Bronchoscopic lung volume reduction as a bridge to lung transplantation in patients with chronic obstructive pulmonary disease

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is the leading indication for lung transplantation; however, these patients rarely gain priority on the waiting list until very late. The clinical status can be improved by surgical lung volume reduction; this procedure, although carries significant morbidity, has been repeatedly advocated as a bridge. Recently, bronchoscopic lung volume reduction (BLVR) has been proposed to improve functional parameters in patients with emphysema; however, it has never been reported as a bridge to lung transplantation so far.

Methods: We hereby report our experience with BLVR as a bridge to lung transplantation in four patients (males, mean age 51 years).

Results: All patients underwent unilateral BLVR (two right upper lobe (RUL), one right lower lobe (RLL), and one left upper lobe (LUL); mean 3.5 valves per patient). No morbidity and mortality were observed. Three out of the four patients successfully reached transplantation after 6, 7, and 6 months, respectively. Two patients received single-lung transplantation and one sequential double-lung transplantation. The fourth patient died of respiratory failure 13 months after valve placement. BLVR was able to reduce the residual volume and improve the 6-min walking test and Medical Research Council (MRC) score.

Conclusions: BLVR allowed to improve the functional status and quality of life of these patients. In a selected group of COPD patients awaiting lung transplantation, the reported short- to medium-term objective improvement may play an important role to ameliorate the clinical status and reach the time of surgery.

Keywords: Bronchoscopic lung volume reduction; COPD; Lung transplantation; Waiting list

1. Introduction

Emphysema-related end-stage lung disease is the most frequent indication for lung transplantation [1]. However, the shortage of suitable donors has dramatically contributed to increase the length of the waiting time as well as morbidity and mortality on the waiting list; at our institution, the latter reaches 15% each year, although chronic obstructive pulmonary disease (COPD) patients are less affected. To improve the quality of life and survival of COPD patients awaiting lung transplantation, surgical lung volume reduction (LVRS) has been increasingly proposed as a bridge [2–7]; however, this surgical procedure still carries a substantial morbidity [8–10], even if mortality is low at the centers with large experience [9,11]. Above all, patients with the most advanced functional deterioration show a higher surgical mortality and less encouraging functional results, suggesting that LVRS might be more carefully considered in these situations [10].

Bronchoscopic lung volume reduction (BLVR) has been recently experimented with in the animal laboratory [12] and subsequently employed in selected clinical settings [13–18]; it has been postulated that blocking an airway supplying the most overinflated parts of the emphysematous lung could favor a decrease in lung volumes; partial or complete atelectasis mimics LVRS and may contribute to alleviate symptoms. The basis of this procedure is endoscopic placement of one-way valves in the segmental bronchi; like a Heimlich system, they allow only expiratory airflow from the emphysematous area preventing air entering, with consequent decrease of lung volumes.

BLVR showed low morbidity and encouraging medium-term results [16,17]. We have employed this technique in a selected group of patients with advanced heterogeneous emphysema; we have also offered BLVR to a small number of lung-transplant candidates with unceasing functional deterioration, with the intent to reduce morbidity and mortality during the transplant waiting time.
This report focuses on our initial experience with unilateral BLVR in four lung-transplant candidates; this technique has never been reported as a bridge to lung transplantation so far.

2. Patients and methods

We have performed a prospective, non-randomized, single-center longitudinal study to evaluate safety and short-term efficacy of BLVR in patients with end-stage heterogeneous emphysema; the inclusion and exclusion criteria have been previously reported [16]. Four patients were on our lung-transplantation waiting list and their functional status and quality of life were rapidly deteriorating; this report focuses only on these four cases. The study was approved by the ethical committee of the University of Rome Sapienza — Policlinico Umberto I; an informed consent was signed by all patients.

One-way endobronchial valves (Emphasys, Redwood City, CA, USA; now Pulmonx Corporation, Redwood City, CA, USA) were placed in the segmental or subsegmental bronchi supplying the most hyperinflated parts of the emphysematous lungs. These devices are stent-supported valves made of silicone and nitinol; they prevent air entering the target lung but allow air and mucous to exit. All the procedures were performed in the operating room with the patient under intravenous anesthesia with propofol and spontaneous assisted ventilation through an endotracheal tube (size 8 or 9) or a laryngeal mask; local anesthesia (2% lidocaine) was administered before inserting the valves, to prevent coughing. Valve deployment was performed through the fiberoptic bronchoscope under direct visualization, according to the standard technique previously described [16,17]. In three patients, we placed the first-generation endobronchial valves while, in the last one, we used the last-generation 'Zephyr' valves. The differences between the two types are related to the need of a guidewire and a different delivery catheter for the first-generation valves [17]; however, they work in the same way.

Preoperative demographics and technical details are reported in Table 1. Three patients had COPD related to smoking and one had alpha-1 antitrypsin deficiency. All patients were on supplemental oxygen at the time of evaluation for transplantation and at the time of BLVR.

All patients underwent standard pre-transplant thorough evaluation before being included in the waiting list. Functional and radiological work-up (including computed tomography, perfusion scan, body plethysmography, and arterial blood gas analysis) as well as 6-min-walk test and Medical Research Council (MRC) chronic dyspnea score assessment were repeated before BLVR and after 24/48 h, and 1 and 3 months; two patients remained on the waiting list at 7 and 13 months, respectively; thus, they also underwent 6-month and 1-year assessment.

3. Results

All patients underwent unilateral BLVR, three on the right and one on the left side. No morbidity and mortality were observed after the endoscopic procedure. No infectious complications were recorded after BLVR, while all patients experienced at least one infectious exacerbation between transplantation listing and BLVR.

Three out of the four patients successfully reached transplantation after 6, 7, and 6 months, respectively. Two patients received single-lung transplantation on the side of the previous BLVR and one sequential double-lung transplantation (side with BLVR transplanted first). The fourth patient died of respiratory failure 13 months after valve placement without having the chance of being transplanted. In this patient, during the last hospitalization, fiberoptic bronchoscopy was performed through tracheostomy and all the valves previously placed were patent and in place. Table 2 reports the functional variables of the four patients at the time of listing for lung transplantation, when valves were placed, and during the follow-up after BLVR, waiting for the transplant. The mean MRC score was 3.5 at the time of listing for transplantation, 4.25 at BLVR, 3.5 after 24/48 h, and 2.5 and 2.75 after 1 and 3 months, respectively. All patients decreased the need of supplemental oxygen after BLVR, but no one was completely weaned from it.

At transplantation, all the valves were in place and patent, with the exception of one that was partially obstructed by the overgrowing granulation tissue. All the lobes where the valves were previously placed were partially deflated, but not fully atelectatic; collateral ventilation probably contributed to partially refill these lobes; however, the valves contributed to macroscopically reduce hyperinflation when compared with the rest of the lung. The lobes remained in this semi-atelectatic state also after removal.

After transplantation, one patient is alive and well after 6 months and two died; one had massive hemoptysis due to a broncho-arterial fistula, and the second one (bilateral transplantation) had complications related to pulmonary aspergillosis that was not present in the lungs explanted at the time of transplantation.

4. Discussion

COPD is recognized as a progressive disease; symptoms, functional parameters, clinical status, frequency and length
of hospitalizations, and quality of life unceasingly worsen with time. When patients reach the area of chronic respiratory failure, these limitations are markedly evident and each exacerbation may increase disability and risk of death. At this stage, patients become candidates to lung transplantation if contraindications do not coexist. However, when compared with other disorders (cystic fibrosis and idiopathic pulmonary fibrosis), the deterioration rate is slower [19] and, with the new allocation score system [20], COPD patients rarely gain priority on the waiting list until very late in the natural history of their disease.

The progression of the disease on the way to transplantation could be slowed down by either surgical or bronchoscopic lung volume reduction. LVRS has proved to objectively ameliorate functional parameters in a well-selected group of patients with heterogeneous emphysema, allowing improvements that can last up to 5 years. It has been demonstrated that LVRS can bridge the time on the waiting list for transplantation by an average length longer than 2 years without a significant increase of post-transplant morbidity and mortality [2]; this capability can be expressed to a greater extent with bilateral LVRS when compared with unilateral LVRS.

In the cohort of patients with heterogeneous emphysema, BLVR has proved to be feasible, safe, and effective in the short- and medium-term, although results are less remarkable when compared with LVRS, and longer follow-up has not yet been reported. However, the morbidity of the endoscopic procedure is low and mortality is virtually nonexistent; for these reasons, BLVR could play an important role in the group of patient candidates to lung transplantation. Patients with homogeneous emphysema are less likely to improve with these procedures due to the increased collateral ventilation, although some authors have reported encouraging results with LVRS [21]; BLVR has not yet been attempted in this subset of patients.

BLVR is still under evaluation and the preliminary results, although encouraging, need to be confirmed and validated in large cohorts of patients with longer follow-up. In this small and preliminary group of patients, we have performed unilateral BLVR on the worse side; a contralateral procedure should have been considered when the functional status would have started to deteriorate again; this is an approach similar to that considered for staged LVRS. Our report confirms that, in selected cases, this technique can offer some functional advantages on the medium term also in the population of patients candidates to lung transplantation; the benefit rarely lasts as long as for LVRS; however, in this group of patients, long-lasting results might not be so crucial because the endoscopic procedure is done to improve the quality of life on the waiting list and not to avoid lung transplantation; the latter procedure was clearly still indicated after BLVR. This temporary improvement could play an important role when functional deterioration starts to significantly limit daily activities, capability to undergo rehabilitation, and quality of life. In three out of four patients receiving BLVR as an interim procedure, we were able to temporarily slow down the symptomatic and functional deterioration, optimizing the clinical status and enabling them to reach the transplant with an improved clinical status. BLVR allowed to reduce the need of supplemental oxygen, improve functional status, stress tolerance, quality of life, and dyspnea score. No infectious exacerbations were observed after the endoscopic procedure. Histology performed on the specimen removed at the time of transplantation did not show any modification related to valve placement, with the exception of granulation tissue partially obstructing the proximal orifice of one of them. The outcome after the transplant, although not satisfactory in two out of three of our patients, was not hampered by pre-transplant valve placement.

BLVR certainly requires larger prospective clinical studies to be validated as an effective tool in the surgical arena; however, in a selected group of COPD patients awaiting lung transplantation, the reported short- to medium-term objective improvement may play an important role to ameliorate the functional status and quality of life.

Table 2. Functional variables.

<table>
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<tr>
<th></th>
<th>Tx listing</th>
<th>Pre BLVR</th>
<th>24/48 h</th>
<th>1 m</th>
<th>3 m</th>
<th>6 m</th>
<th>1 year</th>
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<td>78 (2)</td>
<td>62 (2)</td>
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<td>79 (1)</td>
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<td>3</td>
<td>69 (2)</td>
<td>62 (4)</td>
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<td>81 (3)</td>
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Tx: transplantation; BL VR: bronchoscopic lung volume reduction; h: hours; m: months.
References


