Lung volume reduction for severe emphysema: scalpel or bronchoscope?

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Comment on: Kouritas V, Tcherveniakov P, Milton R, *et al.* Impact of the type of initial intervention on the outcomes of lung volume reduction for emphysema: a propensity matched study. Ann Transl Med 2022;10:1275.

Keywords: Severe emphysema; hyperinflation; lung volume reduction surgery; endobronchial valves (EBV)

Submitted Jan 05, 2023. Accepted for publication Feb 01, 2023. Published online Feb 09, 2023.
doi: 10.21037/atm-2023-1
View this article at: https://dx.doi.org/10.21037/atm-2023-1

Lung volume reduction (LVR) in severe emphysema improves elastic recoil in lung tissue, thus decreasing expiratory airway collapse, and allows respiratory muscles to work at less mechanical disadvantage. It was first performed by surgeons as early as in the 1950s by removing the most affected area of emphysematous lung in an open operation (1).

The perceived risk of lung volume reduction surgery (LVRS), however, has stimulated the development of less invasive bronchoscopic methods of LVR. Endobronchial valves (EBV) are placed in the airways supplying the most emphysematous lobe to create lobar atelectasis (2). Interlobar collateral ventilation (CV) can prevent efficacy, as the valve occluded lobe refills with air from adjacent lobes via incomplete interlobar fissures. There has been much effort to develop bronchoscopic alternatives for CV-positive situations, using coils, heated water vapor and polymer foam (2). But a paucity of clinical data and uncertainties about the risk benefit ratio of these alternative approaches delay their clinical implementation.

So, if LVR is considered, in most settings—like in the German health care system—LVRS and EBV are the only available approaches in clinical routine. In properly selected patients both can improve pulmonary function, exercise capacity, quality of life and survival (2,3). So far, however, both methods have only been studied in large clinical trials against optimized standard care including smoking cessation, pharmacotherapy and pulmonary rehabilitation, but not compared with each other. There is much overlap between the indications for LVRS and EBV, and there is uncertainty about which is preferable in patients who are eligible for both modalities. It is clinical practice at most emphysema treatment centers to initially use EBV as the less "dangerous" option, reserving LVRS for those patients, who do not benefit from EBV.

Published on *Annals of Translational Medicine*, a study from Kouritas *et al.* (4) presents retrospective data from their single-center LVR database. They retrospectively identified 111 patients in the period between 2012 and 2017, who could have been assigned to both LVRS and EBV. In the search for the "nearest neighbor" using propensity score matching in relation to age, gender, performance status, body mass index and lung function, comorbidities and exercise tolerance, two patient groups with comparable baseline characteristics were formed. Finally, from this patient pool 44 EBV patients were compared with 44 matching LVRS patients.

At a median follow-up of 32 months, they found similar morbidity and mortality in both groups. EBV had a shorter hospital stay (median 6 *vs.* 10 days, P=0.006) while LVRS necessitated fewer but more severe reinterventions (median 1 *vs.* 2 interventions, P<0.01). They also found better improvement in breathing and quality of life in the LVRS group.

There are relevant limitations to this retrospective single-center study. Most importantly, there had been no uniform protocol for follow-up in the period under review. So, there

is no consistent follow up data regarding lung function and 6-minute-walk-distance. Efficacy is assessed using only COPD Assessment Test (CAT) scores and subjective patient ratings of "breathing ability" (recorded as same, better or worse). Therefore, despite efforts at propensity matching, the study is certainly prone to bias and cannot be used to establish the superiority of LVRS over EBV and to describe an algorithm for treating severe emphysema that is equally applicable to both LVRS and EBV. Confirmation in rigorous randomized prospective trials is required.

In the meantime, however, it is still worth taking a look at these preliminary data. They can support us in every day practice explaining the advantages and disadvantages of both modalities to our patients. Obviously, the perception that LVRS is more "dangerous" cannot be confirmed. It has evolved from an open surgery sometimes with a sternotomy to video-assisted or even robotic-assisted thoracoscopic surgery (VATS/RATS), which involves less trauma with less morbidity and mortality. On the other hand, EBV is not a "harmless" alternative. Thus, EBV does not always have to have priority in the case of equal suitability. Obviously LVRS is a more definitive treatment approach, requiring a longer in-hospital recovery period but producing a fairly stable effect with less need for re-interventions. EBV, on the other hand, is associated with a shorter recovery but a more variable effect due to migration of valves and the occurrence of pneumothorax requiring repeated bronchoscopy or placement of chest tubes.

Prospective randomized trials are on their way. The Comparative Effectiveness of Lung volume reduction surgery for Emphysema and Bronchoscopic lung volume reduction with valve placement (CELEB) trial was designed to prove the superiority of LVRS over EBV (5). Results have already been published in abstract form (6). With enrollment between September 2016 and July 2019 the follow up period of this study coincided with the coronavirus disease 2019 (COVID-19) pandemic, leading to relevant logistical problems in data collection and leaving some patients with incomplete data at the 12-month follow-up. Comparing 41 LVRS- with 47 EBV-patients, the trial appears to confirm the fact, that morbidity and mortality are the same for both treatment modalities. The primary efficacy endpoint was change from baseline in the i-BODE score. This composite measure of disease severity comprises body mass index, airway obstruction [forced expiratory volume in 1 second (FEV_1)], dyspnea [Medical Research Council (MRC) Dyspnea scale] and exercise capacity (incremental shuttle walk test). Neither the improvement in the i-BODE composite score (LVRS: −1.10, BLVR: −0.82, P=0.54) nor in its individual components differed between treatment arms, so that the superiority threshold was not reached. Both treatments also resulted in similar improvements in gas trapping (residual volume % predicted: LVRS −36.1, BLVR: −30.1, P=0.81). Interestingly, post-randomization six patients randomized for LVRS but only one patient randomized for EBV decided against having the procedure. This again points towards exaggerated concerns about the risk of the surgical procedure, which need to be addressed in careful and well-informed patient education. Another study, the SINCERE trial, has been recruiting since September 2020 and results are not expected until the second half of 2024 at the earliest (NCT04537182).

For the time being, the question of whether scalpel or bronchoscope is preferable for LVR cannot be answered unequivocally. Finally, it must be mentioned, that the available data of Kouritas *et al.* (4). and those of the CELEB study do only apply to the situation of equal suitability for both LVRS and EBV. There are certain situations with clear advantages for one modality or the other. Emphysema with marked intralobar heterogeneity or predominance in the upper lobes or paraseptal regions may be better suited for LVRS. Frail patients and patients with certain comorbidities like pulmonary hypertension may be better served with EBV.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Translational Medicine*. The article did not undergo external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-2023-1/coif). WG has received lecture fees from Pulmonx GmbH. HH reports receiving payment from AstraZeneca, BMS, MSD, and Medela; he also reports participation on a Data Safety Monitoring Board or Advisory Board of AstraZeneca, and BMS; leadership or fiduciary role in IASLC-SPFC. None related to the present manuscript.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Gesierich W, Hoffmann H. Lung volume reduction for severe emphysema: scalpel or bronchoscope? Ann Transl Med 2023;11(3):140. doi: 10.21037/atm-2023-1

