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# Impact of the type of initial intervention on the outcomes of lung volume reduction for emphysema: a propensity matched study

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**Background:** The type of initial intervention i.e., endobronchial valve (EBV) implantation or lung volume reduction surgery (LVRS) to be offered as initial intervention remains vague in the treatment of emphysemachronic obstructive pulmonary disease (COPD) patients. Aim of the present study was to compare the outcomes of EBV with that of LVRS in emphysema patients who could have both offered as an initial intervention.

**Methods:** The outcomes of 44 EBV patients were retrospectively compared to the outcomes of 44 matched LVRS patients (matched for age, gender, performance status, body mass index (BMI), lung functions, comorbidities and exercise tolerance, matching tolerance 0.2) treated in a single institute within a 5-year period. The median follow-up was 32 months (maximum duration 84 months).

**Results:** Mean age was 61.91±9.48 years and 55 (62.5%) were male. Postoperative morbidity was similar but length of stay (LOS) was longer in the LVRS group (median 10 vs. 6 days, P=0.006). Re-interventions were more frequent in the EBV versus LVRS group (52.3% vs. 20.5%, P=0.002) and so was the overall number of re-interventions (median 2 vs. 1, P<0.01). Breathing improved in more LVRS patients (86.4% vs. 70.5%, P<0.002). The decrease of the COPD Assessment Test (CAT) score was less significant in the EBV group (P=0.034). Survival was similar between 2 groups (P=0.350).

**Conclusions:** EBV or LVRS as initial intervention are similar in terms of morbidity and mortality. EBV showed shorter LOS whilst LVRS necessitated less but more severe re-interventions and led to better overall quality of life.

**Keywords:** Emphysema; endobronchial valve implantation (EBV); lung volume reduction surgery (LVRS); chronic obstructive pulmonary disease (COPD); initial

Submitted May 08, 2022. Accepted for publication Nov 09, 2022.

doi: 10.21037/atm-22-2429

View this article at: https://dx.doi.org/10.21037/atm-22-2429

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#### Introduction

Chronic obstructive pulmonary disease (COPD) is projected to induce an important sector of strain in healthcare systems as it is connected with high number of exacerbations, needs for medical treatment, admissions to hospital and deaths (1,2).

Lung volume reduction for emphysema [lung volume reduction surgery (LVRS) or endobronchial valves (EBVs)] can improve survival when compared to medical treatment in appropriately selected patients (3,4).

These interventional modalities are offered to patients after discussion at a dedicated emphysema multidisciplinary team (MDT), as recommended by the National Institute of Clinical Excellence (NICE) guidelines (5,6).

The decision to select one modality over the other is not always straight forward, with many cases being suitable for both. The difficulty in reaching a decision with regards to which modality to offer as initial treatment i.e., EBVs or LVRS in those cases, is augmented by the lack of studies comparing the outcomes of these 2 modalities.

The objective of the present study was to compare the outcomes of LVRS versus EBVs performed in patients who could have both offered as an initial treatment. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-2429/rc).

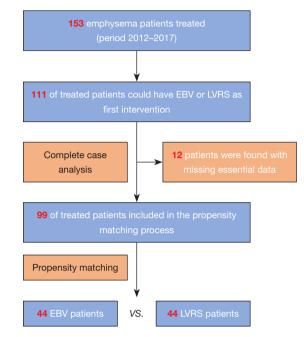
#### **Methods**

After retrospectively reviewing 153 emphysema patients treated with an intervention between 2012–2017 at our institute, 111 were identified as potential candidates for both EBVs or LVRS to be offered as the initial intervention (the rest 42 were shifted towards one intervention because of incomplete fissures on imaging or patient fitness etc., and hence were excluded from the study, *Figure 1*). This decision was either documented in the notes after discussion at the emphysema MDT or was made by a group of physicians with a special interest in emphysema interventions (prior to the establishment of the MDT) with patients having unobstructed and equal access to these modalities. All interventions were performed by board certified surgeons/respiratory physicians with a special interest in emphysema.

None of the patients included in this study was referred for lung transplantation following the LVR intervention and during the study period.

All decisions were based on NICE guidelines and on

Impact of the type of initial intervention on the outcomes of Lung Volume Reduction for emphysema: a propensity matched study FLOW CHART



**Figure 1** Flowchart of study design. EBV, endobronchial valves; LVRS, lung volume reduction surgery.

the findings of the National Emphysema Trial (NET) trial (*Table 1*) (3,6-8) Patients who fulfilled the criteria for LVR intervention and had developed fissures [proved on thin slice computed tomography (CT) scan and the Strat-X analysis] could also be eligible for EBVs apart from LVRS (6). In the cases where both modalities could be offered as initial potential treatments (and are included in this study), the final decision about what type of intervention to offer was made after discussing the risks and the benefits with the patients.

# Data

All data collected included; age and gender, preinterventional pulmonary function [forced expiratory volume in 1 sec (FEV<sub>1</sub>), diffusional lung capacity for carbon monoxide (DLCO), total lung capacity (TLC), residual volume (RV)], comorbidities (not COPD/emphysema), exercise tolerance (as noted during a 6-minute walking test-6MWT or as documented by the physician in the notes) and performance status [Eastern Cooperative Oncology Group

Table 1 Criteria to offer LVR as per NICE guidelines and NET findings

Age 40-80 years

MRC Dyspnea score ≥4

CAT score ≥20

Heterogenous, apical emphysema

Completion of fissures on 1 mm CT and favorable Strat-X (for EBV mainly)

 ${\sf FEV_1}$  between 20–40% (different levels are considered per patient)

RV above 200% (different levels are considered per patient)

Smoking cessation for at least 6 months

At least one course of rehabilitation completed

BMI >18 (for LVRS mainly)

Performance score (ECOG) 0-3

ECG, ECHO acceptable

Co-morbidities or other issues considered per patient

LVR, lung volume reduction; NICE, National Institute of Clinical Excellence; NET, National Emphysema Trial; MRC, Medical Research College; CAT, COPD Assessment Test; CT, computed tomography, Strat-X platform Pulmonics®; EBV, endobronchial valve; FEV<sub>1</sub>, forced expiratory volume in 1<sup>st</sup> second; RV, residual volume; BMI, body mass index; LVRS, lung volume reduction surgery; ECOG, Eastern Cooperative Oncology Group; ECG, electrocardiogram; ECHO, echocardiograph.

(ECOG classification)]. Also, the quantity and whether EBV or LVRS was performed and re-interventions (also for complications) were noted. Additionally, post-interventional morbidity, quality of life/breathing change post-intervention as subjectively reported by the patients at 3–6 months appointment after their interventions (captured as same, better or worse) and overall quality of life change by determining a COPD Assessment Test (CAT) score during these follow up appointments. The total length of stay (LOS) i.e., the LOS of all in-hospital stays (total number of days of all admissions) was captured for both modalities as well as the 30-day mortality (mortality documented throughout all in-hospital stays for all interventions when more than one) and survivorship (deaths up to the end of the study).

All data were collected from our on-line Patient Pathway Manager Plus domain (PPM+), the dedicated emphysema intervention database of the Thoracic Surgery Department and the patient case notes wherever appropriate.

For LVRS group, a re-intervention mainly involved re-

operation for morbidity i.e., bleeding, prolonged air leak etc. as intervention on the contralateral side was perceived as a separate case. For EBV group, any intervention on the valves after their implementation i.e., repositioning, changing or removed. Also, for both modalities insertion/reinsertion of chest drain was perceived as a re-intervention. Chartis<sup>TM</sup> catheter assessment for collateral ventilation alone was not considered as a separate intervention.

Morbidity was captured as respiratory (chest infection but not exacerbation of COPD, respiratory failure), cardiac (arrhythmia, myocardial infarction, cardiovascular failure), surgical (surgical emphysema, pneumothorax, wound infection, prolonged air leak, empyema) and other complications (for example renal, stroke etc.).

## Follow-up

Follow-up documentation was noted up to January 2020. The median follow-up was 32 months (range, 0–84).

# Description of interventions

LVRS was performed via biportal or 3-port video-assisted thoracic surgery (VATS) with buttressed bovine pericardium (Peristrips<sup>TM</sup>) staplers. At the end 1 or 2 drains were variably left into the chest. Only lung parenchyma shaving but no anatomical lung resections i.e., lobectomies were performed.

EBV insertion was conducted under general anesthesia and the use of rigid bronchoscope via which a flexible bronchoscope with adequate size working channel was used to deliver the measurement catheter with the valve (Zephyr<sup>®</sup>, PulmonX Corporation, CA, USA). This event happened after performance of a Chartis<sup>TM</sup> assessment i.e., absence of collateral ventilation.

All procedures were unilateral i.e., no bilateral procedures simultaneously were performed. During the period of the study our institute offered intervention only in patients with heterogenous and apical distribution of emphysema. Contralateral procedures for disease progression were perceived as separate treatment.

All patients recovered on a ward setting which includes a high dependency unit operated by specialist personnel apart from our team. Standard protocols of treatment (i.e., analgesia, anticoagulation and thromboprophylaxis, physiotherapy etc.) were utilized for all patients according to the type of intervention (EBV or LVRS).

Table 2 Population characteristics (N=111) BEFORE propensity score matching

Variables	LVRS, n=48	EBV, n=51	P value
Age in years (mean ± SD)	61.5±9.7	61.7±10.3	0.908*
Male gender (n, %)	29 (60.4)	33 (64.7)	0.041**
BMI (kg/m $^2$ ) (mean $\pm$ SD)	22.86±9.3	24.4±8.7	0.039*
Performance status, median [lowest-highest]	2 [1–3]	2 [1–3]	0.150#
Pulmonary function (mean ± SD)			
FEV <sub>1</sub>	39.8±16.1	32.5±9.3	0.004*
DLCO	37.4±11.2	35.3±11.4	0.347*
TLC	122.9±20.8	129.5±20.6	0.031*
RV	184.4±53.5	213.9±48.9	0.013*
Exercise tolerance in meters (mean ± SD)	193.3±26.1	157.3±23.8	0.032*

<sup>\*,</sup> Student's *t*-test; \*\*, Chi-square test; \*, Mann-Whitney Test. LVRS, lung volume reduction surgery; EBV, endobronchial valve; SD, standard deviation; BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in 1<sup>st</sup> second; DLCO, diffusional lung for carbon dioxide; TLC, total lung capacity; RV, residual volume.

# Study design

In order to exclude biased patient selection for treatment (*Table 2*) matching was performed for age, gender, BMI, pulmonary function, performance status, and exercise tolerance with propensity scores occurring from binary logistic regression and using the "nearest neighbor" technique—matching tolerance of 0.2 and matching in a 1:1 basis. Forty-four (44) matched pairs were yielded and were used for analysis. Because of the limited number of patients, the scoring was conducted based on these limited values excluding other potential ones.

The primary endpoint was the survival probability between the 2 modalities. Secondary endpoints were; the performance of another intervention (1<sup>st</sup> re-intervention) after initial intervention, the total number of reinterventions and hazard of re-interventions by time, and other outcomes such as the quality of life change reported by patients and the overall quality of life calculated via CAT scores on follow-up, the LOS, the morbidity and inhospital/30-day mortality.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was discussed with the Research and Development department of The Leeds Teaching Hospitals NHS Trust and a NHS Research Ethics Committee was not considered appropriate. The R&D department waived the need for ethical approval and consent which was verified by the clinical governance meeting of the department.

# Analysis

The data were captured by a data manager who was unaware of the outcomes of the study and therefore data accumulation was blinded. The analysis was done by 2 authors of the study separately therefore data analysis was not blinded. Both are not members of the MDT.

The IBM SPSS Statistics for Macintosh, Version 22.0. Armonk, New York: IBM Corp was used for analysis. *Figures 2,3* were produced with R version 3.6.2.

All numerical data were presented as mean ± standard deviation (SD). Skewed data were presented as median (lower value – higher value). Categorical data were presented as number of observations and percentages.

Statistically significant level was accepted at P<0.05.

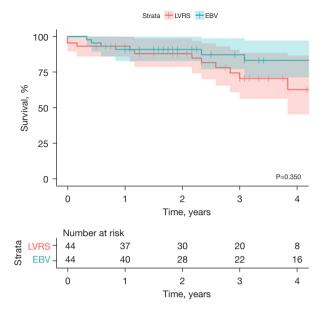
In order to capture the hazard of all re-interventions per modality by time a Nelson-Aalen analysis was performed.

Missing data were handled by conducting complete case analysis with decision to exclude appropriate cases.

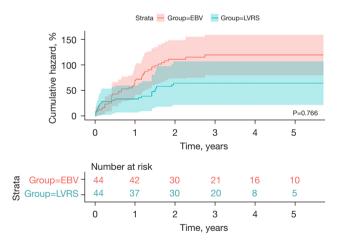
Kaplan-Meier's survival curves and long-rank were used to investigate long survival. The last date investigated was the  $18^{\rm th}$  January 2020.

#### **Results**

In the initial unmatched population, the gender, the pulmonary function tests (FEV<sub>1</sub>, TLC, RV), the BMI and the exercise tolerance were different between patients treated with EBVs and patients treated with LVRS (*Table 2*).



**Figure 2** Survival probability by time (in years) according to whether initial intervention was EBV insertion or LVRS. CI is set to 95%. LVRS, lung volume reduction surgery; EBV, endobronchial valve; CI, confidence interval.



**Figure 3** Cumulative risk of re-interventions as repeated events (Nelson-Aalen analysis) by time (in years) according to whether initial intervention was EBV insertion or LVRS. CI is set to 95%. EBV, endobronchial valve; LVRS, lung volume reduction surgery; CI, confidence interval.

After complete case analysis, 12 cases were found to have missing values from essential data (from the 111 eligible patients) and therefore were not included in the propensity matching process.

After propensity matching (pool of 99 patients, Figure 1),

the 2 groups were consisted of 44 pairs of patients with similar characteristics (*Table 3*) and comorbidities (*Table 4*).

The mean age of the 88 matched patients included in the study was 61.91±9.48 years and 55 (62.5%) were males.

Eleven deaths were captured in the LVRS group and 8 in the EBV group (P=0.437). Excluding the 30-day mortality, patients died because of their disease progression in the form of respiratory issues. However, survival was similar between the 2 groups (log-rank 0.002, P=0.350, CI: 58.832–72.730, *Figure 2*).

The total number of re-interventions was higher in the EBV group and more patients from this group had at least 1 re-intervention necessitated throughout the study (*Table 5*). However, the hazard of re-interventions as repeated events by time was not shown to be different between the 2 modalities (P=0.766, *Figure 3*).

Twelve patients (27.3%) underwent initial reintervention with re-positioning of their valves because the volume reduction effect was lost (in 10 of them EBVs had to be repositioned for more than 1 times). In 6 cases (13.6%) the valves were coughed out by the patient (and were repositioned) and in 2 (4.5%) the valves had to be removed because of bleeding post insertion (these patients finally underwent LVRS). The median number of valves inserted was 3 [2–6]. In 4 cases a chest drain was necessitated to be inserted for pneumothorax (mentioned also below).

In the LVRS group, re-intervention included surgery for morbidity (as described in the methods section). More specifically, 3 patients (6.8%) had to be reoperated for significant postoperative air leak and another 3 (6.8%) for empyema. In 2 (4.5%) patients, redo LVRS was attempted. In 1 case (2.3%) the reason of reoperation/re-intervention was not documented. The LOS was longer in the LVRS group (*Table 5*).

Overall morbidity was similar in the 2 groups (*Table 5*). Morbidity in the EBV group regarded mainly pneumothorax development after implantation in 7 patients (15.9% with a chest drain inserted in 4 of them i.e., reintervention for pneumothorax) and respiratory failure with pneumonia in the rest 2 patients (4.5%). In the LVRS group, morbidity mainly regarded prolonged air leak in 6 cases (13.6%, 2 of which were discharged home with a drain *in situ* and 2 required a blood patch) and respiratory failure with/without pneumonia in 3 (6.8%). A patient developed a stroke and another one sustained myocardial infarction (2.3% respectively).

Within 6–12 months from the intervention, the CAT score was improved in both groups (*Table 5*) but the one

Table 3 Population characteristics (N=88) AFTER propensity score matching

Variables	LVRS, n=44	EBV, n=44	P value
Age in years (mean ± SD)	60.98±9.4	62.74±9.6	0.363*
Male gender (n, %)	29 (65.9)	26 (59.1)	0.436**
BMI (kg/m²) (mean ± SD)	28.25±11.1	25.85±10.3	0.388*
Performance status, median [lowest-highest]	2 [1–3]	2 [1–3]	0.150#
Performance status analytically (n, %)			0.827**
1	8 (18.2)	7 (15.9)	
2	28 (63.6)	31 (70.5)	
3	8 (18.2)	6 (13.6)	
Pulmonary function (mean ± SD)			
FEV <sub>1</sub>	36.8±14.2	36.7±11.3	0.970*
DLCO	37.31±11.5	36.82±11.32	0.844*
TLC	125.11±20.97	121.64±19.4	0.537*
RV	192.35±55.4	196.78±45.97	0.717*
Exercise tolerance in meters (mean ± SD)	189.94±23.9	184.17±29.3	0.504*

Standard differences calculated using the mean or proportions. \*, Student's *t*-test; \*\*, Chi-square test; \*, Mann-Whitney Test. LVRS, lung volume reduction surgery; EBV, endobronchial valve; SD, standard deviation; BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in 1<sup>st</sup> second; DLCO, diffusional lung for carbon dioxide; TLC, total lung capacity; RV, residual volume.

Table 4 Co-morbidities of 88 patients (AFTER matching)

Variables	LVRS, n=44	EBV, n=44	P value
Cardiovascular (n, %)	16 (36.4)	16 (36.4)	0.899 <sup>‡</sup>
CAD/Angina/MI	10	11	
НТ	4	2	
PVD	1	1	
Arrhythmia/AF	1	2	
Respiratory other than COPD/emphysema (n, %)	4 (9.1)	5 (11.4)	0.911 <sup>‡</sup>
Bronchiectasis/Pneumonia	1	1	
Cannabis induced lung pathology	1	2	
Asthma	2	2	
Previous cancer (non-lung) (n, %)	6 (13.6)	2 (4.5)	0.667 <sup>‡</sup>
Musculoskeletal/Rheumatologic (n, %)	5 (11.4)	6 (13.6)	0.997**
Other (n, %)	5 (11.4)	6 (13.6)	0.997**
No other co-morbidities (n, %)	19 (43.2)	18 (40.1)	0.866**

<sup>\*\*,</sup> Chi-square test; <sup>‡</sup>, Fischer's Exact test. LVRS, lung volume reduction surgery; EBV, endobronchial valve; CAD, coronary artery disease; HT, hypertension; PVD, peripheral vascular disease; AF, atrial fibrillation; COPD, choric obstructive pulmonary disease.

Table 5 Outcomes after initial treatment of 88 patients

Variables	LVRS, n=44	EBV, n=44	P value
LOS in days, median [lower-higher]	10 [0–28]	6 [1–32]	0.006#
Morbidity (n, %)	11 (25.0)	9 (20.5)	0.611**
Total number of interventions, median [lower-higher]	1 [1–4]	2 [1–6]	$0.005^{\ddagger}$
At least 1 re-intervention (n, %)	9 (20.5)	24 (54.5)	0.002**
MDT involvement in decision (n, %)	26 (59.1)	14 (31.8)	0.010**
CAT Improvement (mean ± SD)	7.89±1.2	3.67±1.9	$0.034^{\dagger}$
Same or better overall quality of life and breathing ability after intervention (patient report) (n, $\%$ )	38 (86.4)	31 (70.5)	0.002**
30-day mortality (n, %)	2 (4.5)	1 (2.3)	0.557 <sup>‡</sup>

<sup>\*\*,</sup> Chi-square test; \*, Mann-Whitney test; \*, Fischer's Exact test; †, Paired *t*-test. LVRS, lung volume reduction surgery; EBV, endobronchial valve; LOS, length of stay; SD, standard deviation; MDT, multidisciplinary team; CAT, COPD assessment test.

calculated in the LVRS group (from 26.33 preoperatively to 18.44 postoperatively) was significantly more intense than the CAT difference calculated in the EBV group (from 25.67 preoperatively to 22 postoperatively, P=0.034). More patients reported the same or improved quality of life and breathing ability after intervention from the LVRS group than from the EBV group (*Table 5*).

The in-hospital and 30-day mortality were similar in the 2 groups and regarded 1 empyema patient after LVRS with multi-organ failure, 1 patient with respiratory failure after LVRS and 1 patient who developed respiratory failure after EBV insertion (*Table 4*).

#### **Conclusions**

The 2 modalities showed similar survival probability. Patients who were offered EBV insertion as the initial treatment had more re-interventions performed. Apart from LOS, which was longer in the LVRS group, the morbidity as well as the in-hospital/30-day mortality were similar between the 2 groups. Improvement of their overall health was better after LVRS as subjectively reported by the patients and objectively measured with CAT scores.

In this study, the number of re-interventions was secondarily investigated as the treated patients had already reached the ceiling of improvement with medical treatment, and hence a small number of re-interventions would be ideally better for their post-intervention life. The difference in the number of re-interventions could partially be attributed to the fact that the LVRS is an irreversible procedure whilst EBVs can be undone i.e.,

removed or repositioned. Although less re-interventions were necessitated for patients receiving LVRS as the initial intervention, re-intervention risk by time was not different between the 2 modalities and therefore this outcome needs further investigation.

Another outcome was the impact on the overall health of the patients. More patients in the LVRS group reported improvement of this including their breathing ability. Additionally, their CAT score was more effectively reduced. CAT score has been shown to correlate with post-interventional overall health status (9,10).

Morbidity was similar in the 2 groups. Its treatment necessitated re-interventions in both groups and in many occasions a return to theatre with general anaesthesia was required. Additionally, pneumothorax was an important type of morbidity for the EBV group in this study and this agreed with literature (11).

Likewise, the LOS was lengthier in the LVRS group. This finding implies that LVRS intervention recovery necessitates prolonged in-hospital stay which was not the case for EBVs although the more re-interventions needed.

LVRS, despite evolving over the years from an open sternotomy to VATS or Robotic techniques offering less trauma, quicker recovery and lower morbidity and mortality (12-14), it still involves a surgical procedure. EBVs on the other hand, are performed without invasive surgery and in some in some cases without general anaesthesia (15). Consequently, LVRS has notoriously been perceived as more "dangerous", making EBVs a safer choice (16,17). Results from this study show that this notion was not verified.

The benefit of EBV insertion on respiratory function, improvement of exercise tolerance and quality of life without increased exacerbations and mortality, has extensively been proven in the literature (18-20). Similarly, the surgical lung volume intervention can achieve survival benefit when compared with patients who have only received medical treatment (3,13). The two interventional modalities, therefore, have been extensively compared with the optimized medical treatment but not amongst them.

Clear guidelines as to when or to whom to offer one or the other modality do not exist. Practice up to recent years considered that LVRS is more dangerous and therefore should not be offered to compromised patients (17), in whom EBVs would seem to be a better alternative. This study shows that the 2 modalities present similar morbidity and mortality and therefore both could be safely offered.

Even outside the MDT (which can be the case in many countries/departments, private sector etc.), patients received treatment based on NICE guidelines and NET findings. Chartis assessment ensured that EBV insertion would work. Although it was previously shown that the MDT would shift cases towards LVRS, in this study cases could have both modalities offered and therefore this previous finding was not perceived as relevant while setting up the present study.

This study has several limitations. It is a retrospective, small and single institute study, investigating a short period of study time without long-term data regarding breathing improvement. Another limitation was that lung function tests (LFTs) or 6MWT post intervention were requested variably by physicians and MDT and therefore a meaningful analysis regarding breathing improvement post-intervention could not be performed, hence objective measurement of the improvement of the breathing ability was not performed. Moreover, patients were included in the study based on what was documented and therefore it was not possible to check if decisions for both modalities were correctly taken. Finally, some important variables could have been included in the analysis of the propensity matching but that would limit substantially the included in the study cases making a reasonable analysis unfeasible. Based on the above and on the fact that this was not a blinded study, bias could be involved in the results and therefore results should be considered with caution.

Although results from this study do not allow the formulation of an "algorithm" as to what type of intervention to be offered first, it provides an insight of the pros and cons of each modality and attempts, with

limitations, the first comparison, to our knowledge, between these two modalities. The results of the randomized trial CELEB study, which is designed to compare EBV vs. LVRS in patients who could offered both interventions, are expected to come out soon (21).

In conclusion, this study shows that both modalities are safe and therefore can be considered as an initial treatment to emphysema patients. EBVs showed shorter LOS whilst LVRS necessitated less re-interventions but led to better overall health improvement than EBVs. We hope that our small study will prove to be a springboard for future efforts to rectify the current dearth of data, of such an important aspect of Lung Volume Reduction.

# **Acknowledgments**

Parts of this study were presented at the Society For Cardiothoracic Surgery in Great Britain and Ireland, March 2018, Glasgow and at the European Association for Cardiothoracic Surgery annual meeting in Milan, October 2018.

Funding: None.

#### **Footnote**

Reporting Checklist: The authors have completed the STROBE checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-2429/rc

*Data Sharing Statement:* Available at https://atm.amegroups.com/article/view/10.21037/atm-22-2429/dss

*Peer Review File*: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-2429/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm. amegroups.com/article/view/10.21037/atm-22-2429/coif). VK serves as an unpaid editorial board member of Annals of Translational Medicine from December 2021 to November 2023. The other authors have no conflicts of interest to declare.

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. The study was conducted in accordance with the Declaration of Helsinki

(as revised in 2013). The study was discussed with the Research and Development department of The Leeds Teaching Hospitals NHS Trust and a NHS Research Ethics Committee was not considered appropriate. The R&D department waived the need for ethical approval and consent which was verified by the clinical governance meeting of the department.

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Cite this article as: Kouritas V, Tcherveniakov P, Milton R, Papagiannopoulos K, Brunelli A, Karthik S, Dimov D, Kefaloyannis E, Chaudhuri N. 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(23):1275. doi: 10.21037/atm-22-2429

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