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Editorial

Bronchoscopic Lung Volume Reduction: 7 Lessons Learned☆

Reducción de volumen pulmonar por broncoscopia: 7 lecciones aprendidas

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It's true. We have learned a lot in the short time since bronchoscopic lung volume reduction (BLVR) was introduced. Now we can better define the indications and the steps required to treat this numerous group of patients. With the experience acquired over the last five years, patient groups susceptible to improvement have been better defined. We have been able to learn from our mistakes, and the best treatment for each patient has been determined. All this, along with the technical advances made in endobronchial devices for the endoscopic treatment of emphysema, open a promising future for this patient group.

In both the surgical treatment as well as the endoscopic treatment of emphysema with air trapping, the therapeutic objective is similar: diminish pulmonary hyperinflation. In these patients with narrowing of the airway, destruction of the alveolar walls and reduced elasticity, air trapping reduces inspiratory capacity, which produces a lower tolerance to exercise, increasing diaphragm pressure and requiring the use of accessory muscles. BLVR is able to: reduce respiratory effort and pressure on the diaphragm and chest wall, improve lung elasticity, reduce airway resistance, reduce so-called "dynamic hyperinflation" with exercise, improve the ventilation/perfusion ratio and therefore oxygenation and improve breathing dynamics by reducing dyspnea and increasing tolerance to exercise.[1]

It is surprising to know that in the 1990s more than 4000 lung volume reduction surgeries were done annually in the United States, but today only about 200 procedures are done.[2] The famous NETT[3] study revealed some chilling data about this surgical treatment: mortality 5%, intraoperative complications 9%, postoperative complications >50% (reintubation 21.8%; arrhythmia 18.6%; pneumonia 18.2%; readmittance to ICU 11.7%; tracheotomy 8.2%), 28% of the patients required hospitalizations of more than one month, and only 30% of those treated experienced an improvement.

We have gained experience from the surgical treatment of lung volume reduction in emphysema and, although the beginnings have not been clear in BLVR, we now know that we are headed in the right direction. The group that responded to the bronchoscopic procedure presented several advantages over those with surgical treatment: less morbidity, almost no mortality, the ability to retreat, the treatment is reversible in the case of valves, lower cost and shorter hospital stay. Although the price is lower than that of the surgical alternative, in these times of economic crisis and control over health-care expenses, it cannot be forgotten that the cost of each treatment is about 15000 euros.[4]

Currently, the most widely used devices for BLVR are: endobronchial valves, foam sealant, metallic coils and thermal ablation with vapor. As of yet, none of these treatments for BLVR have been approved by the FDA for this procedure (although the valves have been approved for the treatment of persistent air leaks), while in Europe both the valves as well as the foam sealant have attained the CE mark and approval for their use in LVR. Thermal vapor ablation[5] and coils[6,7] are currently in the approval phase. The use of endobronchial blockers has been rejected due to their frequent migration.[8] Airway bypass stenting has also not been successful in homogeneous emphysema because it is a complex technique that is not without risks and has shown no long-term improvement when studied.[9,10]

In BLVR treatment with valves, there are two options available: endobronchial valves (EBV) (now called Zephyr, previously Pulmonx[11] and Emphasis[12]) that have a duck-bill shape; and intrabronchial valves (IBV) (Spiration[13]) that are umbrella-shaped. Among the numerous studies published about these valves is the VENT study,[14] which evaluated the clinical efficacy of Zephyr valves in 321 patients with severe emphysema. Unfortunately, this study was done hastily and was very heterogeneous: only unilateral treatments were applied, there was no blinded control group and the existence of collateral pulmonary ventilation was not assessed. The approval from the FDA was not attained after this study, but it demonstrated an overall improvement in FEV_1 of 6.8%, an increase in the distance walked in the 6-min walk test of 5.8% and a modest increase in the St-George's quality-of-life questionnaire. Later, upon analyzing the subgroups, in patients with lobar exclusion there was an observed improvement in FEV_1 of between 20% and 40% and in residual volume of more than 225%. What remained clear was that, before treatment with valves, the integrity of the scissures must be assessed on CT and collateral circulation must be studied with the so-called Chartis system.[15,16]

Foam sealants may be biological, like the fibrin-thrombin compound or the so-called biological hydrogel,[17] which is made up of

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fibrin, chondroitin sulfate and L-lysine. There are also innovative synthetic foam sealants, like AeriSeal,[18] which is an easy-to-apply polymer that has provided hopeful results in preliminary studies.

Many experts coincide in their opinion that sales pressure, confusion in protocols and the variability in the response require us to once again analyze the steps that should be taken while taking a step back in order to be able to decide the right direction to go from a new perspective.

In the brief but intense journey from the time when patients first started to be treated for LVR, we have learned many things. The following seven points stand out:

1. Treatments with endobronchial valves are effective in heterogeneous emphysema if there is "complete lobar exclusion", meaning that the scissures are whole and that there is no collateral communication with other pulmonary lobes or segments.
2. When possible, it is recommended to use endobronchial valves; this is a reversible procedure as they can be easily extracted if the patient's condition either worsens or does not improve (which is not possible with foam sealant, coils or vapor).
3. As they do not depend on pulmonary ventilation, neither foam sealant, nor coils nor vapor ablation requires complete lobar exclusion to be effective.
4. Foam sealant and vapor in particular can mask over lung cancer and should not be used in lobes with nodules, scarring or bronchial thickening.
5. Coils cause a very important mechanical retraction of the pulmonary parenchyma, and if there is a peripheral air leak it may be very difficult to resolve.
6. The patients who demonstrate the best response are those who have a higher degree of air trapping, with a residual volume higher than 225%. Patients with very severe COPD and diffusion below 20% or FEV_1 lower than 20% should not be treated.
7. When the emphysema is very homogeneous on CT, valves cannot be used. In these cases, pulmonary perfusion gammagraphy should be done in order to determine the most pathologic areas to be selected for treatment with foam sealant or vapor.

Although more statements could be added to this list, this is mainly what has been learned in order to correctly manage BLVR in this patient group.

One clear idea is that these treatments should be done in Bronchoscopy Units at tertiary hospitals with experience in interventionist bronchoscopy that have complete lung function laboratories and COPD outpatient consultations. The treatment of these patients is multidisciplinary, involving the physician, the bronchoscopist and the lung function laboratory specialist. This is the only way to correctly understand the best treatment for each patient in all its complexity. The Bronchoscopy Units should have all BLVR treatments available in order to individualize the best treatment for each patient.

Briefly, we can say that a series of very precise steps must be followed in order to adequately treat only those patients who are likely to improve with BLVR treatment:

- Select symptomatic patients or those with progressive deterioration who meet the functional criteria of RV >225%, FEV_1 20%–45% and diffusion 20%–59%. Perform the St. George's quality of life survey to determine the response to treatment.
- Carry out high-resolution chest CT in order to characterize the most affected areas of emphysema. Classify the emphysema as predominantly homogenous or heterogeneous. In the case that it is homogeneous, also do a pulmonary perfusion gammagraphy.
- When on CT the emphysema is heterogeneous, the first option should be valves because this treatment is reversible. Complete lobar exclusion should be previously confirmed, assessing the integrity of the scissure on CT and performing a collateral air circulation study.
- When on CT the emphysema is homogeneous, or instead if it is heterogeneous but there is collateral communication, the best treatment is the application of foam sealant.

A year has passed since in *Archivos de Bronconeumología*[19] endoscopic treatment of emphysema was discussed and, due to the advances and changes in this area, half a decade seems to have already gone by. We cannot be pleased with the current results, but we have learnt a lot and we are aimed in the right direction. Certainly BLVR is a cutting-edge treatment that can potentially be applied in a very wide range of patients. Thus, it is very important to outline which cases should be treated in order to establish the best treatment, and this should be a joint effort between clinicians and bronchoscopists.

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