BMJ Open Respiratory Research

Bronchoscopic lung volume reduction: model for assisted target lobe selection

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To cite: Hostetter L, Brown LM, Rajagopalan S, *et al*. Bronchoscopic lung volume reduction: model for assisted target lobe selection. *BMJ Open Respir Res* 2025;**12**:e002903. doi:10.1136/bmjresp-2024-002903

Received 16 December 2024
Accepted 28 April 2025

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ABSTRACT

Introduction Bronchoscopic lung volume reduction with endobronchial valves (EBV) is an effective procedure for patient with severe emphysema to improve lung function, exercise tolerance, dyspnoea and quality of life. Optimisation of patient and treatment lobe selection is essential for successful EBV outcomes. While clinical selection criteria are rigorous, many centres use a multidisciplinary team and rely on previous clinical experience for the selection process. To aid objective clinical decision making, we present a mathematical model to facilitate patient and target lobe selection.

Methods A multidisciplinary team reviewed quantitative high-resolution computed tomography (HRCT) analysis from 119 patients to select candidates for EBV and to select a treatment lobe. Two logistic regression models, (1) candidacy for EBV placement and (2) target-lobe selection, were developed based on the normalised distributions of the four quantitative HRCT variables (fissure completeness score, per cent of voxel density with HU < −910 and HU < −950, and lobar volumes) across all five lung lobes. An external cohort of 50 patients (25 candidates and 25 non-candidates) was used to validate the prediction model.

Results Performance measures of the training cohort demonstrated an area under the curve (AUC) of 0.91, accuracy of 81%, sensitivity of 93% and specificity of 78% compared with the multidisciplinary teams' target lobe selection. The validation cohort demonstrated an AUC of 0.89, accuracy of 84%, sensitivity of 88% and specificity of 83% compared with the multidisciplinary team decision making.

Conclusions Endobronchial valve lung volume reduction remains a potent palliative measure to improve quality of life in patients with hyperinflated emphysema. Our model for target lobe selection harnesses the multidisciplinary experience at a tertiary care centre to objectively select candidates and target lobes to assist clinicians' decision making. Future studies investigating prediction of lobar collapse and functional improvement after target lobe selection using our model are needed.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patient selection for endobronchial valve placement is rigorous with only 20%–30% of patients evaluated for endobronchial valves undergoing the procedure, and of those who undergo the procedure even fewer derive clinical benefit. Currently, patient selection is based on clinical experience and using a multidisciplinary team which may not be widely practised. We conducted this study to develop a tool to harness the experience at two multidisciplinary centres to aid in clinical decision making of selecting target lobes for endobronchial lung volume reduction.

WHAT THIS STUDY ADDS

⇒ We developed a mathematical model (harnessing a multidisciplinary approach) to assist clinicians at choosing candidates and target lobes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We hope to use our model to expand awareness of endobronchial valves and to aid in clinical decision making for optimal patient selection.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) negatively impacts physical health, mental health and quality of life, with dyspnoea being described as the leading component impacting quality of life scores.[1] Dyspnoea is especially prevalent in those with an emphysematous phenotype where obstruction and hyperinflation contribute to breathlessness and are minimally responsive to maximal inhaler therapy. Bronchoscopic lung volume reduction (BLVR) is a valuable tool to address dyspnoea in patients with hyperinflated emphysema and has been shown to improve forced expiratory volume in one second (FEV1), exercise tolerance, dyspnoea and quality of life.[2–8]

Patient selection and target lobe selection are critical for successful endobronchial valve (EBV) placement. Inclusion/exclusion criteria have been well defined with most centres using selection criteria from the LIBERATE trial.[6] First, a high-resolution computed tomography (HRCT) is obtained and analysed with a quantitative analysis programme.[8] This quantitative analysis provides information on fissure completeness, emphysema severity (lung density measures) and lobar volumes. When a patient is deemed a candidate for EBV placement, target lobe is decided based on expert opinion using these quantitative data. Some centres use a multidisciplinary approach for patient and target lobe selection including COPD subspecialists, radiologists, interventional pulmonologists, thoracic surgeons experienced in lung volume reduction surgery, and lung transplant pulmonologist—highlighting the difficulties in the selection process.[9] However, many practices do not have access to a multidisciplinary team leaving treatment planning to a single proceduralist. Our study presents the development and validation of a multivariate prediction model for patient candidacy and treatment lobe selection to augment clinical decision making for physicians performing BLVR.

METHODS

A retrospective cohort of patients with hyperinflated emphysema referred for EBV evaluation from January 2019 to May 2021 was reviewed and StratX (PulmonX Corporation, Redwood City, CA) analysis of HRCT scans from 119 patients had been previously obtained to assess EBV candidacy. Cases were obtained from three Mayo Clinic sites including Arizona, Florida, and Rochester, Minnesota. A multidisciplinary team of physicians with expertise in COPD and BLVR reviewed 119 patients of which 83 were deemed to be candidates for EBV placement and 36 patients were not candidates. Candidacy was determined from randomised controlled trials to date with clinical criteria derived from the LIBERATE trial and prior clinical experience.[6] Inclusion criteria included ages 40 to 75, quit smoking for more than 6 months, stable prednisone requirements of 20 mg or less, patients who had less than two COPD exacerbations or episodes of pneumonia in the last year, no lung nodules being monitored for malignancy, systolic pulmonary artery pressure less than 45 mm Hg on echocardiography, $PaCO_2$ less than 50 mm Hg, post-bronchodilator FEV_1 of 15%–45% predicted, total lung capacity greater than 100% predicted, residual volume greater than 175% predicted, diffusion capacity (DLCO) greater than or equal to 20% predicted, 6-min walk between 100 and 500 metres, and prior completion of pulmonary rehabilitation. Two logistic regression models were developed: (1) a candidacy prediction model and (2) a model for assigning probabilities to lobar segments to identify target lobe(s) for treatment. To capture inter-lobar heterogeneity, the candidacy model was developed based on the coefficient of variation of fissure completeness score, per cent voxel density with HU < −950 and lobar volumes; additionally, the maximum of the per cent voxel density with HU < −950 and fissure completeness was also used. The model for the target lobe was based on normalised distributions of the four StratX variables (fissure completeness score, per cent voxel density with HU < −910 and HU < −950, and lobar volumes) across all five lung lobes. An external cohort of 50 patients (25 candidates and 25 non-candidates) from Vanderbilt University in Tennessee previously referred for EBV evaluation was used to validate the prediction model. Patients treated at Vanderbilt similarly undergo a multidisciplinary review with a pulmonologist, radiologist, thoracic surgeon and interventional pulmonologists. Performance measures (area under the curve (AUC), accuracy, sensitivity and

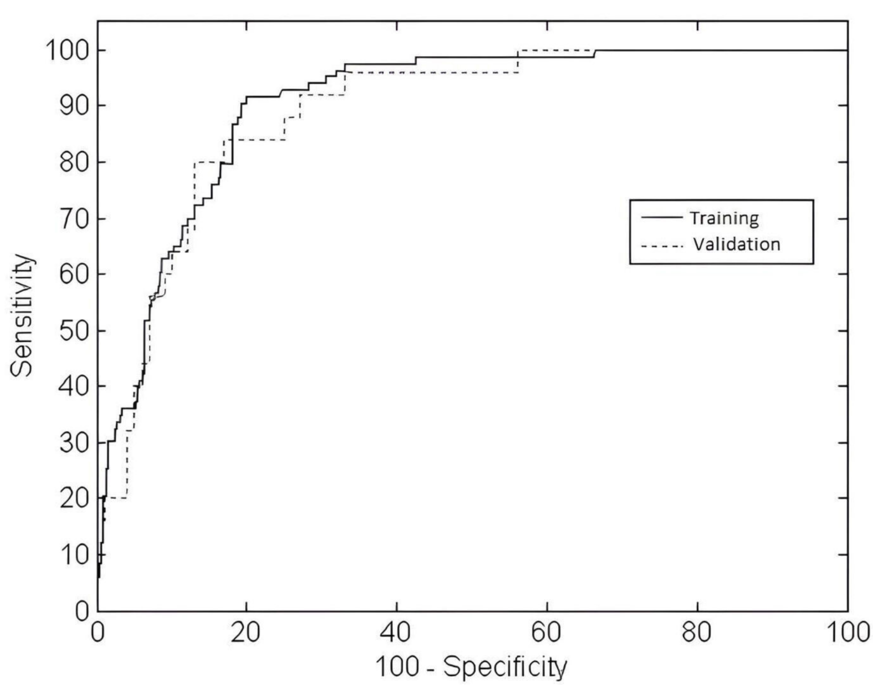

Figure 1 Receiver operating characteristic of sensitivity and specificity for the training and validation cohorts. AUCs were 0.91 and 0.89, respectively. AUC, area under the curve.

Table 1 Logistic regression model to predict the candidacy for bronchoscopic lung volume reduction

Variable	Coefficient	SE	Wald	P value
Max				
HU −950	0.15058	0.035664	17.8276	**<0.0001**
Fissure integrity	0.062339	0.0226949	7.5759	**0.0059**
Coeff of variation				
HU −950	5.72415	2.08451	7.5407	**0.0060**
Fissure integrity	−13.54899	3.82725	12.5326	**0.0004**
Lobar volume	−22.67233	6.65668	11.6005	**0.0007**
Constant	−3.23687	2.57604	1.5789	0.2089

Bold values indicate statistical significance of $p < 0.05$.

specificity) were computed for the training and validation cohort. Probability cut-off values for target lobe assessments were derived from the Yule's coefficient. This study was deemed exempt by the institutional review board (IRB) at both study sites (IRB# 21-005149) and (IRB# 212032).

Patient and public involvement

Outside of the institutional IRB process, as this was a retrospective study, there was not additional public involvement in the development or conduct of this study.

RESULTS

The candidacy model demonstrated an AUC of 0.92 (95% CI: 0.865 to 0.967) for the training set and 0.87 (95% CI: 0.81 to 0.93) for the validation cohort. The target lobe model training cohort demonstrated an AUC of 0.91 (95% CI: 0.878 to 0.937), accuracy of 81%, sensitivity of 93% and specificity of 78% when compared with the multidisciplinary team's target lobe selection. For the validation cohort, the performance measures were 0.89 (95% CI: 0.833 to 0.947), 84%, 88% and 83% respectively (figure 1). This demonstrates excellent intra-institutional repeatability and high efficacy at candidacy and target lobe selection. The linear regression model variable coefficients used to derive first, patient candidacy for the procedure and second, target lobe probabilities are available in tables 1 and 2 respectively.

DISCUSSION

Bronchoscopic lung volume reduction is a potential treatment option for select patients with hyperinflated emphysema to improve functional status, FEV1 and quality of life. Selection criteria are in place to identify candidates for EBV placement, but treatment lobe selection requires expert opinion based on quantitative HRCT analysis and clinical history. To improve patient outcomes, some centres use a multidisciplinary team to identify candidates and determine a target lobe for treatment. The multidisciplinary selection process, while effective, is resource and time intensive and may not be accessible to all centres performing BLVR.

As a practical approach to patient evaluation, our model, in the form of a clinical calculator, could help expand awareness of the procedure and assist non-pulmonologists to identify patients who may be candidates for the procedure and prompt referral to a centre able to perform the bronchoscopy. Second, our model may make BLVR more accessible to centres beyond high-volume tertiary centres where a conventional multidisciplinary approach may not be feasible to augment clinical decision making. Similarly, this model may expedite patient review at high-volume centres with an added benefit of assigning probability to all five lobar segments—creating a priority ranking or 'backup target lobes' if the initial target is unsuccessful intraoperatively due to collateral ventilation.

Table 2 Logistic regression model to predict target lobe for bronchoscopic lung volume reduction

Variable (normalised values)	Coefficient	SE	Wald	P value
Fissure integrity	77.46221	15.85791	23.8609	**<0.0001**
HU −910	2.66658	11.54581	0.05334	0.8173
HU −950	27.29646	6.84576	16.4868	**<0.0001**
Lobar volume	−8.19511	4.3327	3.5776	0.0586
Constant	−22.3033	3.79583	34.5242	**<0.0001**

Bold values indicate statistical significance of $p < 0.05$.

As indicated in our results, the calculator had high efficacy to identify candidates and target lobes in conjunction with the multidisciplinary teams, but we must also give discrete attention to when the calculator and the multidisciplinary team differ. Interestingly, in a retrospective analysis of the validation cohort, there were 11 patients selected as candidates by the multidisciplinary team but deemed to NOT be candidates for the EBV procedures by the calculator. Of these 11 patients, one was lost to follow-up, four received subjective improvement in dyspnoea, two had positive collateral ventilation intra-operatively, three had the valves removed due to lack of response and one patient had a post-procedural pneumothorax and died postoperatively. In the seven cases, where the multidisciplinary team declined the patient for EBV but the calculator selected as candidates, the cited reasons for denial included: severe bilateral disease, target lobe in the healthier lung, diffusion capacity less than 20%, chronic non-tuberculous mycobacterium infection, fissure incompleteness, and in one case, perfusion imaging showed worse perfusion to the non-target lung. Identifying the ideal candidate for endobronchial lung volume reduction (EBLVR) is complex and there is not a single tool sufficient to identify optimal candidates, but utilisation of our tool may be helpful to achieve optimal outcomes for patients undergoing EBLVR. We advocate for this tool be used supplementally for decision making within the constructs of existing multidisciplinary teams. While this tool has high correlation with our multidisciplinary teams process, it is not designed as a stand-alone tool and does not replace physician judgement in the evaluation of patients. Certainly, clinical factors such as symptom burden, functional capacity, candidacy for lung transplantation, lung nodule management and others must be considered prior to moving forward with EBV evaluation. Rather, our model is designed to reduce the inter-observer variability and reduce the subjective nature of target lobe selection. We hope that applying a quantitative rather than qualitative approach to target lobe selection would increase response rates to the procedure. As indicated by Hartman *et al*, "It's all about the target lobe," shows that non-responders (even though they were clinically approved for the procedure) had less target lobe destruction, less heterogeneity, more target lobe perfusion and less target lobe air trapping.[10] Our tool, when used as an adjunct to decision-making process, may help in identifying the target lobe with the highest chance of post-procedure success and symptom improvement. Our calculator may be further refined by including cohorts of responders vs non-responders to enhance the calculator utility.

There are several limitations to our study. First, our model is based on decision-making practices at two centres whose practice may differ from other institutions as some may take more conservative vs broad approach to patient candidacy. Thus, our model may exclude some patients who may otherwise have been considered for EBV placement. Second, for building the candidacy model based on the training set with 30% non-candidates and five predictive variables, the minimum number of samples required is 166 in comparison to the 119 cases used in this study. Hence, future validation studies are needed. Third, perfusion imaging has become increasingly used to inform lobe targeting and provides useful perfusion information not captured in this model and should be considered.[11] Fourth, while clinical history is not included in this model (for example, prior pleurodesis, lung nodules or para-septal emphysema), these could be easily integrated into a clinical calculator to exclude target lobes for treatment. However, even with these additions, patients must still be evaluated by clinicians for appropriateness of candidacy including symptoms, exacerbation, sputum production, etc. Finally, it is important to note, our model does not predict collateral ventilation nor successful lobar collapse. We do not advocate for standalone use of this model and clinical information on perfusion and Chartis for collateral ventilation is still a critical aspect to perform BLVR. Further studies are needed using our model to assess efficacy to achieve lobar collapse compared with a multidisciplinary discussion and, more importantly, to identify responders to endobronchial valve placement.

Acknowledgements All authors contributed to the conception and writing of this manuscript.

Contributors LH, SR, BJB and TP contributed to study design and conception; LH, LMB, BJB, TP, FM, RL and MGL contributed to implementation and supervision of the study; LH, SR, TP and BJB contributed to study planning. LH, LMB, SR, MMD-E, ESE, MGL, FM, RL, BJB and TP contributed to conducting the study; LH, LMB, MGL, FM, RL and SR contributed to acquisition of data; SR, LH and LMB performed the statistical analysis, interpretation of data and TP, MGL, RL and FM verified its accuracy. All authors had full access to the data. LH drafted the manuscript and LH, LMB, SR, MMD-S, ESE, MGL, FM, RL, BJB and TP participated in critically revising the manuscript. All authors approved the final version of the manuscript. TP is the guarantor of the paper, taking responsibility for the integrity and work as a whole.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study was deemed exempt by IRB at both study sites, Mayo Clinic (IRB# 21-005149) and Vanderbilt (IRB# 212032).

Provenance and peer review Part of a Topic Collection; Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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