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ORIGINAL RESEARCH

Two-year Results of Bronchoscopic Lung Volume Reduction Using One-Way Endobronchial Valves: Real-World Single Center Data

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Background: Bronchoscopic lung volume reduction (BLVR) using one-way endobronchial valves (EBV) is a minimally invasive treatment for patients with advanced emphysema and severe hyperinflation. While several randomized controlled trials have demonstrated improvements in lung function, exercise performance, and quality of life, information on long-term outcomes of BLVR outside clinical trial settings are limited.

Objective: This study provides real-world data with a follow-up of up to two years, incorporating the BODE index (Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index), as part of the follow-up assessments.

Methods: Data were collected for all patients treated with BLVR at the University Hospitals of Leuven, Belgium, including lung function parameters, 6-minute walking distance, respiratory questionnaires, and the BODE index at intervals of 3, 6, 12, and 24 months. A composite outcome combining FEV1 (forced expiratory volume in 1 second), 6MWD (6-minute walk distance), and SGRQ (St. George's Respiratory Questionnaire) was used to evaluate the overall impact of BLVR. Mixed model analyses were performed.

Results: All outcome parameters, including FEV1, residual volume (RV), 6MWD, modified Medical Research Council (mMRC) and SGRQ exhibited significant improvement up to 1 year of treatment. RV and mMRC maintained statistical significance compared to baseline at the 2-year follow-up. The BODE index as well, revealed a significant improvement persisting up to 2 years of treatment. Response rate for the composite outcome was 86% (44/51) at one year and 71% (17/24) at 2 years follow-up.

Conclusion: Follow-up data of a real-world setting show maintained benefits of bronchoscopic lung volume reduction with endobronchial valves up to 2 years after treatment, for patients of whom the valves are still in situ. A potential survival benefit of BLVR, based on BODE, and high response rate on the composite outcome was present, in patients who remained in follow-up.

Keywords: COPD, bronchoscopic lung volume reduction, emphysema

Introduction

Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disease of the lung leading to chronic bronchitis and lung emphysema, presenting with irreversible expiratory airflow limitation.[1] COPD still poses a significant global health burden, affecting millions of individuals and giving rise to significant mortality and morbidity rates. Despite the availability of both pharmacological and non-pharmacological interventions, patients with moderate-to-severe disease remain symptomatic with a high burden of dyspnea, which adversely affects their quality of life and exercise capacity. In emphysema patients, airflow obstruction and loss of elastic recoil contributes to expiratory airflow limitation, leading to air trapping and a subsequent decline in inspiratory capacity. This phenomenon, called hyperinflation, is particularly important during exercise when expiration time is shortened.[2]

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Bronchoscopic lung volume reduction (BLVR) utilizing one-way endobronchial valves (EBV) is a minimally invasive treatment, used in patients with advanced emphysema and severe hyperinflation.[3] In well-selected patients, it leads to a decrease in residual volume and alveolar compression, thereby leading to a better elastic recoil, improved expiratory airflow and better respiratory muscle mechanics due to an upward displacement of the diaphragm.[2] It has shown short-term (3 to 6 months) clinical important improvements on lung function, exercise capacity and quality of life in multiple randomized controlled trials.[4–8] In these studies, forced expiratory volume in 1 second (FEV1) improved on average with 22%, residual volume (RV) with −570 mL, 6-minute walk distance (6MWD) with 49 m and St. George's Respiratory Questionnaire by (SGRQ) with −9 points between 3 and 12 months of follow-up.[9]

Based on these trials, BLVR with endobronchial valves has been included in the GOLD recommendations with level A evidence in selected patients with advanced emphysema.[1] Crucial for treatment success are the presence of an emphysematous target lobe and the absence of interlobar collateral ventilation assessed by quantitative computed tomography (CT) analysis and the Chartis system (PulmonX Corp., Redwood City, CA).[10,11]

To date, reports on long-term outcomes of BLVR using real-world clinical data remain limited. Extended observational data of BLVR cohorts from RCTs show treatment effect until 12 months follow-up.[8,12,13] Only a few studies report clinical data with three years follow-up.[14–17] These studies report effects on conventional endpoints such as airflow obstruction, exercise capacity and quality of life separately, using a unidimensional approach to evaluate disease outcomes. Recent trials demonstrate that the use of multicomponent composite endpoints, such as clinically important deterioration (CID), might hold more value in evaluating disease activity and progression.[18] In addition, survival benefit has been suggested in patients undergoing BLVR,[19–21] yet only a few studies incorporate BODE index *(body-mass index, airflow obstruction, dyspnea, and exercise capacity index)*, known as a predictor of mortality in COPD,[22] in long-term follow-up.

To address these limitations in existing literature, the aim of the current study was to investigate long-term effect of BLVR based on real-world clinical data, including uni- and multidimensional endpoints and provide insight into the clinical evolution of these patients. Therefore, the study describes long-term data of the routine clinical practice of patients who underwent BLVR with EBV in an expert center for COPD in Belgium.

Methods

Participants

For this observational, single-center cohort study, follow-up data of all patients treated with BLVR at the University Hospitals of Leuven (Belgium) between November 2017 and October 2023, were prospectively collected up to two years. The study was approved by the ethical committee UZ/KU Leuven (S60207 and S64530). All participants provided written informed consent prior to data collection. All patients were extensively screened and discussed at the multidisciplinary emphysema expert meeting (MEET), as described elsewhere.[23,24] Briefly, all treated patients had obstructive spirometry and hyperinflation, suffered from dyspnea and reduced exercise capacity despite optimal pharmacological and non-pharmacological treatment. Recommended inclusion criteria and contra-indications were applied in line with expert recommendation and the Belgian reimbursement regulations.[25] The extent and distribution of emphysema and the fissure integrity was evaluated using quantitative HRCT analyses.

Procedure and Study Design

Prior to the intervention, all patients performed a baseline assessment (see below). Fissure completeness was estimated by visual and quantitative CT analysis (LungQ software Thirona, Nijmegen, the Netherlands). If fissure integrity was between 80 and 95%, interlobar collateral ventilation was assessed by using the Chartis System (PulmonX Corp., Redwood City, CA). If fissure integrity was above 95%, no Chartis System was used, in line with the national reimbursement regulations. The intervention was performed under general anesthesia in intubated patients with mechanical ventilation support. Zephyr valves (PulmonX Corp., Redwood City, CA) were used in all cases. According to our protocol, patients were hospitalized for five days after the intervention. One month after the procedure, a chest CT was

performed to evaluate the position of the valves and the presence or absence of lobar atelectasis. All patients were invited for a follow-up visit at 3, 6, 12 and 24 months post intervention.

Outcome Measurements

The following clinical assessments were performed before treatment and during the follow-up visits: 1) pulmonary function by post-bronchodilator spirometry (according to the ATS/ERS guidelines), retrieving FEV_1 and FVC; body plethysmography (according to the ATS/ERS guidelines), retrieving RV and TLC; and lung diffusing capacity for carbon monoxide, retrieving TLco; 2) functional exercise capacity by 6-minute walk distance (6MWD) (according to the ATS/ERS guidelines);[26] 3) severity of dyspnea by the modified Medical Research Council (mMRC) dyspnea scale; 4) health-related quality of life by the Saint-George Respiratory Questionnaire (SGRQ) and COPD Assessment Test (CAT); 5) anthropometric measurements (weight and height); 6) occurrence of COPD exacerbations in the year prior to the intervention and during follow-up (based on self-report). An exacerbation was defined as an increase in respiratory symptoms with the need for a course of antibiotics or systemic corticosteroids (moderate) and/or hospitalization (severe). The BODE index was calculated using data on FEV1, 6MWD, mMRC and BMI.[22] Information on procedures, re-interventions and mortality were collected during follow-up.

Statistical Analysis

Patient characteristics, procedural outcomes and data on adverse events are reported using descriptive statistics (mean (SD), median (25th-75th percentiles) or proportions – depending on data distribution). Changes in clinical outcomes from baseline are evaluated using linear mixed model analyses, retrieving the time effect. Response rates are calculated based on the following minimal important differences (MCID): FEV1 $\geq$ 100 mL, [27] RV $\leq$ 430 mL, [28] 6MWD $\geq$ 26 m, [29] and SGRQ $\leq$ 7.1 units. [30] Given the absence of a validated MCID for BODE, we defined a change of 1 as clinically relevant as used in previous studies. [31], [32] Finally, a composite outcome, indicating a response exceeding the MCID in either FEV1, 6MWD and/or SGRQ, was employed to evaluate the comprehensive impact of BLVR. This composite outcome was derived from the composite tool "clinically important deterioration". [18,33,34]

Statistical analyses were performed using SAS statistical package (V9.4, SAS Institute, Cary, North Carolina, USA) and Graph Pad statistics. P-values less than 0.05 were considered significant.

Results

Study Population

In total, data on 88 procedures performed in 83 individual patients were collected. In two patients, BLVR was performed additionally at the contralateral side, and in three patients the contralateral side was treated after extraction of valves at the initial side because of no response.

At baseline, the study population was on average 66 ± 6 years old. The study group had severe airflow obstruction and static hyperinflation, with a mean FEV1 of 0.82 ± 0.23 liter (31% predicted) and RV of 4.72 ± 0.89 liter (221% predicted). Exercise capacity was severely impaired (6MWD 342 ± 84 meter) and BODE index was 6 ± 2. Of the treated patients, 77% had heterogeneous emphysema, defined as ≥15% difference in percentage of voxels below -950HU of the target lobe compared to the ipsilateral lobe. The left upper lobe was most often treated (36%), followed by the left lower lobe (33%). All baseline characteristics are summarized in Table 1.

At 6 months, data of 75 patients were collected. At one- and two-years follow-up, data of, respectively, 51 and 24 patients were retrieved. The reasons for missing data are shown in Table 2.

Procedural Outcomes

The median (IQR) number of valves used was 4 (4–5). The median (IQR) length of stay was 6 (5.3–7) days. One month after BLVR, complete atelectasis of the treated lobe was attained in 43 patients (49%), a partial atelectasis was attained in 29 patients (33%), and no atelectasis was observed in 16 patients (18%) (as assessed by CT). After one or more revision bronchoscopies, complete atelectasis was observed in 47 patients (53%).

Table 1 Baseline Characteristics of Study Population Presented as Mean ± Standard Deviation Unless Mentioned Otherwise (n = 88)

Sociodemographics	
Age (years)	66 ± 6
Gender (female), n (%)	49 (55.68)
Packyears (years)	37.32 ± 18.57
Alpha 1 anti-trypsin deficiency, n (%)	2 (2.27)
BMI (kg/m²)	23.22 ± 3.42
pO2, mmHg	71.82 ± 10.29
pCO2, mmHg	39.82 ± 6.57
BODE	5.65 ± 1.52
Exacerbations per year	1.2 ± 1.17
Hospitalisations per year	0.48 ± 0.84
Lung function	
FEV_1 (l)	0.82 ± 0.23
FEV_1 (%)	31 ± 8
FVC (l)	2.49 ± 0.68
FVC (%)	74 ± 16
RV (l)	4.72 ± 0.89
RV (%)	221 ± 35
RV/TLC	0.65 ± 0.07
TLco (%)	35 ± 8
Exercise capacity and symptoms	
6MWD, m	342 ± 84
mMRC, points	3.07 ± 0.89
CAT, points	22.43 ± 4.84
SGRQ, points	64.49 ± 13.71
Therapy	
Inhaled corticosteroids, n (%)	76 (86%)
Oral corticosteroids, n (%)	12 (14%)
Azitromycin, n (%)	38 (43%)
Long-term oxygen therapy, n (%)	18 (20%)
Target lobe for BLVR	
Left upper lobe, n (%)	32 (36%)—
Left lower lobe, n (%)	29 (33%)
Right upper lobe, n (%)	13 (15%)

(*Continued*)

Table 1 (Continued).

Right middle lobe, n (%)	0 (0)
Right lower lobe, n (%)	10 (11%)
Right upper and middle lobe, n (%)	4 (5%)
Heterogenity, n (%)	68 (77%)
Voxels below -950HU, %	48.62 ± 12.36
Volume, mL	1714 ± 417.47

Abbreviations: BMI, body mass index; pO2, partial pressure for oxygen; pCO2, partial pressure of oxygen; BODE, Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity; Tlco, transfer capacity of the lungs for carbon monoxide; 6MWD, 6-minute walk distance; mMRC, modified Medical Research Council; CAT, COPD assessment test; SGRQ, St. George's Respiratory Questionnaire.

Table 2 Number of Subjects Who Completed Follow-Up and Reasons for Missing Data. Patients Who are Between Follow-Up Measurements (Eg Follow-up Measurement is Scheduled According to Plan), are Labeled as "Follow-up Ongoing"

	Baseline	3 months follow-up	6 months follow-up	12 months follow-up	24 months follow-up
Completed follow-up	88	76	75	51	24
Follow-up ongoing	NA	0	3	14	31
Reasons for missing data	NA	Lost to follow-up: n = 3 Revision: n = 5 Pneumothorax: n = 2 - LVRS - Bullectomy Primary LVRS: n = 1	Lost to follow-up: n = 4 Revision: n = 1 Pneumothorax: n = 2 - LVRS - Bullectomy BLVR other side: n = 1 Primary LVRS: n = 2	Lost to follow-up: n = 6 Died: n = 1 Pneumothorax: n = 2 - LVRS - Bullectomy BLVR other side: n = 3 Primary LVRS: n = 11	Lost to follow-up: n = 6 Died: n = 2 Pneumothorax: n = 2 - LVRS - Bullectomy BLVR other side: n = 5 Primary LVRS: n = 17 SSLTX: n = 1

Abbreviations: LVRS, lung volume reduction surgery; BLVR, bronchoscopic lung volume reduction; SSLTx, sequential single of double lung transplantation.

Effectiveness

All outcome parameters (FEV1, RV, 6MWD, mMRC, SGRQ) demonstrated significant improvement up to one year of treatment (Table 3 and Figure 1). In addition, RV, mMRC and BODE index showed a significant benefit throughout the entire two-year follow-up period compared to baseline.

Table 3 Mean ± Standard Error of the Mean at Baseline and Follow-Up for Clinically Relevant Outcomes.* Indicates Significant Difference (p-value < 0.05) Compared to Baseline

	Baseline	3 months FU	N	6 months FU	N	12 months FU	N	24 months FU	N
FEV_1 (L)	0.82±0.03	1.03±0.03*	*76*	0.97±0.03*	*75*	0.93±0.03*	*51*	0.84±0.04	*24*
RV (L)	4.69±0.11	3.97±0.11*	*76*	4.09±0.11*	*74*	4.10±0.12*	*50*	4.44±0.15*	*23*
6MWD (m)	344±10	376±11*	*74*	375±11*	*72*	379±12*	*48*	352±15	*22*
mMRC (points)	3.0±0.1	1.9±0.1*	*72*	2.4±0.1*	*75*	2.3±0.1*	*46*	2.4±0.2*	*23*
SGRQ (points)	63.7±1.9	47.7±2.0*	*62*	50.1±2.0*	*64*	54.1±2.3*	*41*	61.4±3.0	*17*
BODE (points)	5.6±0.2	3.8±0.2*	*72*	4.5±0.2*	*72*	4.4±0.2*	*46*	4.8±0.3*	*22*

Abbreviations: FEV1, forced expiratory volume in 1 second; RV, residual volume; 6MWD, 6-minute walk distance; mMRC, modified Medical Research Council, SGRQ: St. George's Respiratory Questionnaire; BODE, Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index; FU, follow-up; N, number of patients.

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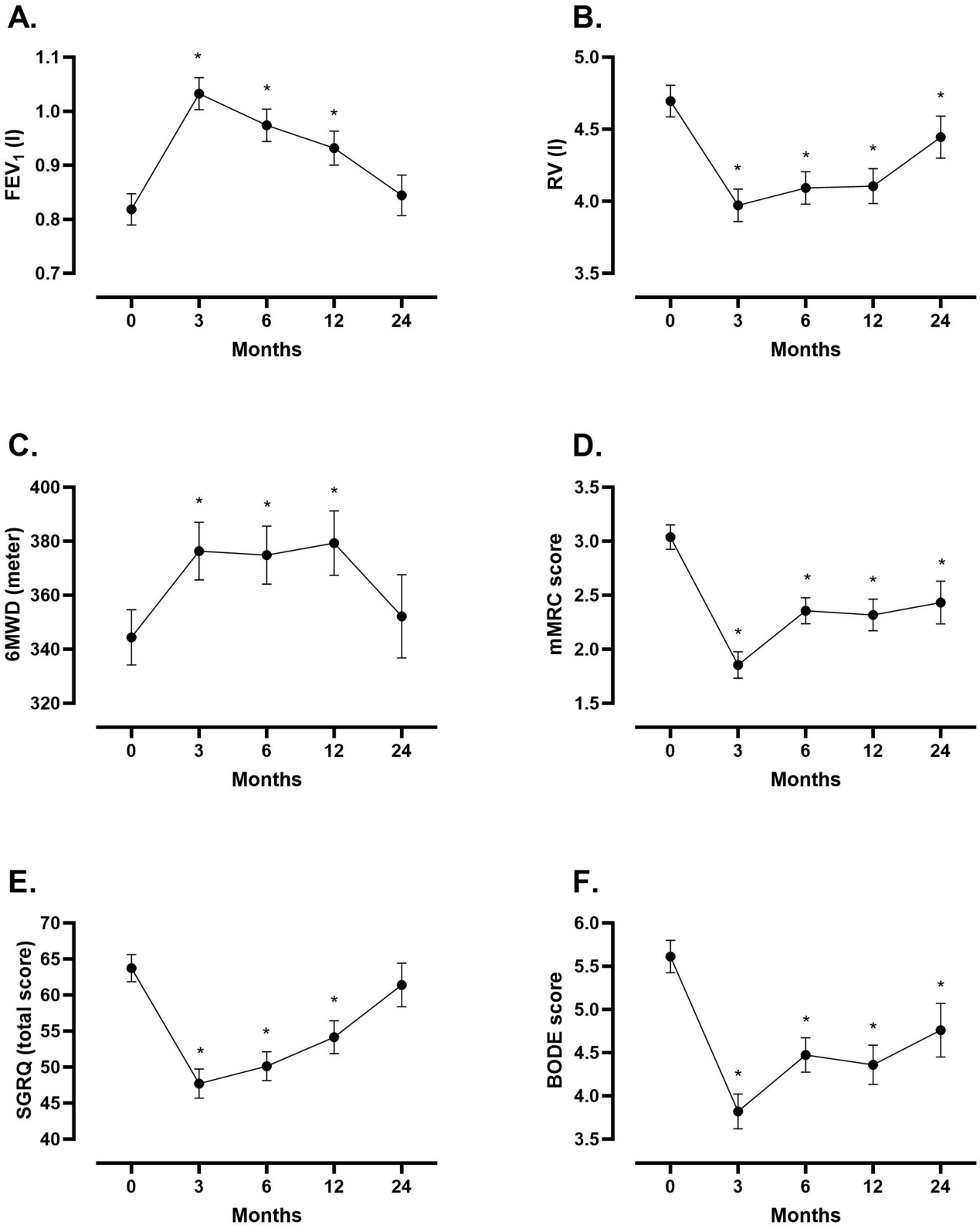

Figure 1 Mean ± standard error of the mean at baseline and follow-up for (**A**) FEV1, (**B**) RV, (**C**) 6MWD, (**D**) mMRC, (**E**) SGRQ and (**F**) BODE* Indicates significant difference (p-value < 0.05) compared to baseline.

Table 4 Responder Rates (Expressed as %) for Important Clinical Outcomes at Follow-Up, Using the Minimal Clinical Important Difference. [$]The Composite Outcome Indicates a Favorable Response in Either FEV_1, 6MWD and/or SGRQ

	3 months follow-up	6 months follow-up	12 months follow-up	24 months follow-up
FEV_1 ≥ 100mL	72 (55/76)	53 (40/75)	49 (25/51)	42 (10/24)
RV ≤ 430mL	71 (54/76)	64 (47/74)	68 (34/50)	48 (11/23)
6MWD ≥ 26m	62 (46/74)	54 (39/72)	58 (28/48)	45 (10/22)
SGRQ ≤ 7.1 units	60 (37/62)	67 (43/64)	61 (25/41)	41 (7/17)
BODE ≤ 1 unit	74 (54/72)	61 (44/72)	76 (35/47)	68 (15/22)
Composite outcome[$]	88 (67/76)	84 (63/75)	86 (44/51)	71 (17/24)

Abbreviations: FEV_1, forced expiratory volume in 1 second; RV, residual volume; 6MWD, 6-minute walk distance; SGRQ, St. George's Respiratory Questionnaire; BODE, Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index.

Responder Analysis

The percentage of responders by terms of minimal important differences for the full database is shown in Table 4 and Figure 2. At 12 months of follow-up, 49% (n = 25 of 51) of the patients showed an increase in FEV1 above the MCID (+100mL), 68% (n = 34 of 50) showed a decrease in RV ≤ -430ml, 58% (n = 28 of 48) demonstrated an improvement in 6MWD of ≥ +26m and 61% (n = 25 of 41) experienced a reduction in SGRQ of ≤ −7 points. Subsequently, there was a gradual decline in response rate for all outcomes at 24 months of follow-up, with 42% (n = 10 of 24) and 48% (n = 11 of 43) of the patients being responders on FEV1 and RV, respectively. The BODE index showed a response of 76% (n = 35 of 47) at one year and 68% (n = 15 of 22) at two years. Response rates for the composite outcome were 86% (n = 44 of 51) at one year, and a sustained response in 71% (n = 17 of 24) of patients at two years.

Safety

Three patients were temporarily admitted to the intensive care unit: two patients because of a pneumothorax and one patient because of hypoxic respiratory failure due to a combination of hemoptysis, infection, and pulmonary edema.

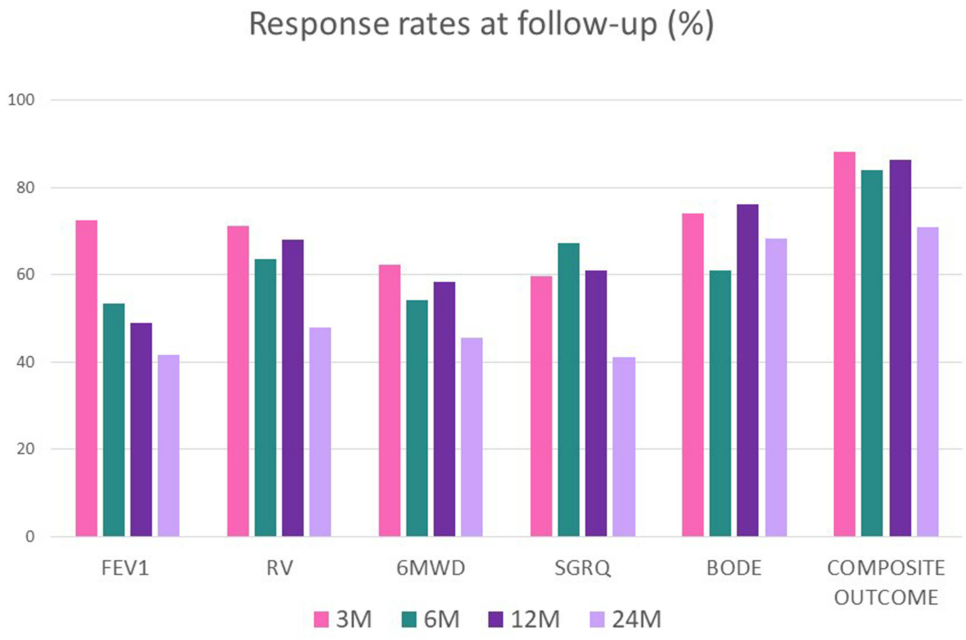

Figure 2 Responder rates (expressed as %) for important clinical outcomes at follow-up, using the minimal clinical important difference (MID). The composite outcome indicates a favorable response in either FEV_1, 6MWD and/or SGRQ.

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Table 5 Respiratory Adverse Events After BLVR

	0–3 months	3–6 months	6–12 months	12–24 months
Exacerbation, n (%)				
Mild-Moderate	19* (25%)	17 (23%)	11 (22%)	3 (13%)
Severe	4 (5%)	75 (7%)	7 (14%)	6 (25%)
Hemoptysis, all minor n (%)	5 (6%)	1 (1%)	0	0
Pneumothorax, n (%)	10 (11.4%)			
Chest drainage	6			
EBV removal	4			
Surgery	1			

Note: *6 patients had an exacerbation in-hospital, immediately after the procedure, these were considered non-severe.
Abbreviation: EBV, endobronchial valve.

During the first three months after BLVR, 21 patients (24%) had an exacerbation, 21 patients (24%) had temporary more oxygen, 17 patients (19%) had a respiratory infection, 5 patients had an episode of minor hemoptysis (one of them because of valve migration), and one patient expectorated a valve during an acute exacerbation. Respiratory adverse events during follow-up are shown in Table 5.

Pneumothorax occurred in 10 patients (11.4%) before three months follow-up, with a median (IQR) of 3 days (1.25–6.25) after treatment. In four patients, the pneumothorax resolved spontaneously (ex-vacuo), in 6 patients chest tube drainage was performed, in four patients a valve was (temporary) removed, and one patient eventually proceeded to surgery (Table 5). The pneumothorax was always at the ipsilateral side.

Clinical Pathway

A flowchart from our clinical cohort is presented in Figure 3, including information on revision bronchoscopies, surgical procedures, and removal of valves (Figure 3).

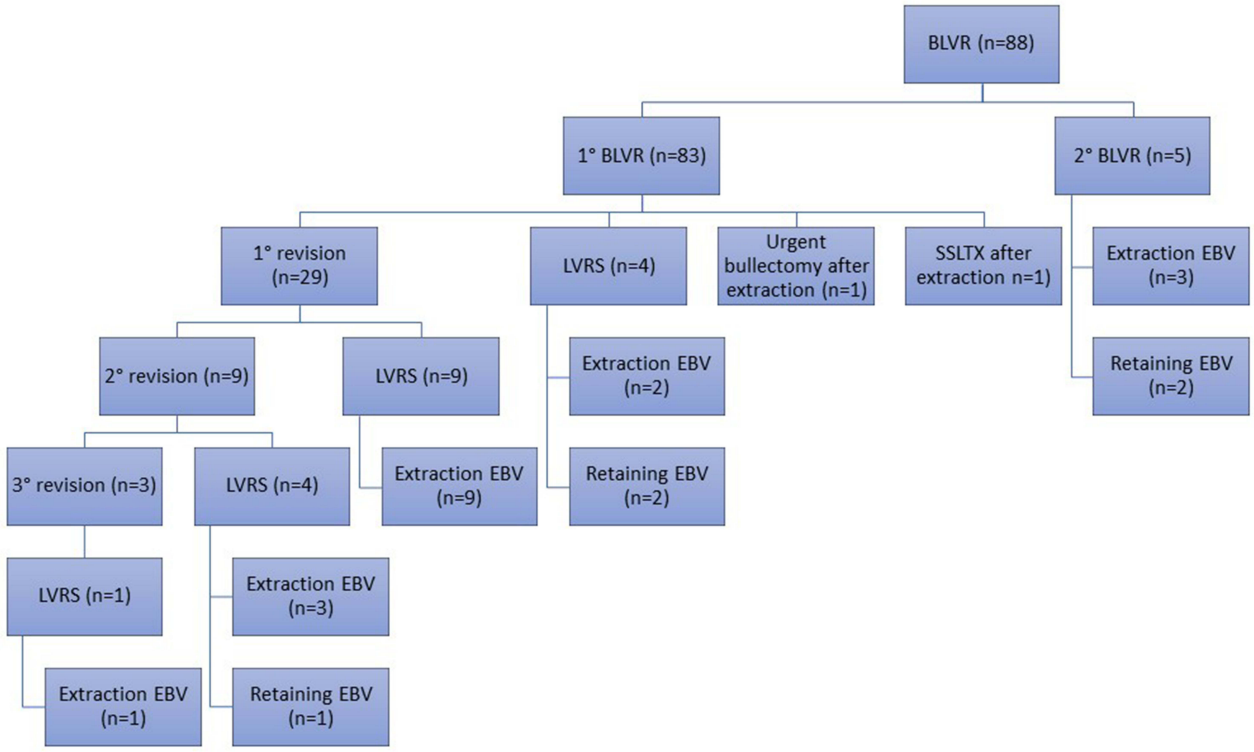

Figure 3 Flowchart of the clinical pathway of the individuals included in the follow-up.

Revision Bronchoscopy

A revision bronchoscopy was performed in 31 patients (35%) with a median (IQR) of 77 (37–158) days after EBV placement. The main reasons for revision bronchoscopy were limited or absent atelectasis (n = 19, 2 with suspicion of dysfunctional valve during bronchoscopy), loss of atelectasis (n = 6, 2 with suspicion of dysfunctional valve during bronchoscopy), extraction of valve in the context of pneumothorax (n = 4), hemoptysis due to valve migration (n = 1) and expectoration of a valve (n = 1). A second revision bronchoscopy was performed in 10 patients (11%), because of limited or absent atelectasis (n = 7), loss of atelectasis (n = 1), valve replacement after resolution of pneumothorax (n = 1) and hemoptysis due to dislocation of a valve (n = 1). A third revision bronchoscopy was performed in two patients: one due to loss of atelectasis and one because of hemoptysis due to a lower respiratory tract infection. Complete atelectasis eventually occurred in five patients after the first revision (16%), in three patients after the second revision (30%) and in none after the third revision.

Step-Up Care

Nineteen patients (22%) in our cohort underwent lung surgery within the two-year follow-up window. One of these underwent a surgical intervention in the context of a pneumothorax. Eighteen patients underwent lung volume reduction surgery (LVRS). In 15 patients, EBV were removed before surgery because lack of response. In three patients, LVRS was performed at the contralateral side, for an additional LVR effect while retaining the effective endobronchial valves at the other side. The median (IQR) time to LVRS was 396 (253–732) days. One patient proceeded to a bilateral lung transplantation 23 months after BLVR.

Mortality Rate

During the reported follow-up period, two patients died with a median of 483 days after the procedure. The reason for death was respiratory failure due to disease progression, not related to the BLVR procedure.

Discussion

In this single center prospective observational study, outcomes up to two years after BLVR using one-way endobronchial valves were reported. Besides evaluating conventional outcomes such as lung function, exercise capacity and quality of life, we evaluated the impact of BLVR on the BODE index, a known predictor of mortality among patients with COPD and on a composite outcome including changes in FEV1, 6MWD and SGRQ, to evaluate the multidimensional impact of BLVR. Our results confirm sustained effects up to two years after treatment for the BODE index, static hyperinflation and symptoms of dyspnea in patients who remained in follow-up. Response rates for the composite outcome, determined on minimally clinically important differences in FEV1, 6MWD and/or SGRQ, were 86% (n = 44 of 51) at one year and 71% (n = 17 of 24) at two years of follow-up.

After three months of follow-up, our findings closely paralleled those reported in other real-world data sources.[14–16,35] The results in our cohort revealed an average improvement from baseline to 3 months in FEV1 by 214 ± 19 mL, a reduction in RV by 724 ± 77 mL, a 32 ± 9 meter increase in the 6MWD, a 16 ± 2 point improvement in SGRQ, a decrease of −1.2 ± 0.1 points on the mMRC dyspnea scale and a −1.8 ± 0.2 point alteration on the BODE index. The short-term intervention effect was similar as reported in other RCTs.[5,7,8] For the long-term effect, a gradual loss of treatment effect was observed in all clinical outcomes. Whereas airflow obstruction, exercise capacity and quality of life was not statistically different at two years compared to baseline, effects on static hyperinflation, symptoms of dyspnea and survival remained present after two years. This is in line with previous cohorts reporting long-term follow-up.[14,15] A five-year follow-up of the LIBERATE trial showed a similar trend for FEV1, even five years after the intervention.[36] Nevertheless, we need to acknowledge the possible selection bias in our results, as we can only report on the changes of patients who remained in follow-up (58% of the initial sample at 1 year follow-up; 27% of the initial sample at 2 years follow-up).

When evaluating the responder rates for clinical outcomes, >40% of the patients who completed the follow-up remained responders at two years follow-up. To the best of our knowledge, we are the first to explore the multi-dimensional effect of BLVR on a composite endpoint. From a clinical perspective, such an evaluation appears relevant

since response does not have to be present in all the measured outcomes to obtain an overall success of treatment for an individual patient. Considering multiple outcomes, the response rates of the composite outcome for patients still in the analyses was substantial, reaching 86% after one year and maintaining a commendable 71% after two years.

Evaluating the effect of BLVR on the BODE index has been reported in the Stelvio and Celeb trials.[32,37] In these studies, treatment with EBV demonstrated statistically significant improvements in the BODE index at 6 months and one year of follow-up. Our real-world data strengthen the hypothesis of a survival benefit of BLVR, showing a significant improvement in the BODE index at three months and up until 24 months post intervention in patients of whom the valves are still in situ.

Except for pneumothorax rate, the safety outcomes are comparable to safety outcomes reported in randomized clinical trials and other real-world datasets.[7,14–16] A lower pneumothorax rate may be explained by a hospital stay of 5 days, with bed rest and cough suppression, as discussed before.[23] Revision rate was similar, yet revisions should be considered carefully, as our data show that the benefits obtained from revisions are relatively small, since only four patients achieved complete atelectasis after undergoing revision bronchoscopy.[38]

Our center offers a multidisciplinary care path for patients with end-stage COPD and severe emphysema, including bronchoscopic lung volume reduction, surgical lung volume reduction and lung transplantation. The objective of this manuscript was to also provide insights in the clinical pathways of the patients referred to our expert center. In Figure 3, we depicted the pathway of patients who underwent bronchoscopic lung volume reduction. 21% of the patients were eventually referred for lung volume reduction surgery, mostly because of insufficient effect of the endobronchial valves. This highlights the importance of a multidisciplinary care path, including both bronchoscopic and surgical treatment options for end-stage COPD. Yet, because of the availability of both treatments in our center, results of our real-life approach mainly include patients with a maintained (initial) treatment effect of bronchoscopic lung volume reduction or patients in absence of other treatment options (eg not eligible for surgical lung volume reduction or lung transplantation).

Strengths and Limitations

The major strengths of the present observational cohort study are providing insights into the long-term effect of BLVR in a clinical population at a high-volume center and describing the clinical pathway of these patients. However, a few limitations should be highlighted. First, the sample size at 24-month follow-up was relatively small, which may affect the generalizability of the findings. Although only a minority of missing data was due to lost-to-follow-up, the absence of data due to surgical interventions likely leads to an overestimation of the reported outcomes, as those patients may have experienced possibly less favorable results from BLVR. This limitation highlights the need for cautious interpretation of the results, as the reported positive outcomes may not fully represent the entire population initially treated with BLVR. Previous real-world observational results suffer from the same important limitation, and additionally performed statistical analyses without correction for repeated measurements. In the current study, we aimed to reduce this statistical error by using repeated mixed model analyses. Nevertheless, we are aware that our results need to be interpreted with caution.

Conclusion

This single-center observational study demonstrated favorable long-term effects of BLVR using one-way endobronchial valves up to two years follow-up for patients of whom the valves are still in situ. Our findings are in line with previous research, showing a gradual loss of the intervention effect over time, yet with maintained statistically significant benefits on static hyperinflation, dyspnea scores and survival after two years. In addition, we found in the majority of the patients who remained in follow-up a sustained clinical important effect in either lung function, exercise capacity and/or quality of life two years post intervention.

Data Sharing Statement

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was performed in accordance with the Declaration of Helsinki. The study was approved by the local ethical committee (UZ/KU Leuven Ethical Committee) (S60207 and S64530) and all subjects signed the informed consent prior to data collection.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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