Lung volume reduction surgery for chronic obstructive pulmonary disease with underlying severe emphysema

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Authors' objectives
To determine the effects and overall effectiveness of lung volume reduction surgery (LVRS) in patients with end-stage chronic obstructive pulmonary disease (COPD) due to underlying emphysema, particularly relative to maximum medical therapy including supplemental oxygen and pulmonary rehabilitation.

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched from 1975 onwards and the search strategy is listed. Experts in the field were contacted to identify ongoing or published research and reference lists of retrieved articles were scanned. There were no language restrictions.

Study selection

Case series. The majority of included studies were 'good-sized consecutive case series which were conducted prospectively with minimal losses to follow-up'. Some studies were excluded due to aspects of validity assessment i.e. studies with loss to follow-up of >25%, inadequate management of losses to follow-up, or retrospective study designs were excluded.

Specific interventions included in the review
LVRS (reduction pneumoplasty or pneumectomy). Open and closed procedures, unilateral and bilateral procedures, laser ablation, stapling or both were included. Some had pulmonary rehabilitation for a number of weeks prior to surgery and some did not.

Participants included in the review
Inclusion criteria were people with diffuse severe emphysema with significant functional limitation despite maximum medical therapy. Actually included were: people with COPD including hyperinflation, poor diaphragmatic excursion, pulmonary perfusion and ventilation deficits; advanced emphysema (diffuse, severe); emphysema with severe airflow limitation; emphysema with hyperinflation; New York Heart Association class III-IV with evidence of airflow obstruction and hyperinflation; severe COPD and respiratory failure; severely impaired pulmonary function (forced expiratory volume in 1 second (FEV1) <0.5L); forced expiratory volume (FEV) 20-30% of predicted; dyspnoea severely impairing lifestyle.

Outcomes assessed in the review
Studies were included irrespective of which outcomes they addressed. Included outcomes were: mortality; morbidity; dyspnoea; pulmonary function tests; chronic respiratory disease questionnaire; 6 minute walking distance (6MWD); exercise testing; quality of life; arterial blood gas; bedside maximum inspired pressure and ventilation; steroid and oxygen dependence; pressure/volume relations; elastic recoil.

How were decisions on the relevance of primary studies made?
Inclusion and exclusion criteria were applied by one reviewer using a pre-agreed proforma and cross-checked by another. Any discrepancies were resolved by discussion.

Assessment of study quality
Whether the study was conducted prospectively; whether the method of selection of cases was identified and appropriate; whether the duration and completeness of follow-up was reported adequately. These were used as criteria for inclusion. Additional detail on methodological quality was recorded and tabulated by one reviewer.
Data were extracted by one reviewer using a predetermined form. Data were extracted on: study design; inclusion and exclusion criteria for entry to the study; intervention; outcomes; additional information and results.

Methods of synthesis

How were the studies combined?
A narrative synthesis of the studies was presented. Where necessary the results of individual studies were re-analysed involving the re-calculation of certain data to facilitate comparison such as the conversion of walking distances to metres and the calculation of pre-test/post-test differences. Data was summarised using additional statistics such as interquartile range (IQR) to give an indication of the general size and direction of effect.

How were differences between studies investigated?
Tabulated characteristics and results of included studies were assessed qualitatively particularly with regard to possible sources of heterogeneity. The tabulation process enabled the identification of a range of plausible values for the likely effect of LVRS on key outcomes of interest.

A funnel plot was constructed to investigate publication bias.

Results of the review

Nineteen studies were included (n = 1069).

Mortality at follow up 3-6 months (16 comparisons (14 studies)): IQR for early mortality (occurring within 30 days of surgery, or in hospital) was 0-6%. IQR for late mortality (30 or more days following surgery, or occurring at home) was 0-8%. IQR for overall deaths at 3-6 months follow-up was 0-11%. Late mortality at 2 year follow-up (2 studies) was estimated as between 0 and 3%.

FEV1 (19 comparisons, 16 studies): 3-6 months after LVRS IQR was 0.91-1.07 litres, with a pre-test/post-test difference IQR of 0.23-0.36 litres. At 2 years follow-up (2 studies) post treatment FEV1 was 1.25 and 0.91 litres, and pre-test/post-test difference was 0.42 and 0.22 litres.

FEV1 as percentage of predicted (18 comparisons, 17 studies): short term IQR 35-41%, pre-test/post-test difference IQR 9-13%. After 1 year (1 study) post-treatment result = 36%, pre/post test difference = 12%. After 2 years (same study) post-treatment result 42%, pre-test/post-test difference 15%.

Six minute walking distance (9 studies): IQR 306-434 metres post-treatment, pre-test/post-test difference IQR 32-96 metres. Long term follow-up (1 study) showed a difference of 64 metres and 80 metres at 1 and 2 years respectively.

Quality of life (4 studies): Although only limited data were presented in the studies, improvements in quality of life were observed across all studies and measurement tools.

Dyspnoea (12 studies): 6 studies used the modified medical research council (MMRC) dyspnoea scale, reductions in score ranging from -1.0 to -2.4 were seen, 3/6 were significant improvements. One study used the CRQ scale and recorded a mean improvement of 5.84 (p=0.0001). Two studies used the Borg scale: in one the mean score decreased from 7.6 pre-operatively to 4.65 post-operatively and in the other the mean score decreased from 3.71 to 2.40. Three studies reported baseline dyspnoea index scores as 0.83, 0.9 and 1.0 and transitional dyspnoea index scores as 2.2, 1.65 and 1.72. One study reported an overall baseline focal score (BFS) of 3.36 and a transitional focal score (TFS) of 6.12. Another study reports an overall TFS of 5.1 (p<0.001).

Length of stay (14 studies): IQR was 13-18 days.

Supplemental oxygen: in the short term (3-6 months) the reduction in the percentage of patients requiring supplemental oxygen either continuously or on exertion was 16-42% (IQR). One study reports a reduction of 41% at one year and 52% at two years.
The pattern of results was consistent across individual studies despite a significant degree of clinical heterogeneity.

**Cost information**
A cost-utility analysis undertaken by the review authors found that it was likely that LVRS was cost-effective. Figures were: £9,000 per additional quality-adjusted life-year gained, best-case scenario £7,000, worst-case scenario £24,000.

**Authors’ conclusions**
In the management of patients with severe end-stage emphysema LVRS with or without pulmonary rehabilitation leads to subjective improvements in quality of life and shortness of breath. Mortality rates associated with the operation are consistent across individual studies and compare favourable with those of untreated people with COPD. However the possibility that the results of the individual studies or of the review itself may be open to bias should not be underestimated.

Even accounting for the fact that the observed evidence on its effectiveness is subject to several biases, it seems unlikely that LVRS is less effective than current best practice. The review authors still judge that the benefits of LVRS are likely to outweigh the risks.

The tentativeness of the cost-utility estimates is further compounded by the absence of accurate data on costs and quality of life.

**CRD commentary**
Inclusion criteria are clearly listed and the literature search is comprehensive with no language restrictions. Efforts were made to find unpublished studies and the funnel plot shows it is unlikely that studies were missed. A validity assessment was undertaken and used to exclude some studies but further details are not presented with the review findings. Study details are adequately reported and a narrative synthesis seems appropriate given the heterogeneity in the included studies. The authors’ conclusions do seem to follow from the results.

**Implications of the review for practice and research**
The authors state that, overall, the findings of the review suggest that LVRS is a procedure where further rigorous research evidence on effectiveness is needed before implementation. They state that LVRS should have a high priority among calls on R&D resources because, if the favourable provisional estimates of effects, effectiveness and cost-utility are borne out, the procedure has the potential not only to be effective but also cost-effective.

**Bibliographic details**

**Original Paper URL**

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Dyspnea /etiology /physiopathology; Emphysema /complications /physiopathology; Forced Expiratory Volume; Length
of Stay; Lung Diseases; Lung Diseases, Obstructive /surgery; Pneumonectomy /methods

**AccessionNumber**
11999009350

**Date bibliographic record published**
30/04/2001

**Date abstract record published**
30/04/2001

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.