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Danial Ahmad

Brandon E. Ferrell

Abhiraj Saxena

Diana C. Jiminez

Thomas J. O/Malley

See next page for additional authors

Authors

Danial Ahmad, Brandon E. Ferrell, Abhiraj Saxena, Diana C. Jiminez, Thomas J. O/Malley, Marco DiSpagna, and Vakhtang Tchantchaleishvili

Original Article

Comparative outcomes of lung volume reduction surgery and lung transplantation: a systematic review and meta-analysis

Danial Ahmad[1], Brandon E. Ferrell[1,2], Abhiraj Saxena[1], Diana C. Jimenez[1], Thomas J. O'Malley[1], Marco A. Dispagna[1], Tyler Grenda[3], Vakhtang Tchantchaleishvili[1]

[1]Division of Cardiac Surgery, Thomas Jefferson University, Philadelphia, PA, USA; [2]Department of Cardiothoracic and Vascular Surgery, Montefiore Medical Center, Bronx, NY, USA; [3]Division of Thoracic & Esophageal Surgery, Thomas Jefferson University, Philadelphia, PA, USA

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Correspondence to: Vakhtang Tchantchaleishvili, MD. Assistant Professor of Surgery, Division of Cardiac Surgery, Thomas Jefferson University, 1025 Walnut St., Suite 607, Philadelphia, PA 19107, USA. Email: Vakhtang.Tchantchaleishvili@jefferson.edu.

Background: Lung volume reduction (LVR) and lung transplantation (LTx) have been used in different populations of chronic obstructive pulmonary disease (COPD) patients. To date, comparative study of LVR and LTx has not been performed. We sought to address this gap by pooling the existing evidence in the literature.

Methods: An electronic search was performed to identify all prospective studies on LVR and LTx published since 2000. Baseline characteristics, perioperative variables, and clinical outcomes were extracted and pooled for meta-analysis.

Results: The analysis included 65 prospective studies comprising 3,671 patients [LTx: 15 studies (n=1,445), LVR: 50 studies (n=2,226)]. Mean age was 60 [95% confidence interval (CI): 58–62] years and comparable between the two groups. Females were 51% (95% CI: 30–71%) in the LTx group *vs.* 28% (95% CI: 21–36%) in LVR group (P=0.05). Baseline 6-minute walk test (6MWT) and pulmonary function tests were comparable except for the forced expiratory volume in 1 second (FEV1), which was lower in the LTx group [21.8% (95% CI: 16.8–26.7%) *vs.* 27.3% (95% CI: 25.5–29.2%), P=0.04]. Postoperatively, both groups experienced improved FEV1, however post-LTx FEV1 was significantly higher than post-LVR FEV1 [54.9% (95% CI: 41.4–68.4%) *vs.* 32.5% (95% CI: 30.1–34.8%), P<0.01]. 6MWT was also improved after both procedures [LTx: 212.9 (95% CI: 119.0–306.9) to 454.4 m (95% CI: 334.7–574.2), P<0.01; LVR: 286 (95% CI: 270.2–301.9) to 409.1 m (95% CI: 392.1–426.0), P<0.01], however, with no significant difference between the groups. Pooled survival over time showed no significant difference between the groups.

Conclusions: LTx results in better FEV1 but otherwise has comparable outcomes to LVR.

Keywords: Lung transplantation (LTx); lung volume reduction (LVR); National Emphysema Treatment Trial (NETT); endobronchial lung volume reduction; lung volume reduction surgery (LVRS)

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Introduction

Chronic obstructive pulmonary disease (COPD)/emphysema is the final and irreversible common pathway of various pulmonary pathologies leading to loss of lung elastic recoil, obstructed and hyper-inflated lungs, and severely symptomatic patients (1). In the US, it has consistently been among the top five causes of death, translating to an economic burden of almost 50 billion USD per year (2,3).

Surgical treatment/palliative options for COPD can be considered when medical treatment has been maximally utilized. These include lung volume reduction (LVR) and lung transplantation (LTx) (4). LVR is based on the premise that advanced COPD manifests with structural changes such as loss of elastic recoil and hyperinflation. Resection of such diseased portions should therefore improve lung elastic recoil and chest wall mechanics since the remaining lung would occupy less space within the thorax (5,6). Single or bilateral LTx on the other hand is also indicated in cases of severe COPD refractory to medical management (4). Globally, the most common primary indication for LTx is COPD (7).

These procedures have been used in different populations of COPD patients. The National Emphysema Treatment Trial (NETT) (8) identified subsets (based on physiological lung parameters) of COPD patients who stand to gain the most or the least from LVR. With respect to LTx, indications and absolute contraindications are also clearly elucidated (4). It remains to be seen whether patients who could potentially qualify for either LVR or LTx, such as those with non-upper lobe predominant emphysema and poor baseline exercise capacity, may accrue different benefits from undergoing one procedure compared to the other. However, the magnitude and direction of such benefit, if present, is unknown.

In addition, non-invasive methods of LVR, collectively referred to as endobronchial LVR are increasingly being utilized. These include devices which functionally exclude diseased lung segments without the need for surgery (9) such as endobronchial valves and the newer endobronchial coils. Compared to LVR, they have thus far shown good palliation and functional improvement in COPD patients with some mortality and morbidity benefit as well. However, long term data comparing surgical LVR to endobronchial LVR are scarce (10).

NETT (8) randomized COPD patients into a medical management group and a surgical LVR group. It was able to classify patients based on how beneficial surgical LVR was compared to standard medical management. However, questions remain regarding the place of surgical LVR in the present-day management of advanced COPD as well as the use of its less invasive versions such as endobronchial LVR. To date, there has not been a large-scale comparative study evaluating LVR and LTx. This knowledge gap has been highlighted by NETT investigators as well (11). In addition, endobronchial LVR has not been comparatively studied against surgical LVR.

We sought to bridge this gap in the literature by systematically pooling the existing evidence and performing quantitative meta-analysis. We aimed to answer the question of how LVR and LTx compared to each other in terms of survival as well as improvement in physiological lung parameters. In addition, in a subset analysis, we further compared outcomes between surgical and endobronchial LVR. To reduce noise in the data, these comparisons were made using only prospective studies conducted after the year 2000. NETT itself was not included in the analysis to avoid overlap and double entry of data from its participating institutions. We present this article in accordance with the PRISMA reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-63/rc).

Highlight box

Key findings

- LTx has better FEV1 compared to LVRS, but survival is comparable between the two.

What is known and what is new?

- Both LTx and LVRS are surgical options for end-stage COPD with distinct indications and populations. As highlighted by NETT investigators, there has been no comparison between the procedures for patients who may qualify for both.
- In the absence of head-to-head comparison due to inherent population differences, this manuscript pools existing studies to compare outcomes of the two procedures in an objective manner.

What is the implication, and what should change now?

- These findings highlight the need for direct comparison between the procedures for patients who may benefit from either. Further, it underscores the importance of considering both short- and long-term outcomes, when offering surgical options to patients with end-stage COPD.

Methods

Literature search strategy

An electronic database search was performed in January 2020 using MEDLINE (Ovid SP), Scopus, Cochrane Controlled Trials Register (CCTR), and Cumulative Index to Nursing and Allied Health Literature (CINAHL). To achieve maximum sensitivity, the following terms were combined: "end AND stage AND lung OR respiratory AND insufficiency" OR "pulmonary AND emphysema OR heterogenous AND emphysema OR pulmonary AND disease" AND "lung AND transplantation OR lung AND volume AND reduction AND surgery OR lvr" included as either key words or MeSH terms. A manual search was also performed to ensure all relevant articles were included.

Eligibility criteria

Eligible articles were full-length, prospective studies published from January 2000 to December 2019 in the English literature that included adults undergoing LVR or LTx with an underlying diagnosis of homogenous or heterogenous emphysema. Both surgical and endoscopic techniques of LVR were eligible for inclusion. Studies that were retrospective, included patients not undergoing LVR or LTx, or included patients without emphysema were excluded. Case reports, abstracts, conference presentations, editorials, reviews, and expert opinions were also excluded. When institutions published more than one study including overlapping patient populations, only the most complete reports were included.

Data extraction and critical appraisal

All relevant study level data were extracted from the text, figures, and tables of all eligible articles (BEF, DCJ). Discrepancies between the reviewers were resolved by discussion and consensus. The Newcastle-Ottawa scale (NOS) and Cochrane Risk of Bias (ROB) assessment tool were used to assess the quality of studies and risk of bias. Further details are presented in the supplementary material (Tables S1-S3).

Statistical analysis

Variables were reported as the pooled mean with 95% confidence intervals (CI). For dichotomous variables, a meta-analysis of proportions with logit transformation was conducted. Continuous data were combined via meta-analysis with random-effects model. Heterogeneity was evaluated using I^2 test. Survival data from each study were collected and pooled to retrieve a weighted mean and 95% CI at specific time points. Such data were then graphically displayed to visualize survival over time. The main analysis was undertaken to compare patients undergoing LTx *vs.* lung volume reduction surgery (LVRS). Subgroup analysis was further undertaken for surgical *vs.* endobronchial techniques of LVR. Propensity matching was not done due to the limitations of the meta-analysis method. R software 3.5.0, meta package (R Foundation for Statistical Computing, Vienna, Austria) was used for data analysis. P values <0.05 were considered statistically significant.

Study characteristics

Eligible studies included all prospective studies on patients who underwent LVR or LTx for homogenous or heterogenous emphysema. After removal of duplicate articles, 1,925 of 2,155 articles were excluded after a detailed evaluation of the title and abstract. The remaining 230 articles underwent a full text evaluation, of which 65 articles met inclusion criteria with a collective 3,671 patients. This consisted of 15 LTx studies (n=1,445) and 50 LVR studies (n=2,226). A PRISMA flow diagram illustrating the search strategy is provided as Figure S1, while a detailed list of the studies included is provided as Table S1. A protocol was not prepared a priori, nor was this review registered.

Results

Baseline characteristics

Mean age was 60 (95% CI: 58–62) years and females comprised 32% (95% CI: 24–40%) of all patients with greater preponderance in LTx group [51% (95% CI: 30–71%) *vs.* 28% (95% CI: 21–36%), P=0.05]. Heterogenous alpha-1 antitrypsin deficiency was less common in the LTx group [69% (95% CI: 42–87%) *vs.* 96% (95% CI: 94–97%), P<0.01] however more patients in this group were on home oxygen therapy prior to surgery [95% (95% CI: 77–99%) *vs.* 63% (95% CI: 41–80%), P=0.01]. Further information is provided in *Table 1*.

Preoperative lung parameters

Overall forced expiratory volume in 1 second (FEV1) (%

Table 1 Baseline and preoperative characteristics of patients in lung transplant and lung volume reduction groups

Variable	Lung transplant				Lung volume reduction				Overall				P value
	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	
Age (years)	52 [47, 56]	444	10	52*	63 [62, 65]	1,825	40	0	60 [58, 62]	2,269	50	43*	<0.01
BMI (kg/m^2)	20.6 [17.7, 23.5]	213	3	0	22.9 [22.0, 23.8]	817	18	0	22.7 [21.8, 23.6]	1,030	21	0	0.14
Female (%)	51 [30, 71]	240/415	9	51*	28 [21, 36]	680/1,759	41	68*	32 [24, 40]	920/2,174	50	71*	0.05
Heterogenous A1AT (%)	69 [42, 87]	365/529	6	84*	96 [94, 97]	1,180/1,195	31	13	95 [91, 97]	1,545/1,724	37	73*	<0.01
Home oxygen requirement (%)	95 [77, 99]	429/450	3	93	63 [41, 80]	422/877	22	95*	69 [49, 84]	851/1,327	25	97*	0.01
Smoking (pack years)	27 [0, 56]	188	1	–	48 [39, 58]	873	15	0	46 [37, 55]	1,061	16	0	0.17
6MWT (m)	212.9 [119.0, 306.9]	249	3	0	286.1 [269.4, 302.9]	1,886	38	0	283.9 [267.4, 300.4]	2,135	41	0	0.13
FEV1	0.65 [0.29, 1.02]	488	2	0	0.70 [0.65, 0.74]	1,975	41	0	0.69 [0.65, 0.74]	2,463	43	0	0.83
FEV1 (% pred)	21.8 [16.8, 26.7]	756	6	0	27.3 [25.5, 29.2]	1,892	40	0	26.7 [25.0, 28.4]	2,648	46	0*	0.04
DLCO (% pred)	36.0 [4.6, 67.4]	31	1	–	32.8 [29.0, 36.6]	1,164	21	0	32.9 [29.2, 36.6]	1,195	22	0	0.84
FEV1/FVC	32.0 [5.7, 58.3]	5	1	–	34.0 [29.6, 38.4]	467	12	0	34.0 [29.6, 38.3]	472	13	0	0.88
RV (% pred)	310.0 [12.0, 608.0]	5	1	–	231.3 [204.9, 257.7]	1,382	32	84*	231.8 [205.5, 258.2]	1,387	33	83	0.61
TLC (% pred)	135.0 [56.1, 213.9]	29	1	–	134.5 [131.6, 137.4]	1,078	28	0	134.5 [131.6, 137.4]	1,107	29	0	0.99

*, significant heterogeneity present (P<0.05). CI, confidence interval; BMI, body mass index; A1AT, alpha-1 antitrypsin; 6MWT, 6-minute walk test; FEV, forced expiratory volume; DLCO, diffusion capacity of carbon monoxide; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity.

Table 2 Comparison of post-operative variables between lung transplant and lung volume reduction groups

Variable	Lung transplant				Lung volume reduction				Overall				
	Pooled value, mean [95% CI]	No. of patients	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients	No. of studies	I^2 (%)	P value
BMI (kg/m^2)	24.1 [19.7, 28.5]	89	3	0	24.69 [23.6, 25.77]	119	3	0	24.65 [23.6, 25.71]	208	6	0	0.8
6MWT (m)	454.4 [334.7, 574.2]	61	2	0	408.3 [391.2, 425.5]	1,392	27	0	409.2 [392.3, 426.2]	1,453	29	0	0.45
FEV1 (% pred)	54.9 [41.4, 68.4]	122	5	25	32.5 [30.1, 34.8]	697	17	0	36.8 [32.8, 40.9]	790	22	45*	<0.01

*, significant heterogeneity present (P<0.05). CI, confidence interval; BMI, body mass index; 6MWT, 6-minute walk test; FEV, forced expiratory volume.

pred) was 26.7% (95% CI: 25.0–28.4%) and less in the transplant group [LTx: 21.8% (95% CI: 16.8–26.7%) *vs.* LVR: 27.3% (95% CI: 25.5–29.2%), P=0.04]. The 6-minute walk test (6MWT) was comparable between the groups [LTx: 212.9 (95% CI: 119.0–306.9) *vs.* LVR: 286.1 m (95% CI: 269.4–302.9), P=0.13]. Further details are given in *Table 1*.

Postoperative lung parameters

The postoperative FEV1 (% pred) was significantly greater in the LTx group [LTx: 54.9% (95% CI: 41.4–68.4%) *vs.* LVR: 32.5% (95% CI: 30.1–34.8%), P<0.01]. The postoperative mean 6MWT distance was however comparable between the groups [LTx: 454.4 (95% CI: 334.7–574.2) *vs.* LVR: 409.1 m (95% CI: 392.1–426.0), P=0.45] (*Table 2*).

Significant improvements were seen in postoperative FEV1 (% pred) in both the LTx group [Preop: 21.8% (95% CI: 16.8–26.7%) *vs.* Postop: 54.9% (95% CI: 41.4–68.4%), P<0.01] and LVR group [Preop: 27.3% (95% CI: 25.5–29.2%) *vs.* Postop: 32.5% (95% CI: 30.1–34.8%), P=0.01] (*Figure 1A*). Similarly, significant within-group improvements in 6MWT (m) were seen in the LTx [Preop: 212.9 (95% CI: 119.0–306.9) *vs.* Postop: 454.4 m (95% CI: 334.7–574.2), P<0.01] and LVR groups [Preop: 286 (95% CI: 270.2–301.9) *vs.* Postop: 409.1 m (95% CI: 392.1–426.0), P<0.01] (*Figure 1B*). Further details are in Table S4.

Pooled survival analysis

Survival at 6 months, 1 year, 5 years, and 8 years was 96% (95% CI: 95–97%), 93% (95% CI: 92–95%), 62% (95% CI: 57–67%), and 19% (95% CI: 5–53%) in the LVR group. In the LTx group, it was 93% (95% CI: 82–98%), 88% (95% CI: 80–93%), 60% (95% CI: 60–68%), and 41% (95% CI: 33–49%) respectively. Pooled survival over time (*Figure 2A*) showed no significant difference between the groups.

Subgroup analysis: surgical vs. endobronchial LVR

The subgroups were comparable in all baseline characteristics (Table S5). The mean operation time [116 (95% CI: 58–173) *vs.* 47 min (95% CI: 28–67), P=0.03] and hospital stay [9 (95% CI: 7–12) *vs.* 2 (95% CI: 1–4) days, P<0.01] were longer in the surgical subgroup compared to the endobronchial subgroup. Post-LVR, the rates of significant bleeding [Surgical: 2% (95% CI: 1–4%) *vs.* Endobronchial: 1% (95% CI: 0–3%), P=0.16]

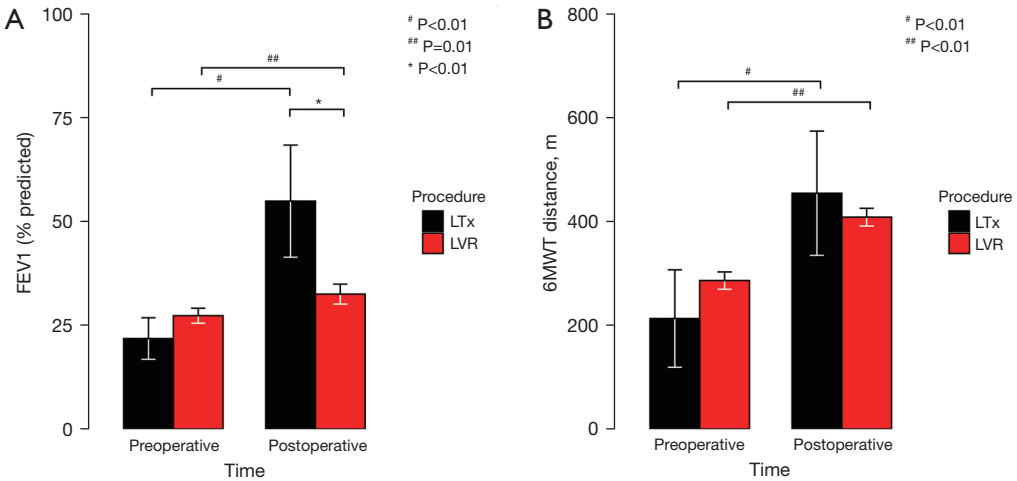

Figure 1 Preoperative *vs.* postoperative comparison of (A) FEV1 (% pred) and (B) 6MWT distance between and within LVR & LTx groups. Bars represent mean & error bars represent 95% confidence intervals. FEV, forced expiratory volume; LTx, lung transplant; LVR, lung volume reduction; 6MWT, 6-minute walk test.

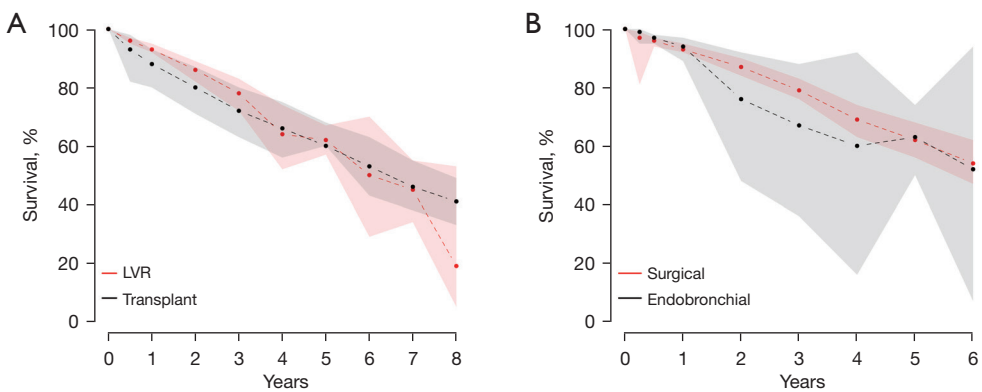

Figure 2 Pooled survival over time after (A) LVR *vs.* lung transplantation and (B) surgical *vs.* endobronchial lung volume reduction. Central dashed line represents pooled means while shaded region represents 95% confidence intervals. LVR, lung volume reduction.

and pneumothorax [Surgical: 3% (95% CI: 1–9%) *vs.* Endobronchial: 4% (95% CI: 2–10%), P=0.62] were also comparable between the subgroups (Table S6).

At 3 months post-procedure, the 6MWT was greater in the endobronchial subgroup compared to the surgical subgroup, however, trends reversed after this time. Similarly, FEV1 peaked in the endobronchial subgroup at 3 months post-LVR followed by a decline while it peaked in the surgical subgroup at 6 months followed by a decline at one year. Figure S2 compares the trends in physiologic lung parameters between both subgroups. Survival was comparable between the subgroups as shown in *Figure 2B*.

Discussion

NETT (8) was undertaken to compare maximal medical treatment with surgical LVR. One benefit of this extensive study was the clarity it provided in the indications for LVR and the subset of patients who were most likely to benefit from it. These were patients who had predominantly upper-lobe emphysema with poor preoperative exercise capacity (8). Patients with an FEV1 (% pred) ≤20% with either a diffusion capacity of carbon monoxide (DLCO) ≤20% or homogenous emphysema were the least likely to benefit from LVR (12) and such patients could potentially benefit from LTx (13). Generally, alongside other criteria,

a patient with a FEV1 (% pred) ≤45% qualifies for LVR. In contrast, for LTx, FEV1 (% pred) criteria for consideration is ≤25 (13,14). The group of patients with FEV1 (% pred) between 20–30 could potentially qualify for either procedure depending on various patient and procedural factors (11,14). Although these procedures are generally used in COPD populations with distinct indications for each, there may exist a potential overlap in indications in the FEV1 (% pred) range alluded to previously, where select patients may stand to benefit from either procedure. The LVR and LTx groups only overlap partially as seen from the 95% CI of baseline FEV1 (% pred) in each.

Despite the benefits seen in advanced COPD from LVR (as described by NETT), it has not gained much traction as a treatment for end-stage COPD (11). The reasons for this could be the high cost, restrictive eligibility criteria, less surgeon experience, and unclear idea of benefits reported by NETT (11,15). However, recent trends in the US indicate increasing utilization of LVR with regional variation in uptake. This increase is being seen simultaneously with lower morbidity and mortality (16).

Patients in this analysis were similar at baseline except for a few key differences. The pooled preoperative mean FEV1 (% pred) was less in the LTx group (21.8%) compared to the LVR group (27.3%) and more LTx (95% *vs.* 63%) patients were on home oxygen therapy. It could therefore be surmised that patients undergoing LTx were more advanced in their pulmonary pathology than those undergoing LVR. This would not be out of place given the different criteria for each procedure. However, since meta-analysis methods do not allow for propensity-matching the populations, the populations can be expected to have key differences at baseline and findings should be contextualized within this limitation.

We found statistically comparable survival between both groups at all assessed time points; however, a greater degree of functional improvement [FEV1 (% pred)] was seen in LTx patients. When taken in the context of the advanced baseline pathology in LTx patients, the comparable survival may hint at a possibly greater survival benefit with LTx as LVRS patients with less advanced baseline pathology show similar long-term survival. In comparison, a single center study of 144 patients by Weinstein *et al.* reported greater overall and subgroup [FEV1 (% pred) 20–30] survival in LVR patients compared to LTx patients (14).

Postoperatively, we found that only FEV1 (% pred) was significantly better in the LTx group compared to LVR group (54.9% *vs.* 32.5%). However, FEV1 (% pred) and 6MWT improved within both surgical groups. This is in agreement with the review by Mora (1) and the study by Weinstein *et al.* (14) who showed greater functional improvement in their subgroup [FEV1 (% pred) 20–30] of patients undergoing LTx who survived more than one year after the surgery.

Our analysis also indicated that surgical LVR had a longer operation time (116 *vs.* 47 min) and hospital stay (9 *vs.* 2 days) compared to endobronchial LVR, however the rates of complications, such as bleeding and pneumothorax were comparable. Survival was also comparable between both subgroups. Of note, general trends indicated that lung function and dyspnea improved quickly after endobronchial LVR; however, improvement in the surgical LVR subgroup occurred later and was greater in magnitude and/or more sustained. One reason for the delayed benefit in the surgical subgroup could be the longer recovery time compared to endobronchial LVR procedures where quicker recovery may lead to earlier improvements post-procedure. It should however be noted that in most endobronchial studies, long term follow-up data was lacking.

Since a history of LVR does not disqualify from future LTx (17-19), it could be argued that in patients opting for initial LVR as "bridge to LTx", especially younger patients, it might be more practical to undergo a single procedure (LTx) which provides greater functional improvement with similar long-term survival. While LTx has been associated with more complications than LVR (4), we were not able to analyze this due to the limited data in the included studies. Thus, this suggestion should be viewed in the context of the lifetime management of emphysema and the greater complexity associated with LTx with risk/benefit assessment individualized to each patient.

The financial aspect of these procedures should also be considered. A single center study reported the total cost of LTx to be $381,732 at a mean follow-up of 2.4±2.5 years compared to $140,637 at a mean follow-up of 5.0±3.1 years for LVR (14). The additional cost of immunosuppression as well as the longer and more frequent follow-up associated with LTx may be behind its higher cost. Nevertheless, both procedures are expensive endeavors, and cost more than medical management (13). Therefore, cost-effectiveness analysis should be part of the patient selection process for these procedures to maximize benefit.

Limitations

Major limitations of this meta-analysis are due to the

inherent inconsistency of reporting patterns that are observed when working with pooled data. Additionally, this meta-analysis was not based on studies with direct comparison between LVR and LTx; which is why we attempted to systematically pool the available evidence on patients undergoing each procedure as the next best way to compare outcomes. While we do report short-term and long-term survival, we were not able to assess changes in physiological lung parameters over time between LTx and LVR. We also did not assess quality of life improvement after both procedures. This may be a major factor in the decision to choose one surgery over the other. Further granularity in the data such as location/extent of emphysema and its impact on choice of procedure, complication rates, and differences in outcomes after single *vs.* double LTx were also lacking.

Conclusions

LTx and LVR are management options in end-stage COPD for highly selective patients. While LTx led to greater improvement in FEV1 (% pred), survival was comparable between both groups. Surgical LVR and endobronchial LVR were also similar in terms of survival, however, surgical LVR led to late and more sustained functional benefits with longer duration of hospital stay.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-63/coif). The 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.

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Supplementary

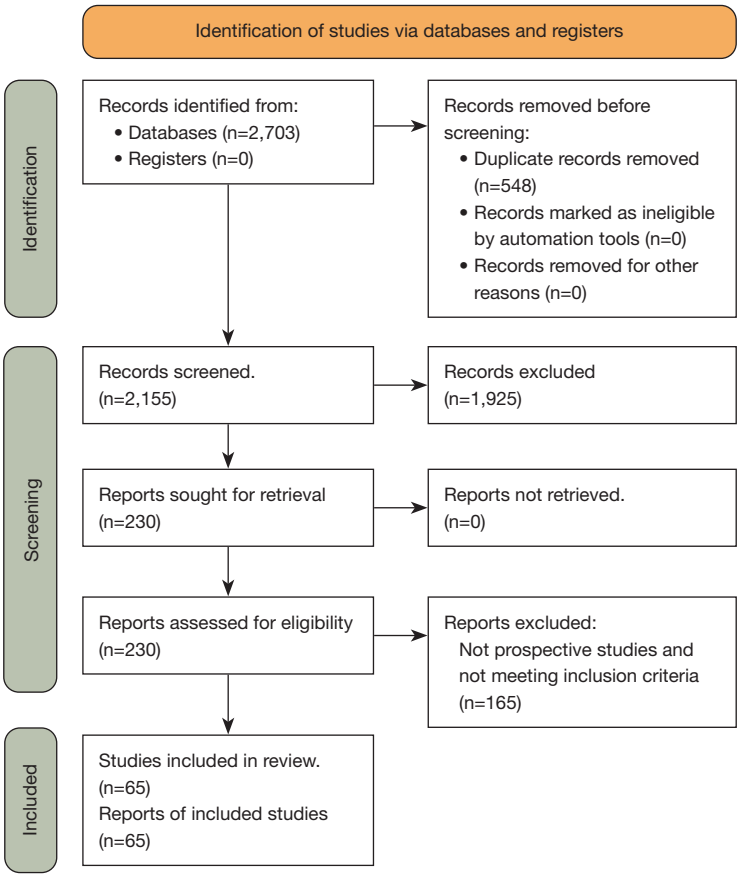

Figure S1 PRISMA flow diagram showing the process of study selection.

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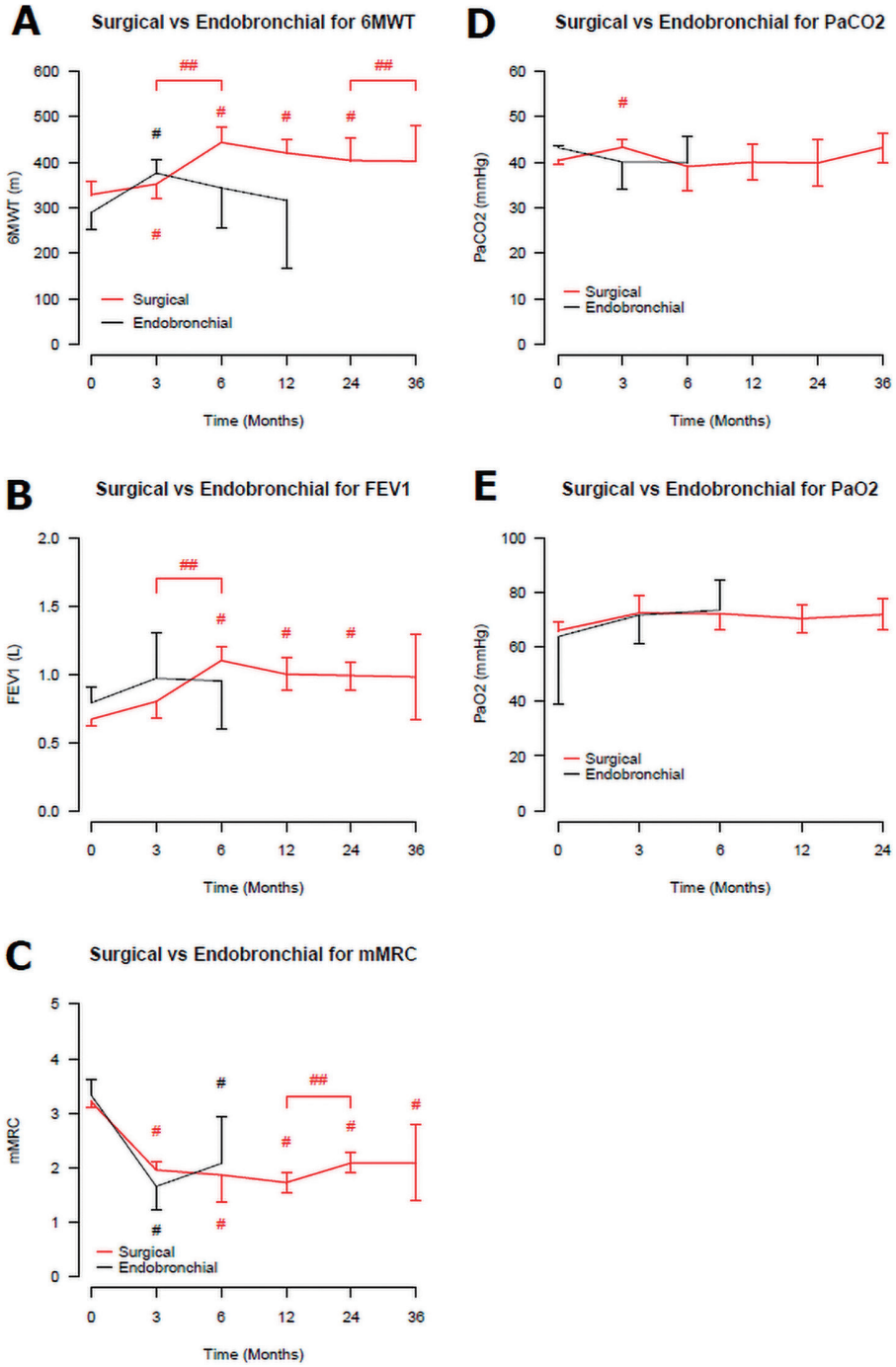

Figure S2 Comparison of trends in functional lung parameters after surgical *vs.* endobronchial lung volume reduction: (A) 6MWT, (B) FEV1 (% pred), (C) mMRC, (D) $PaCO_2$ (mmHg), (E) PaO_2 (mmHg). #, P<0.05 when compared to baseline; ##, P<0.05 for compared timepoints. 6MWT, 6-minute walk test; FEV, forced expiratory volume; mMRC, modified medical research council dyspnea scale; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial pressure of oxygen.

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Table S1 Studies included in the meta-analysis

First author	Title	Year published	Journal	Study date	Type of study	Number of patients	Total NOS score or ROB
Lederer 1	*Obesity and primary graft dysfunction after lung transplantation: the Lung Transplant Outcomes Group Obesity Study*	2011	*Am J Respir Crit Care Med*	2002–2009	Prospective cohort	261	8
Davis	*Pepsin concentrations are elevated in the bronchoalveolar lavage fluid of patients with idiopathic pulmonary fibrosis after lung transplantation*	2013	*Journal of Surgical Research*	2009–2011	Prospective cohort	45	7
Bossenbroek	*Cross-sectional Assessment of Daily Physical Activity in Chronic Obstructive Pulmonary Disease Lung Transplant Patients*	2009	*J Heart Lung Transplant*	1990–2005	Prospective cohort	47	7
Langenbach	*Airway vascular changes after lung transplant: potential contribution to the pathophysiology of bronchiolitis obliterans syndrome*	2005	*J Heart Lung Transplant*	1997–1998	Prospective cohort	11	6
Ekstrom	*Lung transplantation and survival outcomes in patients with oxygen-dependent COPD with regard to their alpha-1 antitrypsin deficiency status*	2017	*International Journal of COPD*	1987–2015	Prospective cohort	171	9
Aharinejad	*Prediction of lung-transplant rejection by hepatocyte growth factor*	2004	*The Lancet*	–	Prospective cohort	65	6
Habedank	*Reversibility of cachexia after bilateral lung transplantation*	2007	*International Journal of Cardiology*	–	Prospective cohort	17	7
Rodrigue	*Are there sex differences in health-related quality of life after lung transplantation for chronic obstructive pulmonary disease?*	2006	*J Heart Lung Transplant*	1994–2002	Prospective cohort	37	6
Ringbaek	*Prognosis of patients with alpha1-antitrypsine deficiency on long-term oxygen therapy*	2014	*Respiratory Medicine*	1994–2010	Prospective cohort	262	7
Ratnovsky	*Mechanics of Respiratory Muscles in Single-Lung Transplant Recipients*	2006	*Respiration*	–	Prospective cohort	5	5
Van Muylem	*Monitoring the lung periphery of transplanted lungs*	2005	*Respiratory Physiology and Neurobiology*	–	Prospective cohort	3	5
Titman	*Disease-Specific Survival Benefit of Lung Transplantation in Adults: A National Cohort Study*	2009	*American Journal of Transplantation*	1995–2006	Prospective cohort	483	8
Gerbase	*Health-Related Quality of Life Following Single or Bilateral Lung Transplantation*	2005	*CHEST*	1993–2004	Prospective cohort	24	6
Wilkens H	*Breathing pattern and chest wall volumes during exercise in patients with cystic fibrosis, pulmonary fibrosis and COPD before and after lung transplantation*	2010	*Thorax*	–	Prospective cohort	5	6
Ley	*Functional Evaluation of Emphysema Using Diffusion-Weighted Helium-Magnetic Resonance Imaging, High-Resolution Computed Tomography, and Lung Function Tests*	2004	*Investigative radiology*	–	Prospective cohort	9	4
Tutic	*Lung-volume reduction surgery as an alternative or bridging procedure to lung transplantation*	2006	*The Annals of Thoracic Surgery*	1994–2005	Prospective cohort	31	8
Haniuda	*Effects of pulmonary artery remodeling on pulmonary circulation after lung volume reduction surgery*	2003	*Thorac Cardiov Surgery*	–	Prospective cohort	12	5
Criner	*Biologic lung volume reduction in advanced upper lobe emphysema phase 2 results*	2009	*Am J Respir Crit Care Med*	2007–2008	NR clinical trial	50	8
McKeough	*Reduction in resting energy expenditure following lung volume reduction surgery in subjects with chronic obstructive pulmonary disease*	2004	*Chronic Respiratory Disease*	–	Prospective cohort	10	5
Herth	*Characterization of outcomes 1 year after endoscopic thermal vapor ablation for patients with heterogeneous emphysema*	2005	*International Journal of COPD*	2009–2011	NR clinical trial	44	8
Fujimoto	*Long-term results of lung volume reduction surgery*	2002	*European Journal of Cardio-thoracic Surgery*	1994–1998	Registry study	88	7
Sievi	*Lung volume reduction surgery does not increase daily physical activity in patients with severe chronic obstructive pulmonary disease*	2018	*Journal of Thoracic Disease*	2010–2016	Prospective case-control	19	7
Yusen	*A prospective evaluation of lung volume reduction surgery in 200 consecutive patients*	2003	*Chest*	1993–1998	Prospective cohort	200	9
Wood	*A multicenter trial of an intrabronchial valve for treatment of severe emphysema*	2007	*The Journal of Thoracic and Cardiovascular Surgery*	2004	Prospective cohort	30	7
Goldstein	*Influence of lung volume reduction surgery (LVRS) on health related quality of life in patients with chronic obstructive pulmonary disease*	2003	*Thorax*	1997–2001	RCT	28	Low risk
Davey	*Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HIFi study): a randomised controlled trial*	2015	*The Lancet*	2012–2013	RCT	25	Low risk
Hopkinson	*Atelectasis and survival after bronchoscopic lung volume reduction for COPD*	2011	*European Respiratory Journal*	2002–2004	Prospective cohort	19	7
Goto	*Improved activities of daily living, psychological state and health-related quality of life for 12 months following lung volume reduction surgery in patients with severe emphysema*	2004	*Respirology*	1996–1999	Prospective cohort	18	7
Ingenito	*Physiological characterization of variability in response to lung volume reduction surgery*	2003	*Journal of Applied Physiology*	1994–2000	Prospective cohort	25	8
Mineo	*Resting energy expenditure and metabolic changes after lung volume reduction surgery for emphysema*	2006	*Annals of Thoracic Surgery*	2000–2003	Prospective cohort	30	9
Pompeo	*Comparative results of non-resectional lung volume reduction performed by awake or non-awake anesthesia*	2011	*European Journal of Cardio-thoracic Surgery*	2007–2010	Prospective cohort	60	7
Deslee 1	*Lung volume reduction coil treatment for patients with severe emphysema: a European multicentre trial*	2014	*Thorax*	2009–2011	NR clinical trial	60	8
Gelb	*Lung function 5 yr after lung volume reduction surgery for emphysema*	2001	*Am Journal Respir Crit Care Med*	1995	Prospective cohort	26	9
Liu J	*Mid-term effects of lung volume reduction surgery on pulmonary function in patients with chronic obstructive pulmonary disease*	2007	*Chinese Medical Journal*	–	Prospective cohort	10	5
Venuta	*Long-term follow-up after bronchoscopic lung volume reduction in patients with emphysema*	2012	*European Respiratory Journal*	–	Prospective cohort	40	7
Bakeer	*Low cost biological lung volume reduction therapy for advanced emphysema*	2016	*International Journal of COPD*	2013–2015	NR clinical trial	15	6
Flaherty	*Short-term and long-term outcomes after bilateral lung volume reduction surgery: Prediction by quantitative CT*	2001	*Chest*	1994–1998	Prospective cohort	89	8
De Oliveira	*Combined bone marrow-derived mesenchymal stromal cell therapy and one-way endobronchial valve placement in patients with pulmonary emphysema: A phase i clinical trial*	2017	*Stem Cells Translational Medicine*	2013–2014	RCT	10	High risk
Homan	*Increased effective lung volume following lung volume reduction surgery in emphysema*	2001	*Chest*	1996–1998	Prospective cohort	36	8
Lederer 2	*Lung-volume reduction surgery for pulmonary emphysema: Improvement in body mass index, airflow obstruction, dyspnea, and exercise capacity index after 1 year*	2007	*The Journal of Thoracic and Cardiovascular Surgery*	2004–2005	Prospective cohort	23	8
Tan A	*Lung volume reduction surgery for the treatment of severe emphysema: a study in a single Canadian institution*	2000	*Canadian journal of surgery*	1995–1997	Prospective case series	10	6
Cremona	*Mechanisms of gas exchange response to lung volume reduction surgery in severe emphysema*	2011	*Journal of Applied Physiology*	–	Prospective cohort	23	5
Ohno	*Oxygen-enhanced MRI, thin-section MDCT, and perfusion SPECT/CT: comparison of clinical implications to patient care for lung volume reduction surgery*	2012	*American Journal of Roentgenology*	2007–2011	Prospective cohort	25	6

Table S1 (*continued*)

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Table S1 (*continued*)

First author	Title	Year published	Journal	Study date	Type of study	Number of patients	Total NOS score or ROB
Liu Z	*Video-Assisted Thoracoscopic Surgery for Treatment of Chronic Obstructive Pulmonary Disease*	2016	*Indian Journal of Surgery*	2002–2012	Prospective cohort	90	6
Koizumi	*Comparison of changes in hemodynamics between unilateral and bilateral lung volume reduction for pulmonary emphysema*	2001	*Annals of Thoracic and Cardiovascular Surgery*	1994–1997	Prospective	16	4
Gorman	*Diaphragm length and neural drive after lung volume reduction surgery*	2005	*American Journal of Respiratory and Critical Care Medicine*	–	Prospective cohort	12	6
Malthener	*Lung volume reduction surgery: Results of a Canadian pilot study*	2000	*Canadian Journal of Surgery*	1995–1997	Prospective case series	24	8
Wilkens H	*Lung volume reduction surgery versus conservative treatment in severe emphysema*	2000	*European Respiratory Journal*	1995–1997	Prospective cohort	29	8
Mineo	*Impact of lung volume reduction surgery versus rehabilitation on quality of life*	2004	*European Respiratory Journal*	1996–1999	RCT	30	High risk
Hillerdal	*Comparison of lung volume reduction surgery and physical training on health status and physiologic outcomes: a randomized controlled clinical trial*	2005	*Chest*	1997–2000	RCT	49	Some concern
Weder	*Persistent benefit from lung volume reduction surgery in patients with homogeneous emphysema*	2009	*The Annals of Thoracic Surgery*	1994–2008	Prospective cohort	250	8
Geiser	*Outcome after unilateral lung volume reduction surgery in patients with severe emphysema*	2001	*European Journal of Cardio-thoracic Surgery*	1996–1999	Prospective cohort	28	7
Soon	*Sequential VATS lung volume reduction surgery: prolongation of benefits derived after the initial operation*	2003	*European Journal of Cardio-thoracic Surgery*	1994–2001	Prospective cohort	29	7
Sharafkhaneh	*Altered thoracic gas compression contributes to improvement in spirometry with lung volume reduction surgery*	2005	*Thorax*	–	Prospective cohort	27	7
Butler	*Underestimation of mortality following lung volume reduction surgery resulting from incomplete follow-up*	2001	*Chest*	1995–1997	Prospective longitudinal	85	7
Laghi	*Effect of lung volume reduction surgery on diaphragmatic neuromechanical coupling at 2 years*	2004	*Chest*	–	Prospective cohort	15	5
Klooster 1	*Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation*	2015	*The New England Journal of Medicine*	2011–2014	RCT	34	Low risk
Herth	*Treatment of Advanced Emphysema With Emphysematous Lung Sealant (AeriSeal®)*	2011	*Respiration*	–	NR clinical trial	25	7
Deslee 2	*Lung Volume Reduction Coil Treatment vs Usual Care in Patients With Severe Emphysema: The REVOLENS Randomized Clinical Trial*	2016	*JAMA*	2013	RCT	50	Low risk
Klooster 2	*Lung Volume Reduction Coil Treatment in Chronic Obstructive Pulmonary Disease Patients with Homogeneous Emphysema: A Prospective Feasibility Trial*	2014	*Respiration*	2011–2012	Prospective cohort	10	8
Bostanci	*Endobronchial coils in treatment of advanced emphysema: A single center experience [İleri amfizem tedavisinde endobronşiyal sarmallar: Tek merkez deneyimi]*	2019	*Turkish Journal of Thoracic and Cardiothoracic Surgery*	2012–2014	Prospective cohort	46	8
Zoumot	*Endobronchial Coils for Severe Emphysema Are Effective Up to 12 Months following Treatment: Medium Term and Cross-Over Results from a Randomised Controlled Trial*	2015	*PLOS ONE*	2010–2011	RCT	45	Low risk
Herth	*Segmental Volume Reduction Using Thermal Vapour Ablation in Patients With Severe Emphysema: 6-month Results of the Multicentre, Parallel-Group, Open-Label, Randomised Controlled STEP-UP Trial*	2016	*The Lancet: Respiratory medicine*	2013–2014	RCT	45	Low risk
Song	*Bronchoscopic Lung Volume Reduction For Pulmonary Emphysema: Preliminary Experience With Endobronchial Occluder*	2013	*Respiratory Care*	2006	Prospective cohort	23	7
Shah	*Bronchoscopic lung-volume reduction with Exhale airway stents for emphysema (EASE trial): randomised, sham-controlled, multicentre trial*	2011	*Lancet*	2006–2009	RCT	208	Low risk

NOS, Newcastle-Ottawa scale; ROB, Risk of Bias; NR, non-randomized; RCT, randomized clinical trial.

Table S2 NOS for included studies

First author	Title	Type of study	Representative of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start of study	Comparability of cohorts on the bases of the design or analysis	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow-up	Total
Lederer 1	*Obesity and primary graft dysfunction after lung transplantation: the Lung Transplant Outcomes Group Obesity Study*	Prospective cohort	1	1	1	0	2	1	1	1	8
Davis	*Pepsin concentrations are elevated in the bronchoalveolar lavage fluid of patients with idiopathic pulmonary fibrosis after lung transplantation*	Prospective cohort	1	1	1	0	1	1	1	1	7
Bossenbroek	*Cross-sectional Assessment of Daily Physical Activity in ChronicObstructive Pulmonary Disease Lung Transplant Patients*	Prospective cohort	1	1	1	1	0	1	1	1	7
Langenbach	*Airway vascular changes after lung transplant: potential contribution to the pathophysiology of bronchiolitis obliterans syndrome*	Prospective cohort	0	0	1	1	1	1	1	1	6
Ekstrom	*Lung transplantation and survival outcomes in patients with oxygen-dependent COPD with regard to their alpha-1 antitrypsin deficiency status (swedish registry)*	Prospective cohort	1	1	1	1	2	1	1	1	9
Aharinejad	*Prediction of lung-transplant rejection by hepatocyte growth factor*	Prospective cohort	1	0	1	1	0	1	1	1	6
Habedank	*Reversibility of cachexia after bilateral lung transplantation*	Prospective cohort	1	1	1	1	1	1	1	0	7
Rodrigue	*Are there sex differences in health-related quality of life after lung transplantation for chronic obstructive pulmonary disease?*	Prospective cohort	1	0	1	0	1	1	1	1	6

Table S2 (*continued*)

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Table S2 (*continued*)

First author	Title	Type of study	Representative of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start of study	Comparability of cohorts on the bases of the design or analysis	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow-up	Total
Ringbaek	*Prognosis of patients with alpha1-antitrypsine deficiency on long-term oxygen therapy (danish oxygen register)*	Prospective cohort	1	1	1	0	1	1	1	1	7
Ratnovsky	*Mechanics of Respiratory Muscles in Single-Lung Transplant Recipients*	Prospective cohort	0	0	1	0	1	1	1	1	5
Van Muylem	*Monitoring the lung periphery of transplanted lungs*	Prospective cohort	1	0	1	1	0	1	1	0	5
Titman	*Disease-Specific Survival Benefit of Lung Transplantation in Adults: A National Cohort Study (UK database)*	Prospective cohort	1	0	1	1	2	1	1	1	8
Gerbase	*Health-Related Quality of Life Following Single or Bilateral Lung Transplantation*	Prospective cohort	1	0	1	1	0	1	1	1	6
Wilkens H	*Breathing pattern and chest wall volumes during exercise in patients with cystic fibrosis, pulmonary fibrosis and COPD before and after lung transplantation*	Prospective cohort	1	0	1	0	1	1	1	1	6
Ley	*Functional Evaluation of Emphysema Using Diffusion-Weighted Helium-Magnetic Resonance Imaging, High-Resolution Computed Tomography, and Lung Function Tests*	Prospective cohort	0	1	1	0	0	1	0	1	4
Tutic	*Lung-volume reduction surgery as an alternative or bridging procedure to lung transplantation*	Prospective cohort	1	1	1	1	1	1	1	1	8
Haniuda	*Effects of pulmonary artery remodeling on pulmonary circulation after lung volume reduction surgery*	Prospective cohort	0	0	1	1	0	1	1	1	5
McKeough	*Reduction in resting energy expenditure following lung volume reduction surgery in subjects with chronic obstructive pulmonary disease*	Prospective cohort	0	0	1	1	0	1	1	1	5
Fujimoto	*Long-term results of lung volume reduction surgery*	Registry study	1	0	1	1	1	1	1	1	7
Sievi	*Lung volume reduction surgery does not increase daily physical activity in patients with severe chronic obstructive pulmonary disease (registry switzerland)*	Prospective case-control	1	0	1	1	2	1	1	0	7
Yusen	*A prospective evaluation of lung volume reduction surgery in 200 consecutive patients*	Prospective cohort	1	1	1	1	2	1	1	1	9
Goto	*Improved activities of daily living, psychological state and health-related quality of life for 12 months following lung volume reduction surgery in patients with severe emphysema*	Prospective cohort	1	1	1	1	1	1	1	0	7
Ingenito	*Physiological characterization of variability in response to lung volume reduction surgery*	Prospective cohort	1	1	1	1	2	1	1	0	8
Mineo	*Resting energy expenditure and metabolic changes after lung volume reduction surgery for emphysema*	Prospective cohort	1	1	1	1	2	1	1	1	9
Pompeo	*Comparative results of non-resectional lung volume reduction performed by awake or non-awake anesthesia*	Prospective cohort	1	1	1	1	0	1	1	1	7
Gelb	*Lung function 5 yr after lung volume reduction surgery for emphysema*	Prospective cohort	1	1	1	1	2	1	1	1	9
Liu J	*Mid-term effects of lung volume reduction surgery on pulmonary function in patients with chronic obstructive pulmonary disease*	Prospective cohort	0	1	1	1	0	1	1	0	5
Venuta	*Long-term follow-up after bronchoscopic lung volume reduction in patients with emphysema*	Prospective cohort	1	1	1	1	1	1	1	0	7
Flaherty	*Short-term and long-term outcomes after bilateral lung volume reduction surgery: Prediction by quantitative CT*	Prospective cohort	1	1	1	1	1	1	1	1	8
Homan	*Increased effective lung volume following lung volume reduction surgery in emphysema*	Prospective cohort	1	1	1	1	1	1	1	1	8
Lederer 2	*Lung-volume reduction surgery for pulmonary emphysema: Improvement in body mass index, airflow obstruction, dyspnea, and exercise capacity index after 1 year*	Prospective cohort	1	1	1	1	1	1	1	1	8
Tan A	*Lung volume reduction surgery for the treatment of severe emphysema: a study in a single Canadian institution*	Prospective case series	0	0	1	1	1	1	1	1	6

Table S2 (*continued*)

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Table S2 (*continued*)

First author	Title	Type of study	Representative of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not present at start of study	Comparability of cohorts on the bases of the design or analysis	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow-up	Total
Cremona	*Mechanisms of gas exchange response to lung volume reduction surgery in severe emphysema*	Prospective cohort	0	0	1	1	1	1	1	0	5
Ohno	*Oxygen-enhanced MRI, thin-section MDCT, and perfusion SPECT/CT: comparison of clinical implications to patient care for lung volume reduction surgery*	Prospective cohort	0	0	1	1	1	1	1	1	6
Liu Z	*Video-Assisted Thoracoscopic Surgery for Treatment of Chronic Obstructive Pulmonary Disease*	Prospective cohort	1	1	1	1	1	1	0	0	6
Koizumi	*Comparison of changes in hemodynamics between unilateral and bilateral lung volume reduction for pulmonary emphysema*	Prospective cohort	0	0	1	1	1	1	0	0	4
Gorman	*Diaphragm length and neural drive after lung volume reduction surgery*	Prospective cohort	0	0	1	1	1	1	1	1	6
Malthener	*Lung volume reduction surgery: Results of a Canadian pilot study*	Prospective case series	1	1	1	1	1	1	1	1	8
Wilkens H	*Lung volume reduction surgery versus conservative treatment in severe emphysema*	Prospective cohort	1	1	1	1	1	1	1	0	8
Weder	*Persistent benefit from lung volume reduction surgery in patients with homogeneous emphysema*	Prospective cohort	1	1	1	1	1	1	1	1	8
Geiser	*Outcome after unilateral lung volume reduction surgery in patients with severe emphysema*	Prospective cohort	0	1	1	1	1	1	1	1	7
Soon	*Sequential VATS lung volume reduction surgery: prolongation of benefits derived after the initial operation*	Prospective cohort	1	1	1	1	1	1	1	0	7
Butler	*Underestimation of mortality following lung volume reduction surgery resulting from incomplete follow-up*	Prospective longitudinal	1	1	1	1	1	1	1	1	7
Laghi	*Effect of lung volume reduction surgery on diaphragmatic neuromechanical coupling at 2 years*	Prospective cohort	0	0	1	1	1	1	1	0	5
Bostanci	*Endobronchial coils in treatment of advanced emphysema: A single center experience [İleri amfizem tedavisinde endobronşiyal sarmallar: Tek merkez deneyimi]*	Prospective cohort	1	1	1	1	1	1	1	0	8
Song	*Bronchoscopic Lung Volume Reduction For Pulmonary Emphysema: Preliminary Experience With Endobronchial Occluder*	Prospective cohort	0	1	1	1	1	1	1	1	7
Criner	*Biologic lung volume reduction in advanced upper lobe emphysema phase 2 results*	NR clinical trial	1	1	1	1	1	1	1	1	8
Herth	*Characterization of outcomes 1 year after endoscopic thermal vapor ablation for patients with heterogeneous emphysema*	NR clinical trial	1	1	1	1	1	1	1	1	8
Wood	*A multicenter trial of an intrabronchial valve for treatment of severe emphysema*	Prospective cohort	1	1	1	1	1	1	1	0	7
Hopkinson	*Atelectasis and survival after bronchoscopic lung volume reduction for COPD*	Prospective cohort	0	1	1	1	1	1	1	1	7
Deslee 1	*Lung volume reduction coil treatment for patients with severe emphysema: a European multicentre trial*	NR clinical trial	1	1	1	1	2	1	1	0	8
Bakeer	*Low cost biological lung volume reduction therapy for advanced emphysema*	NR clinical trial	0	1	1	1	1	1	1	0	6
Herth	*Treatment of Advanced Emphysema With Emphysematous Lung Sealant (AeriSeal®)*	NR clinical trial	0	1	1	1	1	1	1	1	7
Klooster	*Lung Volume Reduction Coil Treatment in Chronic Obstructive Pulmonary Disease Patients with Homogeneous Emphysema: A Prospective Feasibility Trial*	NR clinical trial	0	1	1	1	1	1	1	1	8
Sharafkhaneh	*Altered thoracic gas compression contributes to improvement in spirometry with lung volume reduction surgery*	Prospective cohort	1	1	1	1	1	1	1	0	7

NOS, Newcastle-Ottawa scale; NR, non-randomized.

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Table S3 Cochrane ROB assessment of included studies

First author	Title	Type of study	Randomization process	Deviation from intended intervention	Missing outcome data	Measurement of outcome	Selection of reported result	Overall risk of bias
Goldstein	*Influence of lung volume reduction surgery (LVRS) on health related quality of life in patients with chronic obstructive pulmonary disease*	RCT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Davey	*Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HIFi study): a randomised controlled trial*	RCT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mineo	*Impact of lung volume reduction surgery versus rehabilitation on quality of life*	RCT	Some concern	Low risk	Some concern	Some concern	Low risk	High risk
Hillerdal	*Comparison of lung volume reduction surgery and physical training on health status and physiologic outcomes: a randomized controlled clinical trial*	RCT	Low risk	Low risk	Some concern	Low risk	Low risk	Some concern
Klooster	*Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation*	RCT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Zoumot	*Endobronchial Coils for Severe Emphysema Are Effective Up to 12 Months following Treatment: Medium Term and Cross-Over Results from a Randomised Controlled Trial*	RCT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Herth	*Segmental Volume Reduction Using Thermal Vapour Ablation in Patients With Severe Emphysema: 6-month Results of the Multicentre, Parallel-Group, Open-Label, Randomised Controlled STEP-UP Trial*	RCT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Shah	*Bronchoscopic lung-volume reduction with Exhale airway stents for emphysema (EASE trial): randomised, sham-controlled, multicentre trial*	RCT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
De Oliveira	*Combined Bone Marrow-Derived Mesenchymal Stromal Cell Therapy and One-Way Endobronchial Valve Placement in Patients with Pulmonary Emphysema: A Phase I Clinical Trial*	RCT	High risk	Low risk	High risk	Low risk	Low risk	High risk
Deslee 2	*Lung Volume Reduction Coil Treatment vs Usual Care in Patients With Severe Emphysema: The REVOLENS Randomized Clinical Trial*	RCT	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

ROB, Risk of Bias; RCT, randomized clinical trial.

Table S4 Pre to post-operative comparison within lung volume reduction and lung transplant groups

Variable	Lung transplant			Lung volume reduction		
	Pre-operative	Post-operative	P value	Pre-operative	Post-operative	P value
BMI (kg/m^2)	20.6 [17.7, 23.5]	24.1 [19.7, 28.5]	0.19	22.9 [22.0, 23.8]	24.7 [23.6, 25.8]	0.01
6MWT (m)	212.9 [119.0, 306.9]	454.4 [334.7, 574.2]	<0.01	286.0 [270.2, 301.9]	409.1 [392.1, 426.0]	<0.01
FEV1 (% pred)	21.8 [16.8, 26.7]	54.9 [41.4, 68.4]	<0.01	27.6 [25.7, 29.5]	32.5 [30.1, 34.8]	0.01

Data presented as mean [95% CI]. BMI, body mass index; 6MWT, 6-minute walk test; FEV, forced expiratory volume; CI, confidence interval.

Table S5 Baseline characteristics of surgical *vs.* endobronchial lung volume reduction groups

Variable	Surgical				Endobronchial				Overall				P value
	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	
Age (years)	64 [62, 67]	1,034	26	0	62 [59, 65]	724	16	0	63 [62, 65]	1,758	42	0	0.18
BMI (kg/m^2)	22.7 [21.7, 23.8]	227	7	0	23.3 [21.6, 25.0]	590	11	0	22.9 [22.0, 23.8]	817	18	0	0.58
Female (%)	25 [17, 35]	343/968	23	67*	32 [22, 45]	300/779	18	70*	28 [21, 36]	643/1,748	41	68	0.34
Heterogeneous A1AT (%)	96 [94, 98]	816/831	20	32	95 [92, 97]	348/352	11	0	96 [94, 97]	1,164/1,183	31	13	0.58
Home oxygen requirement (%)	50 [28, 72]	231/519	12	93*	68 [36, 89]	198/358	9	96*	59 [40, 75]	429/877	21	95	0.37
Smoking (pack years)	49 [31, 66]	245	3	0	48 [37, 60]	616	12	0	48 [39, 58]	861	15	0	1

*, significant heterogeneity present (P<0.05). CI, confidence interval; BMI, body mass index; A1AT, alpha-1 antitrypsin.

Table S6 Surgical *vs.* endobronchial lung volume reduction perioperative variables (takes the latest follow-up value per variable)

Variable	Surgical				Endobronchial				Overall				P value
	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	Pooled value, mean [95% CI]	No. of patients (N or n/N)	No. of studies	I^2 (%)	
Operation time (min)	116 [58, 173]	166	3	91*	47 [28, 67]	458	7	51	74 [47, 101]	624	10	85*	0.03
Significant bleeding (%)	2 [1, 4]	8/373	6	0	1 [0, 3]	1/208	1	–	2 [1, 3]	9/581	7	0	0.16
Infection (%)	15 [10, 21]	27/180	5	0	11 [8, 16]	45/387	14	24	13 [10, 16]	72/567	19	8	0.25
Pneumothorax (%)	3 [1, 9]	3/98	2	0	4 [2, 10]	26/536	12	74*	4 [2, 9]	29/634	14	69	0.62
Respiratory failure (%)	10 [3, 27]	27/238	5	82*	8 [2, 21]	3/40	3	0	9 [4, 21]	30/278	8	75	0.68
Arrhythmia (%)	14 [9, 22]	28/194	6	9	5 [0, 61]	6/55	2	72	12 [7, 20]	34/249	8	37	0.51
Hospital stay (days)	9 [7, 12]	438	8	14	2 [1, 4]	190	3	0	6 [4, 9]	628	11	56*	<0.01

*, significant heterogeneity present (P<0.05). CI, confidence interval.

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