

Clinical management of lung volume reduction in end stage emphysema patients

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Abstract: Following the evaluation of surgical lung volume reduction (LVR) in the National Emphysema Treatment (NETT) trial, different endoscopic LVR procedures have been developed for severe emphysema. Among those, endobronchial valve placement is the best evaluated method. All these therapies aim at reducing hyperinflation and at improving respiratory mechanics. It has been shown that these procedures can improve quality of life, lung function and exercise capacity in a significant and clinically meaningful way in suitable patients. Optimal medical therapy, physical rehabilitation, smoking cessation and respiratory insufficiency assessments should be thoroughly evaluated by a multi-disciplinary team before considering any LVR procedure. Clinical experience is necessary to decide if a patient is an appropriate candidate for a surgical or an interventional LVR procedure, to choose the optimal treatment strategy and to provide a high-level of care after the intervention, particularly when complications such as pneumothorax or persistent air leak occur in this already severely ill patient population. High volume emphysema care centers, providing a broad spectrum of different LVR procedures and involving a multidisciplinary team in the diagnostic process, are best suited to provide an optimal outcome. The aim of this manuscript is to describe the structures and procedures required to achieve the best possible outcome even in patients with advanced stage of their emphysema disease, including patients who are candidates for lung transplantation.

Keywords: Emphysema; lung volume reduction (LVR); valves; lung volume reduction surgery (LVRS)

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Introduction

Chronic obstructive pulmonary disease (COPD) is predicted to become the third most frequent cause of death in the world by 2020 (1). Pulmonary emphysema is an important clinical phenotype of advanced COPD characterized by tissue destruction, hyperinflation and ventilation-perfusion mismatch. With the intention to decrease hyperinflation, to improve ventilatory mechanics and diaphragmatic function, and thus to reduce the work of breathing, surgical and more recently bronchoscopic lung volume reduction (BLVR) procedures have been developed and successfully evaluated

for patients with pulmonary emphysema.

The National Emphysema Treatment (NETT) trial has shown that lung volume reduction surgery (LVRS) can reduce mortality and increase exercise capacity in selected patients with heterogenous upper-zone emphysema and reduced exercise tolerance. A moderate increase in exercise capacity was also found in patients with homogenous emphysema and low exercise capacity (2). BLVR procedures (valves, coils, vapor and foam) have been subsequently developed and shown in clinical studies to improve significantly lung function, exercise capacity and quality of life (3-6). For Coils, Vapor and Foam, more evidence

is required regarding their optimal treatment selection algorithms.

For optimal outcomes, accurate patient selection, management and postoperative care are critical (7,8), and less well understood in patients with very severe emphysema, particularly because they have been excluded from treatment in many former studies.

An important issue requiring special consideration is the application of lung volume reduction techniques as a bridge or alternative to lung transplantation. Our center is a tertiary referral center for end-stage emphysema patients that offers all treatment options including a lung transplantation program. This manuscript focuses on the structures and procedures required to safely perform bronchoscopic and surgical LVR, with special focus on patients in very advanced stages of their emphysema.

Patient selection

Lung function

A broad experience in bronchoscopic or surgical LVR and optimal selection of patients is crucial for favorable patient outcome. In many clinical studies, patients with an airway obstruction FEV1 >40% and a hyperinflation with RV <200% were included for bronchoscopic or surgical therapy assessments (2-5,9-12). However, in our opinion this does not reflect current selection algorithms, as tissue destruction and hyperinflation have to be severe enough to allow for significant improvements. Regarding coils, a recently published post-hoc analysis of a multi-center trial showed that patients improve after bilateral coil placement only if their baseline RV exceeds 225% predicted (5), which is higher than the value of 150% described for surgical LVR and Vapor ablation (13,14). It is important to emphasize that all LVR modalities are thought to work primarily by reducing lung hyperinflation, or in operational terms, by reducing residual volume. In our and many other emphysema care centers, patients are usually considered for any type of LVR procedure only if they present with values of FEV1 <40% predicted and RV >200% predicted. These limits are supported by the average baseline characteristics in the major trials (7). Additionally, the RV/TLC ratio may provide further guidance if larger, ideally, than 0.58 as described by Caviezel *et al.* (13). Whether there is a clear lower limit of FEV1 to exclude patients from LVR procedures is still under debate and will be discussed later. A diffusion capacity (DLCO) <20% has been described as a

predictor for increased mortality after LVRS and is usually considered a contraindication for surgical LVR (2).

6-minute walk test (6-MWT)

It is important to evaluate exercise capacity for LVR to exclude patients who will not improve after the procedure. The 6-MWT can be performed in a standardized manner and has become established as the method to evaluate exercise capacity (15). Patients with a 6-MWT above 450 m are not physically limited enough to notice a clinical improvement after LVR and should be excluded from any LVR procedure. Patients with a 6-MWT <200 m are pathophysiologically limited most often by reasons other than dynamic hyperinflation, e.g., reduced skeletal muscle strength, obesity or cardiac issues. Those patients should be sent for intense pulmonary rehabilitation before being re-evaluated for LVR (8). Patients who are not limited by dynamic hyperinflation have a low probability of clinical improvement after LVR. Although it has not been proven by prospective trials and is only based on our clinical experience, if the oxygen saturation does not decrease during a 6-MWT, the patient's exercise capacity may be limited by comorbidities and not by the emphysema. In such a situation LVR should be carefully reconsidered.

Collateral ventilation (patient selection for valves only)

One of the most important results of the VENT trial is that patients with collateral ventilation have to be excluded from BLVR with valves (9). Appropriate patients with no collateral ventilation can expect significant and clinically meaningful improvements in lung function, exercise capacity and quality of life from BLVR with valves (4). When a bronchoscopic procedure with valves is considered, the collateral ventilation status has to be evaluated before making a decision on the appropriate LVR procedure (7). Measuring collateral ventilation by a bronchoscopic procedure (CHARTIS[®]) predicts successful LVR in 70–90% of patients (4,16,17). A surrogate for the presence of collateral ventilation is an incomplete fissure between two lobes assessed on CT scan. While visual analysis of the fissures may be erroneous, software-assisted evaluation together with quantitative CT scan (QCT) can quantify the completeness of the fissure. Fissure completeness below 80% predicts the presence of collateral ventilation and a low probability of successful bronchoscopic LVR with valves. In this situation CHARTIS measurement might not

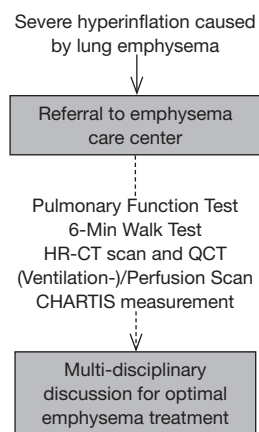


Figure 1 Patient selection and assessment should be standardized and transparent. Decisions should be made by a multi-disciplinary team discussion that includes all specialists responsible for emphysema treatment.

be necessary (18). These patients should be considered for surgical LVR or alternative bronchoscopic methods.

CT scan

The HR-CT scan should be assessed not only for collateral ventilation but also for severity of lobar emphysema. Other pulmonary findings such as significant bronchiectasis and fibrosis disqualify patients for any LVR procedure. A suspicious nodule in the target lobe favors a surgical approach if the patient otherwise qualifies for LVRS. If the CT scan reveals the emphysema is mainly caused by secondary LVR of an adjacent area (i.e., bronchiectasis), patients should not be subjected to further LVR evaluation.

Smoking cessation

Patients who are continuous smokers should be excluded from any LVR procedures. This is more an ethical than evidence-based question. As continuous smoking doubles the loss of lung function over time compared to patients who stopped smoking, any post-treatment lung function improvement gained will vanish within a few years (19). The decision to offer a LVR procedure is a good time to motivate COPD patients to quit smoking.

Multidisciplinary board (MDB)

In cancer treatment, MDBs are routinely established and

lead to improved treatment decisions compared to decisions made by the single specialist. In emphysema treatment, where interventions are performed purely for functional reasons, MDBs have been established only in a few dedicated centers (20).

For the treatment of emphysema patients, endoscopic treatment is frequently performed by interventional pulmonologists whereas surgical LVR is performed by thoracic surgeons. A MDB should at least be attended by thoracic surgeons, interventional pulmonologists and radiologists, to cover all involved specialties, and to guide optimal treatment decisions. Ideally, all patients should be discussed in a MDB prior to any LVR intervention (*Figure 1*). In our center, a MDB that meets on a weekly basis was established in 2016.

Patient management

Patients with severe emphysema suffer from significantly impaired gas exchange and diminished ventilatory capacity. Comorbidities are also frequent in these patients, resulting in an increased risk of peri-interventional complications from any form of LVR procedure. Unstable patients with active infection or cardiac insufficiency should be stabilized before the intervention.

Medical therapy

Pharmacological interventions with bronchodilators significantly improve lung function and hyperinflation at rest and during exercise and reduce the intensity of dyspnea in patients with COPD (21,22). Although Stage IV COPD patients have been assessed only in few randomized controlled trials, these patients should have been under optimal pharmacological treatment according to the GOLD guidelines (1). Patients should only be considered for LVR therapy after optimal medical therapy does not lead to sufficient improvement of disease severity.

Rehabilitation

Severe COPD is not only linked to lung tissue destruction and respiratory muscle dysfunction, but also to limb muscle dysfunction caused by muscle disuse atrophy resulting from low physical activity, chronic systemic inflammation, nutritional factors, drugs and comorbidities (21,23). Exercise training can significantly increase muscle mass and can have a positive effect on exercise capacity, quality

of life and even lung function (24). Patients considered for endoscopic or surgical LVR should be evaluated for limb muscle dysfunction and should undergo a specialized pulmonary rehabilitation program that includes and focuses on a specific exercise-training program. This is especially mandatory when patients are limited not only by dynamic hyperinflation but also because of deconditioning.

Hypoxemia & hypercapnia

Patients with severe hypoxemia or hypercapnia do not have to be excluded from LVR procedures if a significant improvement in blood gas analysis can be achieved, either with supplementary oxygen or non-invasive ventilation. Patients with severe hypoxemia (<55 mmHg, room air) should be treated with supplementary oxygen before performing the LVR procedure. The oxygen flow should be adjusted after the procedure. For patients with significant hypercapnia (>55 mmHg), non-invasive ventilation should be initiated before and adjusted after the procedure. Bronchoscopic LVR can improve respiratory mechanics and increase alveolar ventilation (25).

LVR and lung transplantation

Severe COPD is the most common indication worldwide for lung transplantation. However, when organs are allocated according to the lung allocation score (LAS), as used in Germany and in the USA, patients with COPD have a lower chance of receiving an organ (26). Only limited data are available for endoscopic LVR in patients on waiting lists for lung transplantations. These “Low-FEV1”-patients with an FEV1 \leq 20% predicted are severely impaired by lung emphysema with seriously diminished quality of life and have the highest need for therapy (27). Two separate studies evaluating BLVR using endobronchial valves in LOW-FEV1 patients have shown that EBV therapy is feasible and safe, and improvements of lung function and exercise capacity are comparable to patients with less severely diminished lung function (28,29). BLVR with endobronchial valves improves lung function and quality of life of patients awaiting lung transplantation and does not influence the outcome after lung transplantation. BLVR with valves can therefore be considered an adequate bridging strategy to lung transplantation (30,31).

A pneumothorax after BLVR can occur and lead to a critical situation. Immediate attention and chest tube placement can be necessary. This is even more important in

patients with Low-FEV1, and close supervision, preferably in the ICU, for at least 24 h after the bronchoscopic procedure is recommended (28). For more than 20 years, surgical LVR has been used as an alternative to lung transplantation, and as a bridging procedure to postpone the need for lung transplantation, as well as an option to improve the patient’s condition prior to transplantation (32-34). While early experience of uniformly good results has been described for lung transplantation after LVRS, two reports from the US raised concerns that the long term outcome might be impaired (35,36). Such impairment, however, does not match the authors’ personal experience and has not been confirmed by others. Further, a recent paper from the Zurich group reports that long term outcome after lung transplantation is not negatively effected by prior LVRS (37). Ultimately, patient selection for both procedures remains a crucial issue in achieving good outcomes.

Conclusions

To achieve the best possible outcome, selection and treatment of patients with severe emphysema should be performed in a setting where all treatment options are available and the involved specialists cooperate in in the framework of an emphysema care center. After careful evaluation and pre-interventional preparation, the most appropriate treatment procedure has to be selected by a MDB. Since further evidence on treatment selection algorithms is needed such a setting facilitates prospective clinical trials. When LVR procedures are performed by experienced teams together with close postoperative patient monitoring, LVR treatments are an efficient therapy that might be offered also to patients with very severe forms of the disease.

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Footnote

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