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Bronchoscopic Lung Volume Reduction With Endobronchial Valves Exclusively of the Middle Lobe in Patients With Emphysema

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Bronchoscopic lung volume reduction (BLVR) treatment using 1-way endobronchial valves has been shown to significantly improve pulmonary function, exercise tolerance, and quality of life, and also may lead to a survival benefit, in carefully selected chronic obstructive pulmonary disease (COPD) patients with severe emphysema and hyperinflation.[1–7]

The 1-way endobronchial valves are placed in the most emphysematous lobe. In previous randomized controlled trials, the middle lobe was almost always treated in combination with the right upper lobe.

Only 1 single case has been published before on middle lobe treatment in an emphysema patient, with in that same paper a summary of 5 additional patients treated for a bulla in the middle lobe.[8] However, to our knowledge, this is the first analysis of patients with emphysema who underwent BLVR with Zephyr endobronchial valves (PulmonX) exclusively in the right middle lobe. Our aim was to investigate the efficacy of BLVR with endobronchial valves exclusively of the middle lobe in patients with emphysema.

From January 2008 till February 2021, 15 patients (53% male) with COPD underwent a middle lobe treatment at our center (~3% of the total number of patients treated with valves). All patients were included in the analysis and all provided written informed consent for the scientific use of their data.

At baseline and after endobronchial valve treatment, quantitative analysis was performed on high-resolution computed tomography (HRCT) scans (LunQ; Thirona). Furthermore, pulmonary function tests, quality of life questionnaires (Saint George Respiratory Questionnaire), and 6-minute walk tests were performed at baseline and 6 months after treatment. To test for differences between baseline and follow-up, a Wilcoxon signed-rank test was used. Data is described as median (minimum to maximum). All statistical analyses were performed using IBM SPSS Statistics, version 23 (IBM Corp.), and P values <0.05 were considered statistically significant.

Baseline characteristics were: median age 63 years (range: 36 to 74 y), forced expiratory volume in 1 second 24 (16 to 51) % of predicted, residual volume of 228 (162 to 392) % of predicted, 6-minute walk distance 323 m (165 to 539 m), and SGRQ total score of 46 points (37 to 78 points). Target lobe volume was 908 mL (436 to 2510 mL), and 67% had a $>95\%$ fissure integrity of the right middle lobe fissure [median fissure score of 99% (54% to 100%)]. The destruction of the middle lobe, measured on the HRCT scan was 58% (46% to 84%) on voxel density −950 HU.

Valve placement was performed under general anesthesia in 12 patients, using deep conscious sedation in 2 patients, and under local anesthesia 1 patient. Before valve placement,

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Chartis assessment was performed in 6 patients (40%), in 3 patients the outcome was no collateral ventilation and in 3 patients the outcome was undeterminable due to no flow output. The median procedure time was 3 minutes (1 to 7 min) and in every patient, one endobronchial valve size 5.5 was placed in the entrance of the combined segment RB4/5. The median hospital stay was 1 night (1 to 4 nights) after treatment.

At 6 months follow-up, outcomes significantly improved and were clinically meaningful (Table 1). One pneumothorax occurred 5 days posttreatment and was treated with chest drainage for 9 days. There were no other serious adverse events and no patients died.

Our results showed that BLVR treatment with endobronchial valves exclusively in the middle lobe, leads to a statistically significant and clinically meaningful reduction in target lobar volume, lung function, exercise tolerance, and quality of life (Fig. 1). The results of our study are consistent with the results of 6 previously published case reports, were there was clinical improvement in 5 of 6 patients.[8]

The target lobe with the most pronounced destruction is most often an upper or lower lobe, and therefore chosen as target lobe for lung volume reduction with valves. The right middle lobe is rarely the most destroyed lobe and the lobe volume is usually much smaller compared with the upper and lower lobes. Therefore, closing of the middle lobe with endobronchial valves may have too little effect. However, in this study, we showed that if the middle lobe shows the most pronounced destruction, that treatment of a relatively small volume [middle lobe volume 908 (436 to 2510 mL)] results in clinically relevant outcomes. Furthermore, our analysis demonstrates that occlusion of the middle lobe leads to significant target lobar volume reduction, with 12 of 14 patients (86%) reaching the minimal clinically important difference of > −22.4% for target lobar lobe volume reduction.[9]

The absence of collateral ventilation between target lobe and ipsilateral lobe is key for inducing an atelectasis after endobronchial valve placement. However, measurement of collateral ventilation in the middle lobe is challenging, due to a "no flow" output. Fissure integrity is a surrogate for the absence or presence of collateral ventilation.[10] In our cohort, 67% had a fissure completeness score > 95%, suggesting absence of collateral ventilation.[11]

The first cases were performed with doing a Chartis measurement. At that time, we did not have the quantitative computed tomography (CT) analysis reports available, and therefore no information about the fissure integrity. Since we had the quantitative CT and the fissure was above 95%, we decided not to perform Chartis. Other reasons not to perform a Chartis are: in all cases, the middle lobe was very much expanded and overinflated, so the change that there will be collateral ventilation is really low. Furthermore, also to get a reliable flow output from such an overexpanded lobe, was very difficult. And the time and costs of the Chartis assessment was another argument to just place the valve. By placing one valve, the air cannot directly go to the middle lobe, so the lobe will be less hyperinflated and the patient can still have the benefit of the treatment. In our experience over the years, it became clear that at least an 80% middle lobe fissure integrity score can still be worthwhile to schedule for a Chartis assessment.

Posttreatment CT scan showed significant target lobar volume reduction with a high

TABLE 1. Effectiveness Outcomes: Change From Baseline to 6 Months After Endobronchial Valve Treatment Exclusively in the Middle Lobe (N = 15)

	Baseline	Absolute Change	Relative Change
TLV	908 mL (436-2510 mL)	−835 mL (−2510 to −68 mL)	−98% (−100% to −16%)
FEV_1	0.77 L (0.38-2.28 L)	+60 mL (−130 to +730)	+9.1% (−11.5% to +98.6%)
FVC	2.54 L (1.20-7.55 L)	+310 mL (−210 to +2240 mL)	+11.5% (−4.7% to 102.3%)
RV	4.99 L (3.69-7.58 L)	−305 mL (−1770 to +30 mL)	−6.35% (−38% to 0%)
TLC	7.94 L (6.17-13.74 L)	−140 mL (−1110 to +170 mL)	−1.4% (−11% to +2.7%)
SGRQ	46 points (37-78 points)	−6.5 points (−35 to +6 points)	
6MWD	323 m (165-539 m)	+40 m (−16 to +155 m)	

Values are presented in median (minimum-maximum). All outcomes were statistically significant compared with baseline ($P < 0.05$).

FEV_1 (N = 15) indicates forced expiratory volume in 1 second; FVC, forced vital capacity; 6MWD (N = 11), 6-minute walk distance; RV (N = 14), residual volume; SGRQ (N = 13), Saint George Respiratory Questionnaire total score; TLC (N = 15), total lung capacity; TLV, target lobe volume; TLVR (N = 14), target lobe volume reduction.

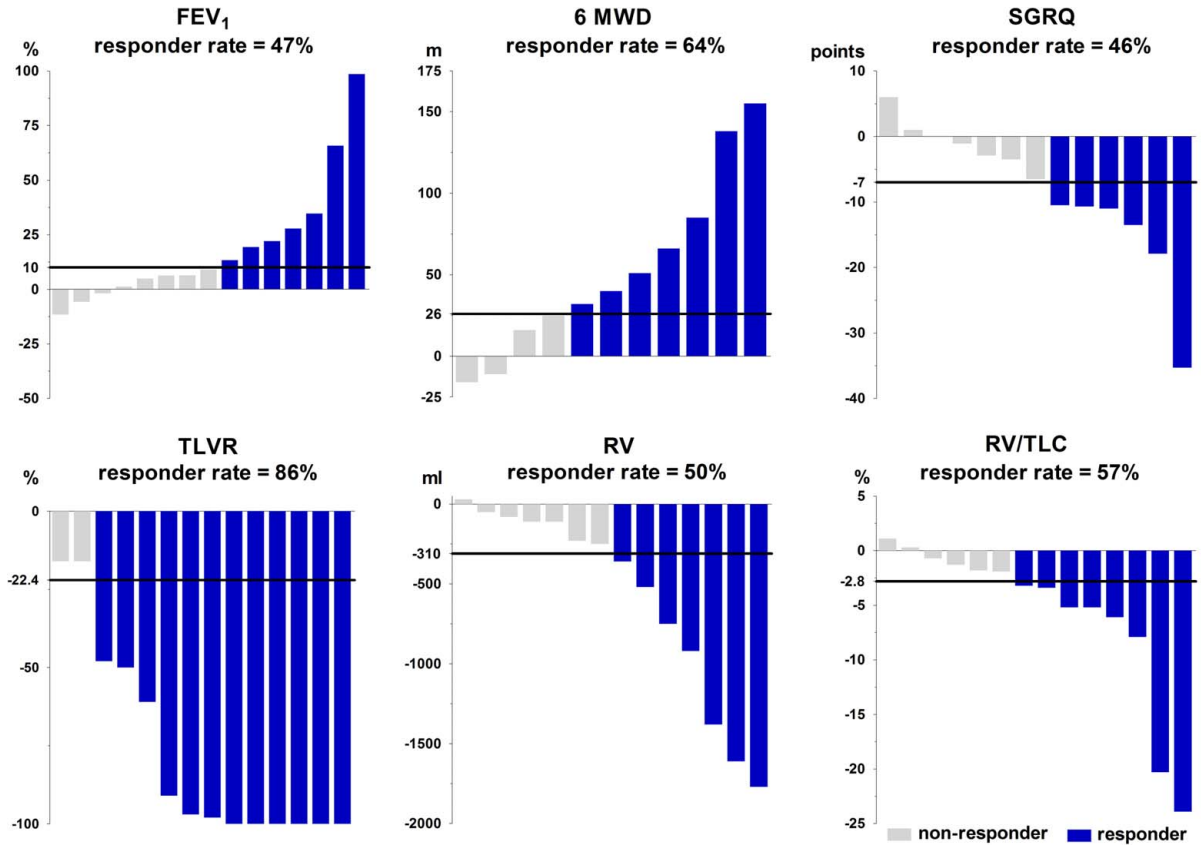

FIGURE 1. Minimal clinically important difference (MCID) responder results at 6 months after endobronchial valve treatment exclusively in the middle lobe. The MCID is shown in the graph as a black horizontal line. Response rates were calculated by counting the number of patients for whom the change at 6 months met or exceeded the MCID. Individual outcomes per patient in change from baseline. FEV_1 (N = 15) indicates forced expiratory volume in 1 second (MCID > +10%); FVC, forced vital capacity; 6MWD (N = 11), 6-minute walk distance (MCID > 26 m); RV (N = 14), residual volume (MCID > −310 mL); SGRQ (N = 13), Saint George Respiratory Questionnaire total score (MCID > −7.1 points); TLC (N = 15), total lung capacity (MCID RV/TLC > −2.8%); TLVR (N = 14), target lobe volume reduction (MCID TLVR > −22.4%); TLV, target lobe volume.

responder rate. In 4 patients, the fissure completeness score was <80%. In 2 of these patients, only slight volume reduction was obtained after treatment. However, 2 patients did show significant volume reduction (−61% and −100% target lobe volume reduction).

Despite the fact that our cohort included only a small sample size, the significant target lobar volume reduction of the middle lobe suggests that with careful patient selection treatment benefit can be achieved. All patients in our cohort had advanced COPD, remained highly symptomatic despite receiving optimal medical, had severe hyperinflation [residual volume of 228 (162 to 392) % of predicted], and a "clear" treatment target lobe with having pronounced destruction of lung tissue in the middle lobe.

To conclude, the benefit of BLVR treatment with Zephyr endobronchial valves is not limited to only patients with upper or lower lobe predominant emphysema. Endobronchial valve treatment exclusively in the middle lobe in patients with emphysema can improve lung function, exercise tolerance, and quality of life. However, careful selection of patients with hyperinflation and a clear treatment target lobe identified on HRCT is key.

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