had already decreased significantly in this group after 30 days. TLC showed no significant change in either group during the follow-up period. In the bilateral treatment group none of the other pulmonary function parameters changed (Tables 2, 3).

Improvement in exercise capacity demonstrated in the 6MWD was only observed in the unilateral group after 30 and 90 days. Seven patients improved by more than 30 m after ELVR, whereas in the bilateral group only one patient was observed to have an

Table 1—*Baseline Characteristics of the Patients*

Variable	Unilateral Group	Bilateral Group	*P* Value[a]
Demographic characteristics			
Age, y	63.02 ± 7.56	63.78 ± 8.24	.519
BMI	23.88 ± 3.63	22.52 ± 5.7	.489
Arterial blood gas levels			
Pa_{O_2}, mm Hg	67.33 ± 5.95	62.62 ± 7.99	.217
Pa_{CO_2}, mm Hg	40.75 ± 5.40	45.20 ± 4.79	**.033**
S_{O_2}, %	95.14 ± 1.56	92.94 ± 3.33	**.058**
Lung function			
FEV_1			
Value, L	0.84 ± 0.19	0.78 ± 0.19	.410
% Predicted	29.4 ± 3.95	31.9 ± 7.62	.652
IVC			
Value, L	2.72 ± 0.73	2.44 ± 0.62	.292
% Predicted	75.9 ± 16.72	79.2 ± 20.19	.606
RV			
Value, L	5.93 ± 1.23	5.76 ± 1.63	.962
% Predicted	264.8 ± 46.98	269.3 ± 66.89	.797
TLC			
Value, L	8.65 ± 1.59	8.24 ± 2.07	.652
% Predicted	142.2 ± 15.31	145.4 ± 24.94	.847
RV/TLC			
Value, %	0.69 ± 0.06	0.69 ± 0.06	.949
Exercise performance			
6MWT distance, m	305.4 ± 68.7	293.2 ± 85.9	.617
Quality of life (SGRQ), points			
Total	59.04 ± 16.33	58.84 ± 14.19	.898
Symptoms	61.33 ± 16.25	57.38 ± 16.01	.748
Activity	78.75 ± 18.17	81.83 ± 14.49	.932
Impacts	47.29 ± 20.17	45.99 ± 16.22	.898
Scores, points			
mMRC dyspnea score	2.64 ± 1.03	3.09 ± 0.94	.326
BODE index	5.73 ± 1.62	6.09 ± 1.7	.459
ADO index	6.27 ± 1.19	6.64 ± 1,43	.601

Data are presented as mean ± SD. 6MWT = 6-min walk test; ADO = age, dyspnea, and airflow obstruction; BODE = BMI, airflow obstruction, dyspnea, and exercise capacity; IVC = inspiratory vital capacity; mMRC = modified Medical Research Council; RV = residual volume; SGRQ = St. George Respiratory Questionnaire; S_{O_2} = oxygen saturation; TLC = total lung capacity.

[a]Wilcoxon-Mann-Whitney test, level of significance $\alpha = 0.2$. Values in bold are statistically significant.

Table 2—*Mean Changes of the Different Parameters in the Unilateral Group After 30 and 90 d*

Unilateral Group	30 d	*P* Value[a]	90 d	*P* Value[b]
Lung function				
△FEV_1, mL	+267 ± 154	**.0010**	+180 ± 90	**.0020**
In % from baseline	+31.8 ± 18.3	…	+21.4 ± 10.7	…
△IVC, mL	+425 ± 451	**.0186**	+453 ± 300	**.0020**
In % from baseline	+15.6 ± 16.6	…	+16.7 ± 11.0	…
△RV, mL	−546 ± 1307	.5370	−872 ± 796	**.0049**
In % from baseline	−9.2 ± 22.0	…	−14.7 ± 13.4	…
△TLC, mL	−86 ± 1222	.1748	−357 ± 874	.3203
In % from baseline	−1.0 ± 14.1	…	−4.1 ± 10.1	…
△RV/TLC, %	−6.3 ± 7.1	**.0322**	−7.4 ± 3.2	**.0020**
In % from baseline	−9.1 ± 10.3	…	−10.7 ± 4.6	…
Exercise performance				
△6MWD, m	+47.8 ± 55.7	**.0137**	+48.9 ± 53.0	**.0244**
In % from baseline	+15.7 ± 18.2	…	+16.0 ± 17.4	…
Quality of life (SGRQ), points				
△Total	−12.2 ± 13.4	**.0029**	−11.8 ± 10.6	**.0068**
△Symptoms	−16.6 ± 26.6	.0537	−12.3 ± 16.2	.0537
△Activity	−8.7 ± 17.3	.1328	−9.0 ± 19.8	.1797
△Impacts	−12.7 ± 12.9	**.0010**	−12.9 ± 11.0	**.0049**
Scores				
mMRC dyspnea score	−1.1 ± 1.1	.0703	−1.2 ± 1.25	**.0234**
BODE index	−2.0 ± 1.3	**.0039**	−1.8 ± 1.47	**.0215**
ADO index	−1.6 ± 1.1	**.0215**	−1.2 ± 1.1	**.0215**

Data are presented as mean ± SD. Values in bold are statistically significant ($P < .05$). Scores on the SGRQ range from 0 to 100, with higher scores indicating a worse quality of life. The MCID is −4 points. Scores on the mMRC scale range from 0 to 4, with higher scores indicating greater severity of dyspnea. The MCID is 1 point. 6MWD = 6-min walk distance; △ = change in value from baseline; MCID = minimal clinically important difference. See Table 1 legend for expansion of other abbreviations.

[a]Wilcoxon signed-rank test.

[b]Sign-test.

Table 3—*Mean Changes of the Different Parameters in the Bilateral Group After 30 and 90 d*

Bilateral Group	30 d	*P* Value[a]	90 d	*P* Value[b]
Lung function				
△FEV_1, mL	+13 ± 140	.7168	−24 ± 117	.6240
In % from baseline	+1.6 ± 17.9	…	−3.1 ± 15.0	…
△IVC, mL	+2 ± 388	1.0000	+15 ± 349	.9180
In % from baseline	0.1 ± 15.9	…	+0.6 ± 14.3	…
△RV, mL	−61 ± 990	.7646	+85 ± 446	.7002
In % from baseline	−1.1 ± 17.1	…	+1.5 ± 7.7	…
△TLC, mL	−117 ± 1038	.8311	+122 ± 563	.7471
In % from baseline	−1.4 ± 12.6	…	+1.5 ± 6.8	…
△RV/TLC, %	+0.7 ± 5.8	.7646	+0.1 ± 3.6	.8311
In % from baseline	+1.0 ± 8.4	…	+0.1 ± 5.2	…
Exercise performance				
△6MWD, m	−25.0 ± 81.5	.5566	−52.3 ± 81.2	.0801
In % from baseline	−8.5 ± 27.8	…	−17.8 ± 27.7	…
Quality of life (SGRQ), points				
△Total	−0.3 ± 9.8	.8311	+2.12 ± 8.5	.5771
△Symptoms	−6.1 ± 15.9	.3652	+6.7 ± 12.5	.1230
△Activity	+1.0 ± 12.9	.6250	−2.3 ± 20.8	1.0000
△Impacts	+0.7 ± 11.7	.7002	+3.5 ± 9.1	.2402
Scores, points				
mMRC dypsnea score	0.0 ± 1.0	1.0000	0.0 ± 1.3	1.0000
BODE index	+0.5 ± 1.1	.2188	+0.6 ± 1.6	.2891
ADO index	+0.1 ± 1.1	1.0000	0.0 ± 1.4	1.0000

Data are presented as mean ± SD. Scores on the SGRQ range from 0 to 100, with higher scores indicating a worse quality of life. The MCID is −4 points. Scores on the mMRC scale range from 0 to 4, with higher scores indicating greater severity of dyspnea. The MCID is 1 point. See Table 1 and 2 legends for expansion of abbreviations.

[a]Wilcoxon signed-rank test.

[b]Sign-test.

improvement 90 days after ELVR. In this group, the 6MWD deteriorated continuously over the follow-up period and eight of the 11 patients were unable to achieve their baseline results.

QoL recorded in the SGRQ was significantly improved in the unilateral group after 30 and 90 days. Improvements were more pronounced within the domains of symptoms and impacts rather than in the activity score, but the significant improvement of the total score appears to be due to improvement in the impact domain. Overall, in nine of 11 patients in the unilateral group, an improvement of > -8 points was observed after 90 days. Furthermore, these patients improved by > -1 point in mMRC score after 30 and 90 days. The improvement was significant after 90 days but not after the first 30 days. In the bilateral and incomplete treatment group, no significant improvement in either SGRQ or mMRC score was observed at any point during follow-up.

Thirty days after ELVR, atelectasis was found on chest radiograph in seven of the 11 patients in the unilateral group, but in none in the bilateral treatment group. After 90 days, complete or partial atelectasis was visible on HRCT scan in five patients with complete closure and one patient of the bilateral group (Fig 2). Visual volume reduction on HRCT scan after 90 days was present in nine patients of the unilateral group and three of the other group. Radiologic evidence of atelectasis and volume reduction is, hence, significantly more common in the unilateral treatment group ($P = .004$ and $P = .030$).

Complications observed were four exacerbations, two per group, requiring antibiotic treatment and/or steroids without the need for hospitalization. In the bilateral group, two additional patients developed respiratory failure 52 and 76 days post ELVR. One patient required noninvasive ventilation; the other patient necessitated intubation at a different hospital and was transferred back to us for successful weaning. Both patients had their IBVs removed without difficulty after 90 days because of lack of clinical improvement.

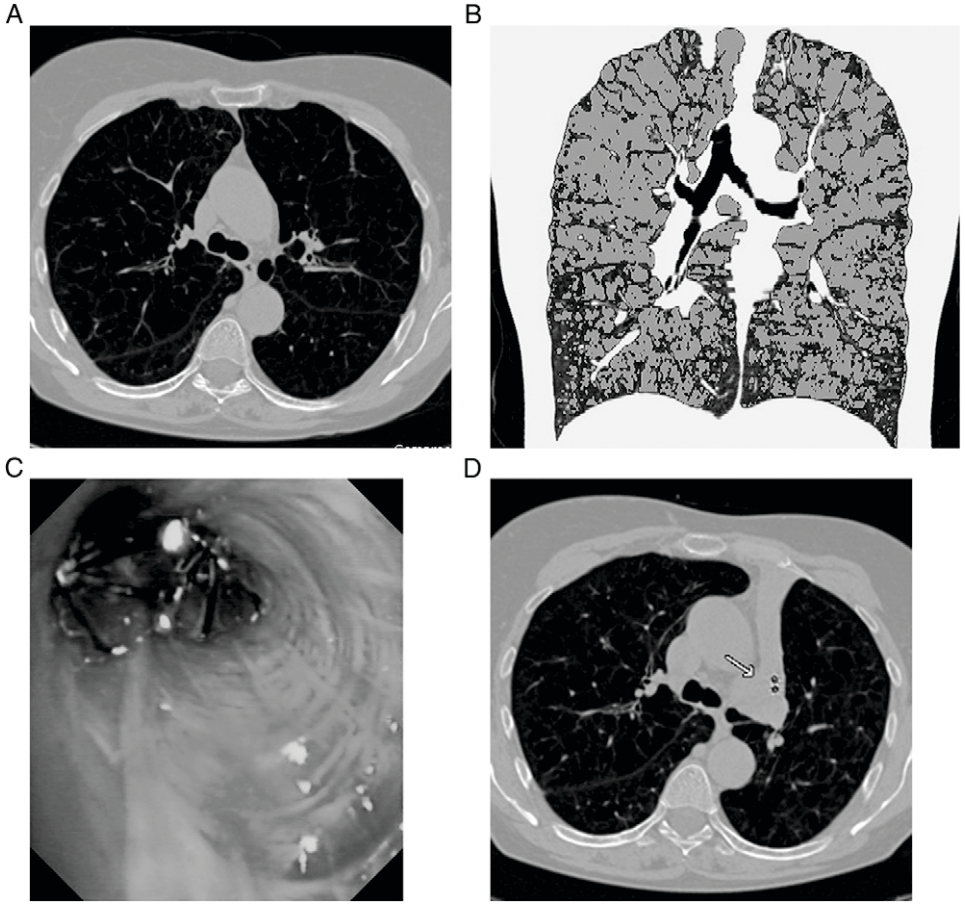

FIGURE 2. Patient No. 7 treated in the unilateral arm with complete closure of the left upper lobe. A, CT scan prior to valve placement. B, Corresponding software analysis shows bilateral upper-lobe-predominant emphysema. C, Endoscopic image with two intrabronchial valves occluding the left upper lobe. D, Corresponding CT scan after 90 d with complete atelectasis of the treated lobe. Arrow indicates two implanted intrabronchial valves.

One patient developed a pneumothorax at day 4 following ELVR with complete closure of his left upper lobe, which required insertion of a chest drain. It was removed after 12 days and the patient was discharged home 16 days after the procedure. He showed significant improvement after 90 days ($\triangle FEV_1$, +15.4%; $\triangle$6MWD, +29.6%). No other complications were observed in either group; there was no migration of valves and no mortality.

Discussion

The aim of unilateral valve treatment with complete closure of all segments of one lobe is a real volume reduction of the most hyperinflated lobe. The maximum volume effect is achieved by developing a complete lobar atelectasis. In the largest published trial on ELVR (Endobronchial Valve for Emphysema Palliation Trial [VENT]) there was an increase of 4.3% in FEV_1 after 6 months in the treatment group, which was significant, but this mean change of 34.5 mL may not be clinically important for the individual patient.[8] However, in patients who had radiologic evidence of an intact fissure as a marker for lack of collateral ventilation, a significantly larger volume reduction of $>$ 700 mL was found. This ultimately led to a greater improvement in PFT and exercise capacity in this subgroup.

The aim during bilateral treatment with incomplete closure is a redistribution of ventilation toward the nontreated parts of the lung. It is postulated that clinical improvement can be achieved through a reduction of dynamic hyperventilation even without causing atelectasis.[10] Coxson et al[20] were able to show through CT scan volumetric measurements that moderate volume reduction of the treated upper lobe can occur with following increase in volume of the untreated lobe of about 300 mL. This change in volume correlates with health-related QoL in the SGRQ but has not been translated into improvements in PFT or 6MWD.[20]

It appears that a clinically relevant improvement in outcome correlates with maximal possible volume reduction, but the two approaches we used have never been compared directly, to our knowledge. Our study confirms that complete occlusion is a prerequisite for the development of atelectasis or visual volume reduction. Comparison of both treatment groups shows a significantly better outcome for patients with complete closure of one lobe as opposed to bilateral incomplete closure (Table 4). Lung function, exercise capacity, and QoL improved in almost all parameters by 30 days, and improvements were sustained at 90 days compared with incomplete occlusion (Fig 3). Only the activity score and TLC showed no significant difference between both groups after 90 days. The reduction in RV and RV/TLC ratio as a parameter for hyperinflation is better demonstrated in the change in IVC rather than in the change in TLC.

For the patient, an improvement in exercise capacity, QoL, and, finally, survival are important. The minimal clinically important difference (MCID) defined by Redelmeier et al[21] is 54 m, but this goal seems to be too high in daily practice, especially for patients with severe COPD.[21,22] For these patients, Puhan et al[23] suggest an improvement in 6MWD of 26 ± 2 m as the threshold for clinical relevance. The

Table 4—*Between-Group Difference in Change From Baseline at Day 30 and Day 90*

Variable	Day 30	*P* Value	Day 90	*P* Value
Lung function				
FEV_1, mL	250 (110 to 360)	**.0003**	200 (110 to 300)	**.0002**
IVC, mL	440 (0.0 to 790)	.0676	460 (140 to 760)	**.0043**
RV, mL	−630 (−1,430 to 160)	.0652	−880 (−1,340 to −480)	**.0010**
TLC, mL	−190 (−810 to 730)	.7130	−350 (−1,120 to 280)	.4672
RV/TLC, %	−7.5 (−12.4 to −2.0)	**.0083**	−7.7 (−10.7 to −4.7)	**.0004**
Exercise performance				
6MWD, m	61 (8 to 127)	**.0201**	94 (39 to 150)	**.0034**
Quality of life (SGRQ), points				
Total	−8.3 (−2.1 to −21.5)	**.0104**	−15.6 (−22.6 to −6.3)	**.0104**
Symptoms	−9.0 (−27.9 to 8.0)	.3653	−18.0 (−31.8 to −4.1)	**.0192**
Activity	−7.3 (−19.6 to 1.2)	.1453	−13.4 (−20.2 to 7.0)	.2843
Impacts	−10.0 (−22.3 to −2.9)	**.0104**	−17.4 (−24.3 to −9.4)	**.0032**
Scores, points[a]				
mMRC dypsnea scale	−1.0 (−2.0 to 0.0)	**.0426**	−1.0 (−2.0 to 0.0)	**.0477**
BODE index	−3.0 (−4.0 to −1.0)	**.0003**	−3.0 (−4.0 to −1.0)	**.0026**
ADO index	−2.0 (−3.0 to −1.0)	**.0026**	−1.0 (−2.0 to 0.0)	**.0416**

For between-group median differences, values were calculated with the use of a Hodges-Lehmann estimator with nonparametric 95% CIs; Wilcoxon signed-rank test; Values in bold are statistically significant ($P < .05$). See Table 1 legend for expansion of abbreviations.
[a]Sign-test.

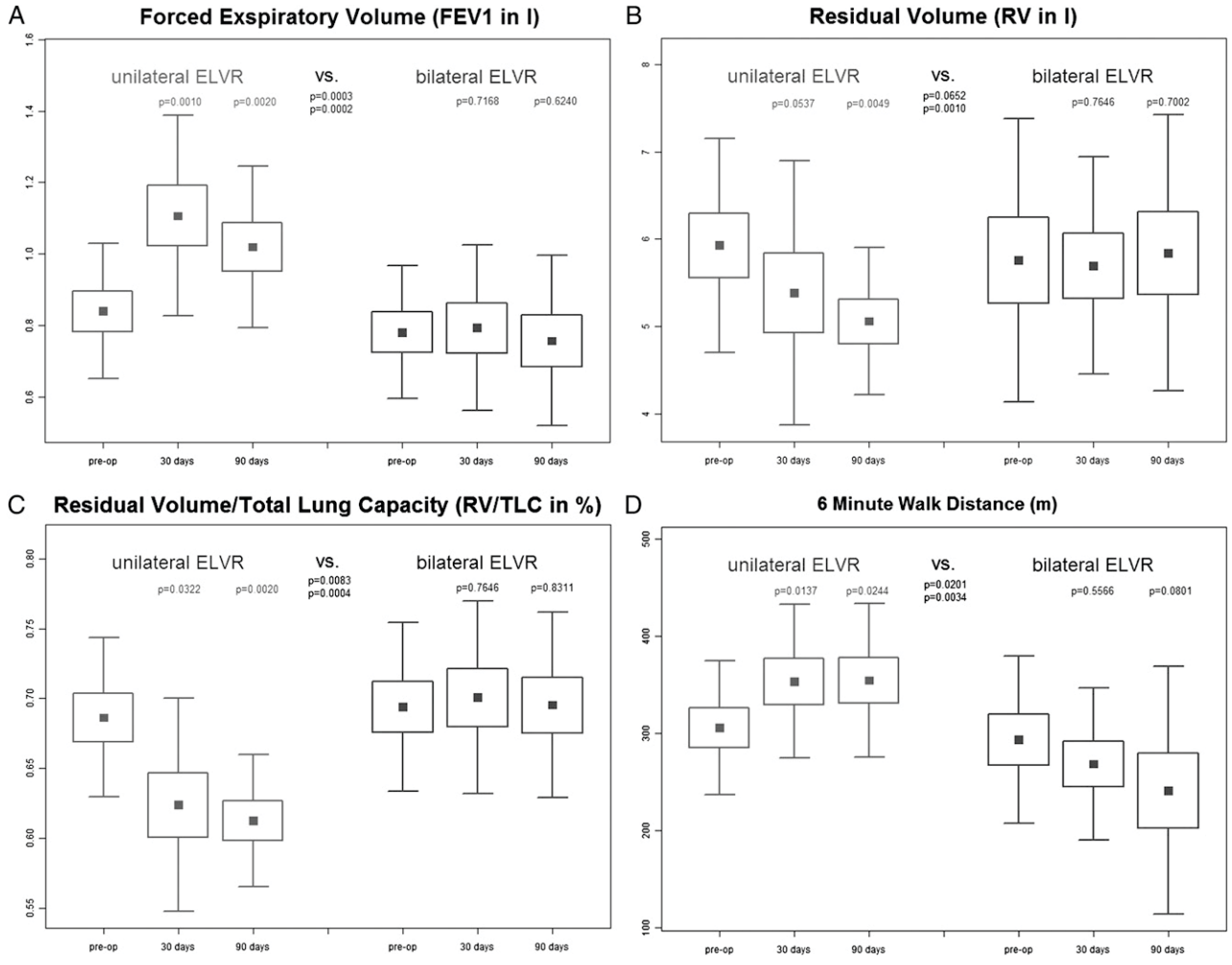

FIGURE 3. A, Change in FEV_1 of both groups after 30 and 90 d. B, Change in RV of both groups after 30 and 90 d. C, Change in RV/TLC of both groups after 30 and 90 d. D, Change in 6-min walk test of both groups after 30 and 90 d. ■ = mean values; □ = ± SD; ⊤ = maximum, ⊥ = minimum. ELVR = endoscopic lung volume reduction.

unilateral group with complete closure surpassed this MCID at nearly 50 m after 30 and 90 days, whereas the bilateral group with partial treatment showed a reduction in walk distance.

The threshold for clinical relevance of the SGRQ is −4 points.[17] At an improvement of −12 points, as achieved in the unilateral group, a placebo effect can be excluded and an actual improvement in QoL can be assumed. Furthermore, the unilateral group achieved an improvement in mMRC of > 1 point, which is the defined MCID for this test, after 30 and 90 days. An improvement in QoL after bilateral incomplete treatment, which was shown in previous trials, was not confirmed in this study.

Hopkinson et al[24] examined the survival of 19 patients after ELVR with valves. Patients who had not developed an atelectasis died according to their ADO index, but all patients with a postinterventional atelectasis were still alive after 6 years. In our study, we were able to show that after unilateral valve placement the ADO and BODE index improve. Hence, it appears that mortality may be reduced with this minimally invasive therapy in patients with stage COPD III/IV and severe emphysema, but it appears unlikely after bilateral treatment because of lack of improvement in lung function and exercise capacity and absence of atelectasis formation.

Even though we did not use HRCT scan analysis of fissures, the results in the unilateral group are well above the values from VENT.[8] It can be assumed that the reason for this is the improvement in patient and target selection and more procedural.[8,25,26] In comparison with the VENT cohort, patients in this study had similarly severe airway obstruction but more hyperinflation (mean FEV_1, 29% ± 4% vs 30% ± 8% predicted; mean RV, 269% ± 47% vs 216% ± 44% predicted). The HRCT scans of all patients were further analyzed with specific software.[15] By visualizing the most destroyed areas, the distribution and heterogeneity of emphysema can be better evaluated

than by specific scores. We further used perfusion scintigraphy for planning of therapy and in the unilateral group treated the lung with lower perfusion. However, future studies should estimate the presence of collateral ventilation based on CT scan analysis and/or bronchoscopic measurements to predict the likelihood of volume reduction and improve the outcome of treated patients.[27]

In unilateral complete closure of one lobe, an increased incidence of pneumothoraces is to be expected, especially after treatment of the left upper lobe with closure of the lingula.[11] Overall, the risk of pneumothorax associated with the procedure appears to be acceptable, and most patients would likely accept the risk in view of the procedure itself having the potential to significantly improve their exercise capacity and QoL. In bilateral ELVR, on the other hand, there is a risk of respiratory failure that is explained by the near complete blocking of two lobes and lack of improvement of respiratory mechanics.

The limitations of this study are its short follow-up period as well as the low patient number, and the performance of procedures in a single center, as is common in pilot studies. Another potential limitation is the fact the average $Paco_2$ was slightly higher in patients with bilateral incomplete treatment, but it is unlikely that this influenced study outcome, as other indicators of disease severity did not show a difference. The results should be verified in a multicenter, prospective study with a larger number of patients with unilateral and complete closure treatment.

Conclusion

Unilateral valve placement with complete closure of a single lobe can improve lung function, exercise capacity, and QoL to a clinically relevant degree in patients with severe bilateral pulmonary emphysema. It is significantly superior to bilateral incomplete treatment. The sole improvement in SGRQ cannot justify the risk of an interventional procedure in our opinion, and, hence, a unilateral treatment should be preferred even in bilateral emphysema.

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Dr Eberhardt: contributed to patient selection, follow-up, and data sampling; performing the procedures; and writing and editing the manuscript.
Dr Gompelmann: contributed to patient selection, follow-up, and data sampling and writing and editing the manuscript.
Dr Schuhmann: contributed to patient selection, follow-up, and data sampling and writing and editing the manuscript.
Dr Reinhardt: contributed to patient selection, follow-up, and data sampling and writing and editing the manuscript.
Dr Ernst: contributed to performing the procedures and writing and editing the manuscript.
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