Sequential Bilateral Bronchoscopic Lung Volume Reduction With One-Way Valves for Heterogeneous Emphysema

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Background. **Clinical benefits of bronchoscopic lung volume reduction with one-way endobronchial valves have been reported for heterogeneous emphysema after unilateral treatment. We assessed the potential role of contralateral treatment to prolong the benefits obtained with the first procedure.**

Methods. **This was a retrospective multicenter study including consecutive patients with heterogeneous emphysema undergoing bronchoscopic valves deployment during the last 4 years. Patients were split into two groups depending on the procedure (unilateral versus bilateral). The intergroup differences were evaluated to assess the viability, effectiveness, and safety of the bilateral procedure.**

Results. **Forty-nine patients were enrolled. Of these, 14 (28%) had a sequential bilateral procedure mainly due to loss of the clinical benefits obtained with the first treatment. A significant improvement of forced expiratory volume in 1 second ($p < 0.05$), forced vital capacity ($p < 0.05$), residual volume ($p < 0.05$), 6-minute walking test ($p < 0.05$), and St. George respiratory questionnaire ($p < 0.02$) was achieved after the second procedure. These results were maintained during follow-up. There was no significant difference regarding the changes of forced expiratory volume in 1 second ($p = 0.4$), forced vital capacity ($p = 0.08$), residual volume ($p = 0.9$), 6-minute walking test ($p = 0.3$), and St. George respiratory questionnaire ($p = 0.1$) between the bilateral and unilateral groups.**

Conclusions. **A sequential bilateral approach seems to be a valid strategy to improve respiratory function in patients with bilateral heterogeneous emphysema who have lost the benefits obtained with the first procedure.**

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Emphysema remains a leading cause of morbidity and mortality. Treatment options include smoking cessation, inhaled medications, systemic corticosteroids, pulmonary rehabilitation, supplemental oxygen, and lung transplantation. Lung volume reduction surgery (LVRS) has been proposed as a viable option for patients with heterogeneous emphysema. Despite the positive results, LVRS shows a significant morbidity rate (20% to 30%) and a relatively high operative mortality rate (7.9%) within 90 days after the procedure in the main series [1]. Therefore, less invasive procedures are desirable.

Several studies have reported that bronchoscopic lung volume reduction (BLVR) with an endobronchial one-way valve (EBV [Zephyr EBV; Pulmonx, Redwood, CA) provides significant functional improvement, namely, in patients with severe heterogeneous emphysema and complete interlobar fissures [2–5]. Bronchoscopic lung volume reduction is able to induce lobar collapse, mimicking the effects of LVRS, allowing air to exit from a pulmonary lobe but not entering. However, the functional improvement obtained with unilateral BLVR may progressively decline to the pre-BLVR level. The usefulness of a second contralateral treatment has been confirmed after unilateral LVSR [6, 7] but remains unclear after unilateral BLVR.

We evaluated the results of bilateral BLVR in a multicenter retrospective study to assess the safety and functional efficacy of such a strategy.

Material and Methods

Study Design

This was a retrospective multicenter study involving four high-volume centers. Data were collected retrospectively from the prospective database of each center. All consecutive patients with bilateral heterogeneous emphysema undergoing BLVR with EBV from January

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Abbreviations and Acronyms

BLVR = bronchoscopic lung volume reduction
EBV = endobronchial valve
FEV_1 = forced expiratory volume in 1 second
FVC = forced vital capacity
HRCT = high-resolution computed tomography
LVRS = lung volume reduction surgery
RV = residual volume
SGRQ = St. George's Respiratory Questionnaire
6MWT = 6-minute walk test

2011 to December 2014 were included. Exclusion criteria were (1) lack of complete clinical and functional follow-up data; (2) previous surgical procedures such as LVRS, bullectomy, and lung transplantation; and (3) endoscopic hybrid procedures (ie, EBV associated with coils).

All patients were reassessed from the functional point of view and quality of life after 3 and 6 months and yearly by follow-up visit. Radiologic monitoring was performed with chest radiograph 24 hours after the procedure, at discharge, and 15 days later; and with high-resolution computed tomography (HRCT) 1 and 3 months after BLVR and then on a yearly basis. Mortality and postoperative morbidity were also recorded. Patients with decline of respiratory function or without benefits after the initial BLVR underwent repeated contralateral BLVR (bilateral group) and were then compared with the remaining patients (unilateral group). The objectives were to evaluate the efficacy and outcome (primary endpoint) and the morbidity, mortality, and survival rate (secondary endpoints) of bilateral BLVR.

Study Population

The selection criteria for BLVRS were the same in both groups according to the Endobronchial Valve for Emphysema Palliation Trial (VENT study) guidelines (Table 1) [8]. Heterogeneity was assessed by HRCT scan with volume rendering and lung perfusion scan; we treated only lobes showing a clear density reduction without perfusion. The presence of interlobar fissures was determined using three-dimensional reconstructions at HRCT and multiplanar evaluation [9, 10]. The timing for contralateral BLVR was determined by a combination of factors such as functional deterioration or the patient's desire for additional improvement.

Pulmonary Function Tests

Pulmonary function tests were performed according to the American Thoracic Society guidelines [11]. Forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), total lung capacity, residual volume (RV), diffusing capacity of lung for carbon monoxide, 6-minute walk test (6MWT), Pa_{O_2} and Pa_{CO_2} (measured at rest while breathing room air) were measured. All pulmonary function data are presented as a percentage of predicted values for the patient's age, sex, and height. Quality of life was measured by the St. George's Respiratory Questionnaire (SGRQ); scores range from 0 to 100, with a higher score indicating a worse quality of life.

Statistical Analysis

Data were expressed as mean ± SD for continuous variables and absolute number and percentage for categoric variables. Comparison of preoperative and postoperative results was evaluated using the χ^2 test or paired Student's *t* test, as appropriate. Analysis of variance test corrected with post-hoc test (if indicated) compared repeated measures over time. Survival curves were calculated with the Kaplan-Meier test, and the statistical difference was assessed by the log rank test. A p value less than 0.05 was considered significant. MedCalc statistical software, version 12.3 (Mariakerke, Belgium) was used for the analysis.

Results

Of 55 eligible patients, 6 were excluded owing to lack of data during follow-up (2 patients) or association with other surgical procedures (4 patients). Therefore, a total of 49 patients (Table 2) were retrospectively evaluated. Of these, 14 (28%) received a repeated BLVR after a median interval of 18 months (range, 2 to 25; Fig 1) from the initial BLVR. In all, 74 valves were deployed (34 during the first procedure and 40 during the second one), with a median of 5 valves (range, 5 to 8) per patient. The 5.5 EBV was used in 35% and the 4.0 EBV was used in 65% of patients.

In 12 patients (43%), the left upper lobe was occluded (6 during the first and 6 during the second procedure), the lower left lobe in 2 cases (7.2%) at the second procedure, the right upper lobe in 11 (39% [6 during the first and 5 during the second procedure]), and the right lower lobe in 1 patient (3.5%) during the first procedure. The middle lobe was treated with the right upper lobe in 1 patient (3.5%) at the time of the first procedure and with the right lower lobe in 1 patient (3.5%) during the second one.

The mean hospital stay was 8.2 ± 2.0 days (median 8; range, 5 to 12), 3 days after the first procedure and 5 days after the second. After the first and after the second procedure, complete lobar atelectasis was observed in 6 patients (43%) and 6 (43%), partial atelectasis in 6 (43%) and 7 (50%), and no atelectasis in 2 patients (22%) and 1 patient (7%), respectively. Combining the results of the first and second procedures, 7% of patients (1 of 14) had no atelectasis on both sides, 14% (2 of 14) had no atelectasis on one side and complete atelectasis on the contralateral side, 29% (4 of 14) had complete atelectasis on both sides, and 50% (7 of 14) had complete atelectasis on one side and partial atelectasis on the opposite side.

Thirty-five (72%) patients had unilateral BLVR. No significant differences were found between the bilateral group and unilateral group regarding the age of population, the treated lobe, the type of the procedure, and functional baseline variables. As expected, the mean number of valves for each patient was significantly higher