Novel Technologies in Endoscopic Lung Volume Reduction

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KEYWORDS

• Emphysema • COPD • Interventional bronchoscopy • Endoscopic lung volume reduction

KEY POINTS

- Endoscopic lung volume reduction (ELVR) presents an effective therapy in patients with advanced emphysema characterized by a forced expiratory volume in one second less than 45% to 50% and a residual volume greater than 150%, preferably greater than 200%.
- Valve therapy is a reversible blocking technique that leads to lobar atelectasis in case of low collateral ventilation and lobar occlusion.
- The partial irreversible lung volume reduction coil implantation and irreversible bronchoscopic thermal vapor ablation are effective treatment approaches independent of collateral ventilation.
- Precise patient selection with respect to pulmonary function test, emphysema distribution, and collateral ventilation are prerequisites for a successful use of the various ELVR techniques.
- The idea of the targeted lung denervation, whose safety and feasibility was confirmed in the pilot trial, is to lead to sustainable bronchodilation by ablation of parasympathetic pulmonary nerves. Further trials evaluating efficacy are warranted.
- To date, there are only a few randomized controlled trials for bronchoscopic therapy in patients with chronic obstructive pulmonary disease, so the various techniques should be performed within clinical trials or registry studies.

Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory diseases worldwide with an increasing morbidity and mortality. In 1990, COPD was ranked sixth as cause of death, but is estimated to become the third leading cause of death in 2020.[1,2] The reason for increased mortality is mainly the expanding epidemic of smoking. Predominant symptoms of COPD include productive cough, shortness of breath, and subsequent limited exercise tolerance due to chronic bronchitis, irreversible bronchoconstriction, and emphysematous destruction of lung parenchyma.

Smoking cessation, pharmacologic therapy, consequent exercise training, and pulmonary rehabilitation are the most important therapeutic options that reduce symptoms and improve exercise capacity. Long-term oxygen therapy is required in patients with chronic respiratory failure and ventilatory support is indicated in patients with significant hypercapnia and related clinical signs. However, so far, there is no curative therapeutic approach. In addition, lung transplantation, which should be discussed in appropriately selected patients with COPD, is associated with a limited long-term prognosis and thus is often considered as palliative treatment approach. Another surgical therapeutic option in patients with severe emphysema is the lung volume reduction surgery (LVRS) that was introduced by Brantigan and colleagues[3] in the 1950s, but was abandoned due to high mortality and morbidity. It was only in the 1990s that Cooper and colleagues[4] reintroduced this surgical approach that aims at the

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reduction of hyperinflation and thus optimizes the respiratory mechanics leading to decreased breathlessness and increased exercise capacity. As lung hyperinflation is an independent predictor for all-cause mortality in patients with COPD, minimizing hyperinflation plays an important role in patients with severe COPD.[5] However, LVRS confers a survival advantage over medical therapy in only a precise selected group of patients with emphysema. Particularly patients with predominantly upper-lobe emphysema and low exercise capacity experience improvement of lung function and exercise tolerance and seem to have a survival benefit from LVRS. However, the 90-day mortality of LVRS with 7.9% was very high in a 2003 published randomised controlled trial; particularly patients with non-upper lobe emphysema and high exercise capacity were poor candidates for LVRS.[6] Therefore, the search for minimally invasive approaches with comparable benefits to LVRS but with less attendant risk was stimulated.

Since 2003, various techniques of endoscopic lung volume reduction (ELVR) that mimics the effect of LVRS are available extending the therapeutic spectrum for patients with severe COPD and emphysema. There are blocking and nonblocking ELVR techniques that are different in degree of reversibility, safety, and toxicity and whose application is dependent on the emphysema type and interlobar collateral ventilation. However, all these methods of ELVR are only worth considering in patients with advanced emphysema characterized by a forced expiratory volume in one second (FEV_1) of less than 45% to 50% of predicted and a residual volume (RV) greater than 150%, preferably greater than 200%.

Reversible implantation of one-way valves represents the blocking ELVR technique, for which there has been the greatest clinical experience worldwide. For valve therapy, which has already been introduced in 2003, comprehensive data including 4 randomized clinical trials (RCTs) are available. The currently available nonblocking techniques include the lung volume reduction coil (LVRC) implantation and the bronchoscopic thermal vapor ablation (BTVA). Another nonblocking technique, the polymeric lung volume reduction is currently not available due to lack of investors despite promising efficacy results. Furthermore, the creation of extra-anatomic airway bypasses that was mainly used in patients with predominant homogeneous emphysema is no longer performed, as the initial benefits following intervention did not persist within the course of 6 months.

Besides ELVR, which focuses on the reduction of hyperinflation, targeted lung denervation (TLD) is the most recent development in the field of bronchoscopic therapeutic options in patients with COPD. This technique simulates the effect of anticholinergic drugs and thus leads to sustainable bronchodilation.

The various bronchoscopic techniques for management of COPD and emphysema are shown in **Table 1**.

VALVE IMPLANTATION

Endoscopic valve implantation that is commercially available in European countries presents the only blocking and the only reversible ELVR technique. By placement of these one-way valves in the bronchi of the most emphysematous lung lobe, air is allowed to escape during expiration but not enter during inspiration and thus inducing a target lung volume reduction (TLVR). The maximum result is a complete lobar atelectasis. The target lobe is thereby defined on the basis of multidetector computed tomography (MDCT), including software emphysema analysis (eg, YACTA, "yet another CT analyzer") and perfusion scan. So far, 2 different types of valves are available that distinguish only in shape but act both as one-way valves (**Fig. 1**). The endobronchial valves (EBVs) (Zephyr; Pulmonx, Inc, Neuchatel, Switzerland; see **Fig. 1**; **Fig. 2**) are similar to bronchial stents made from nitinol and silicone, whereas the intrabronchial valves (IBVs) (Spiration; Olympus, Tokyo, Japan; see **Fig. 1**; **Fig. 3**) have a design like an umbrella with a nitinol skeleton covered by a polyurethane membrane. Different sizes of both valves are available, which are selected depending on the diameter of the bronchi of the target lobe. The valve implantation technique is a straightforward procedure technically that is performed by using a special flexible delivery catheter that can be inserted through a 2.8-mm or larger working channel of a standard bronchoscope.

Impact of Lobar Occlusion and Collateral Ventilation

Endoscopic valve placement is, to date, the best-studied ELVR technique. Since the first publications in 2003, various trials have been performed leading to expanded knowledge with this technique. The first RCT that is currently the largest trial is the Endobronchial Valve for Emphysema Palliation Trial, also known as VENT.[7] Sciurba and colleagues[7] compared 214 patients with emphysema who underwent valve therapy with 101 patients who received standard medical care. Patients who were treated by EBV developed an improvement of 4.3% in FEV_1, whereas the patients of the control group experienced a decrease of 2.5%. Similar benefits were observed