Lung Volume Reduction Surgery for Emphysema

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CCOHTA takes sole responsibility for the final form and content.
Lung Volume Reduction Surgery for Emphysema

**Technology**
Lung volume reduction surgery (LVRS) using buttressing (reinforcing) or no buttressing; staples or laser; unilateral or bilateral procedures; staged or simultaneous procedures; and median sternotomy (MS) or video-assisted thoracoscopic surgery (VATS).

**Disease**
Emphysema is a chronic obstructive pulmonary disease (COPD) that mainly affects adults older than 65. It causes shortness of breath and reduces quality of life (QoL).

**Issue**
LVRS is one treatment option for patients with severe emphysema. It is an expensive procedure, with a high risk of postoperative death. It may be used as a bridge to lung transplantation or when transplantation is unavailable. There is a need to compare LVRS with medical management, and compare different types of LVRS procedures.

**Methods and Results**
A systematic review was performed. Where possible, a meta-analysis was performed to derive statistical summaries. The relative benefit and harm were determined by examining the impact on QoL, mortality, shortness of breath, and pulmonary function; and complications associated with treatment. Seven randomized controlled trials (RCTs) involving 1,412 patients and comparing LVRS with medical management, were identified. Four RCTs and 10 cohort studies comparing different LVRS procedures were identified.

**Implications for Decision Making**
- **There is no reduction in the overall death rate at about two years.** LVRS is a palliative treatment that improves QoL, lung function, and exercise tolerance. It increases the risk of short-term death compared with medical management alone.
- **For certain patients, LVRS offers a survival advantage compared with medical management.** These are patients whose emphysema mainly affects the lung’s upper lobes, and whose baseline exercise capacity is low.
- **Other patients are at high risk of death after LVRS.** These are patients who have a forced expiry volume in one second that is no more than 20% of the predicted value, and who have a homogenous distribution of emphysema in the lung, or a carbon monoxide diffusing capacity that is no more than 20% of the predicted value.
- **There is no definite advantage to any one LVRS procedure, in terms of clinical outcomes or in-hospital costs.**
- **The US National Emphysema Treatment Trial (NETT) shows that the total cost, six months after surgery, was less with VATS compared with the MS procedure.**

1 Introduction

Emphysema is one of several conditions collectively known as chronic obstructive pulmonary disease (COPD).1 It mainly affects adults older than 65, by reducing their exercise capacity and quality of life (QoL). Emphysema may lead to early death by progressively destroying the alveolar wall and hyperinflating the lung.2,3 There is no known cure for emphysema; the aims of treatment are to relieve symptoms and improve QoL.4

With an aging population in Canada, the rate of occurrence of COPD is increasing, and the already substantial related health care costs are projected to increase accordingly. In 1997, emphysema was the fourth leading cause of death in men and the seventh in women, with 9,618 deaths.5 A 1998 survey found that 3.2% of adult Canadians suffered from chronic bronchitis or emphysema,5 and the total cost of COPD that year was $1.67 billion.6 Another survey found that women were affected at the rate of 2.1% in non-smokers, 2.7% in ex-smokers, and 8.2% in smokers7. In men, the corresponding rates were 0.8%, 2.9%, and 3.5%. Preventing COPD largely depends on smoking cessation strategies.

For those with COPD, the symptoms are traditionally managed with bronchodilators, anti-inflammatory medications, oxygen supplementation, and pulmonary rehabilitation. If these fail, lung transplantation or lung volume reduction surgery (LVRS) is considered. The latter may be a bridge to lung transplantation or a substitute when an organ is unavailable. LVRS is expensive and risky for older and severely compromised patients. A comparison of LVRS to medical management, and an assessment of the LVRS techniques, are needed.

LVRS was pioneered in 1957, when Otto Brantigan et al. published a case series of 33 patients.8 Based on the theory that a loss of elastic recoil was the main cause of collapsed expiratory airways in emphysema patients, their technique consisted of a unilateral thoracotomy with a 20% to 30% resection of the lung, coupled with denervation using radical hilar stripping. After the patient had recovered from the first surgery, the operation on the second lung occurred.3

Some think that LVRS works by restoring circumferential traction (elasticity) in small airways.9 Others suggest that an outward circumferential pull on the airways diminishes expiratory airway collapse;10 and that the reduced thoracic volume allows better rib cage and diaphragm movement.3 Brantigan et al. reported increased exercise tolerance and lung ventilation in 75% of patients, but because of the high rates of severe morbidity and mortality (16%), their procedure never gained popularity.

Interest in LVRS was renewed in 1994, when Joel Cooper et al. refined the original technique, based on observations that the hyperexpanded chests and flattened diaphragms of COPD patients quickly reverted to a more normal state after lung transplantation.10 Surgeons now use one of two approaches to LVRS: a median sternotomy (MS) or video-assisted thoracoscopic surgery (VATS).11 Both procedures can be performed unilaterally or bilaterally, although MS is usually bilateral, because the incision in the midline of the sternum allows equal access to both lungs.12 In VATS, instruments such as a light source, a fibre-optic video camera, and a stapler are inserted through small access points.13 Diseased lung is removed using a stapler or laser, usually
the former, because it cuts the tissue while sealing the edges. When stapling is used, the staple line is sometimes buttressed with bovine pericardium or other material to reduce air leaks.

The patients who are most likely to benefit from LVRS generally experience severe expiratory airflow limitation, air trapping, and marked hyperinflation; and have the ability to complete a vigorous preoperative pulmonary rehabilitation program. Patients most at risk from surgery are those with severe pulmonary hypertension, severe comorbidities, low tolerance of exercise, low tolerance of pulmonary rehabilitation, and previous lung surgery; and those who continue to smoke. Surgical procedures do not require licensing by Health Canada.

2 Objectives

Our objective was to evaluate the clinical efficacy of LVRS compared with medical management for emphysema, and to evaluate the clinical benefit and harm of different LVRS procedures.

3 Methods

A protocol for this systematic review was written a priori. It was later modified to produce two systematic reviews. The first report compared LVRS with medical management, and the second report compared different LVRS approaches.

For both reports, literature dating from 1992 was obtained by cross-searching MEDLINE®, EMBASE®, BIOSIS Previews®, PASCAL, and Current Contents Search® databases on the DIALOG® system, using a broad search strategy without language or publication restrictions. The original search was performed in 2002, with database alerts capturing new studies up to September 2004. Parallel searches were also performed in PubMed and the Cochrane Library until September 2004. Grey literature was found by searching the web sites of regulatory agencies; health technology assessment and related agencies; professional associations; and specialized databases. The Internet was searched using Google™ and AlltheWeb search engines.

Selection Criteria

For LVRS versus medical management, trials were selected if they were randomized controlled trials (RCTs) involving patients with emphysema; compared LVRS with medical management (with or without rehabilitation); and reported data on QoL, mortality, complications, dyspnea, pulmonary function, exercise tolerance, or blood gas level. Case series studies in English and involving ≥20 patients were included if they reported surgical complications or mortality.

Studies comparing different LVRS procedures were included if they were RCTs or cohort studies (prospective or retrospective) involving patients with emphysema; compared different LVRS techniques; and reported complications of surgery, mortality, QoL, dyspnea, and pulmonary function.
Two reviewers independently selected studies for inclusion in each review. Differences of 
opinion were resolved by consensus. After the studies were selected, two people working 
independently extracted data using a structured form.

**Strategy for Quality Assessment**

Reviewers assessed the quality of studies using the Jadad five-point scale\textsuperscript{15} for RCTs, and the 
scale by Hailey \textit{et al.}\textsuperscript{16} for cohort studies. In both scales, higher scores denote higher quality 
studies. Allocation concealment was also assessed.\textsuperscript{17}

**Data Analysis**

Most outcomes were reported as continuous data. In the case of outcomes, where data came from 
more than one trial, the information was pooled and summary estimates [weighted mean 
difference (WMD)] and corresponding 95% confidence intervals (CI) were calculated. If data 
came from one trial, then the mean difference (MD) and corresponding 95% CI were calculated. 
The WMD, standardized mean difference (SMD), or MD was statistically significant if the 95% 
CI excluded zero.

Mortality was reported as binary data. Relative risk (RR) and 95% CI were calculated for the 
mortality data. RR<1 indicated reduced mortality and results were considered statistically 
significant if the corresponding 95% CI excluded one.

Results were considered to be significant if p value <0.05.

4 RESULTS

**LVRS versus Medical Management**

Of the 1,643 citations identified in the original search, 1,559 citations were excluded. An 
additional 10 potentially relevant reports were scrutinized for inclusion, resulting in a total of 94 
potentially relevant reports (16 RCT reports and 78 case series reports). Of the 16 RCT reports, 
eight were excluded. That left eight reports describing seven unique RCTs,\textsuperscript{18-24} [including one 
unpublished report describing two unique trials by Dr. John Miller (JM) of McMaster 
University]. Of the 78 case series reports, 16 were excluded, leaving 62 reports describing 59 
unique studies. The latter were used to document additional information on the risks of surgery, 
but they did not provide additional insight and are excluded in this overview.

a) Trial and Patient Characteristics

Of the seven RCTs, two were done in Canada, three in the US, and one each in the UK and Italy. 
The largest RCT\textsuperscript{21,22} had 1,218 patients and a follow-up time to 24 months. The number of 
patients in the other RCTs \textsuperscript{18-20,25,24} (including JM’s) ranged from 37 to 60, with follow-up times 
between three and 12 months. The LVRS was either MS or VATS (unilateral or bilateral). One 
published RCT\textsuperscript{19} and two unpublished RCTs (JM’s) reported the details of medical management. 
The mean age (±SD) of patients, all with severe emphysema, varied between 58.8±6.4 and 
66.7±5.9. Females made up 3.3% to 68.4% of patients.
The seven RCTs scored between two and three on the Jadad five-point scale. Allocation concealment was adequate in one.20

b) Data Analysis and Synthesis

QoL, dyspnea, pulmonary function, and exercise capacity improved in patients who had LVRS compared with those who had their symptoms managed medically. The degree of improvement could have been influenced by the surgical technique, medical therapy, and pulmonary rehabilitation programs used (Table 1).

**Table 1: QoL results using various measurement instruments**

<table>
<thead>
<tr>
<th>Specific Measures Used</th>
<th>Number of Studies</th>
<th>Number of Patients</th>
<th>Time of Follow-up (months)</th>
<th>WMD or MD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRQ-emotion</td>
<td>3</td>
<td>131</td>
<td>6</td>
<td>1.23 (0.80, 1.65)</td>
</tr>
<tr>
<td>CRQ-fatigue</td>
<td>3</td>
<td>131</td>
<td>6</td>
<td>1.48 (0.07, 1.90)</td>
</tr>
<tr>
<td>CRQ-mastery</td>
<td>3</td>
<td>131</td>
<td>6</td>
<td>1.42 (0.98, 1.87)</td>
</tr>
<tr>
<td>SF-36 mental</td>
<td>2</td>
<td>75</td>
<td>6</td>
<td>1.89 (-3.29, 7.06)</td>
</tr>
<tr>
<td>SF-36 physical</td>
<td>2</td>
<td>75</td>
<td>6</td>
<td>8.95 (5.21, 12.70)</td>
</tr>
<tr>
<td>SF-36 overall</td>
<td>1</td>
<td>42</td>
<td>3</td>
<td>11.00 (2.32, 19.68)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>42</td>
<td>6</td>
<td>29.00 (20.03, 37.97)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>32</td>
<td>12</td>
<td>30.00 (15.89, 44.11)</td>
</tr>
<tr>
<td>QWB</td>
<td>1</td>
<td>861</td>
<td>6</td>
<td>0.05 (0.03, 0.07)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>711</td>
<td>12</td>
<td>0.04 (0.02, 0.06)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>448</td>
<td>24</td>
<td>0.05 (0.03, 0.07)</td>
</tr>
<tr>
<td>SGRQ</td>
<td>1</td>
<td>860</td>
<td>6</td>
<td>-13.40 (-15.13, -11.67)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>711</td>
<td>12</td>
<td>-13.60 (-15.67, -11.44)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>449</td>
<td>24</td>
<td>-11.00 (-13.60, -8.37)</td>
</tr>
</tbody>
</table>

CRQ=chronic respiratory disease questionnaire; SF-36=36-item short form questionnaire to determine QoL; QWB=Quality of Well Being questionnaire; SGRQ=St. George’s respiratory questionnaire; WMD=weighted mean difference; MD=mean difference

LVRS patients stayed in hospital significantly longer (p<0.001) and had more days of ambulatory care (p=0.005) during the first 12 months after randomization than medically managed patients.21 Between the 13th and 24th months, this reversed, with medically managed patients requiring significantly more hospitalization. Emergency room visits and supplemental oxygen were not significantly different between the two groups.

For dyspnea, patients undergoing LVRS did significantly better than those managed medically. The WMD at 95% CI were 1.67 (1.22, 2.12), 2.00 (1.31, 2.69), and 1.92 (1.25, 2.59), at six, nine, and 12 months respectively.

Mortality data are presented in Tables 2 and 3. The relative risk of death at three months was significantly greater for patients who underwent LVRS than for those managed medically; this was no longer significant at six and 12 months.
Table 2: Mortality data for subgroups in the NETT\textsuperscript{21}

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Number of Patients</th>
<th>90-day Mortality</th>
<th>Total Mortality*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LVRS</td>
<td>Medical Management</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>All</td>
<td>608</td>
<td>610</td>
<td>6.02 (2.87, 12.62)</td>
</tr>
<tr>
<td>High risk\textsuperscript{†}</td>
<td>70</td>
<td>70</td>
<td>41.00 (2.53, 664.89)</td>
</tr>
<tr>
<td>Other than high risk</td>
<td>538</td>
<td>540</td>
<td>3.51 (1.62, 7.64)</td>
</tr>
<tr>
<td>Upper-lobe emphysema and low exercise capacity</td>
<td>139</td>
<td>151</td>
<td>0.87 (0.24, 3.17)</td>
</tr>
<tr>
<td>Upper-lobe emphysema and high exercise capacity</td>
<td>206</td>
<td>213</td>
<td>3.10 (0.63, 15.19)</td>
</tr>
<tr>
<td>Non-upper-lobe emphysema and low exercise capacity</td>
<td>84</td>
<td>65</td>
<td>11.65 (0.68, 200.27)</td>
</tr>
<tr>
<td>Non-upper-lobe emphysema and high exercise capacity</td>
<td>109</td>
<td>111</td>
<td>11.20 (1.47, 85.29)</td>
</tr>
</tbody>
</table>

*Total mortality rates are based on mean follow-up of 29 months. †High risk patients defined as those patients with FEV\textsubscript{1} (% predicted) $\leq$20% and either homogeneous emphysema on computed tomography or diffusing capacity of carbon monoxide (% predicted) $\leq$20%. “Other than high risk” is defined as all patients except those at high risk.

Figure 1: RR of death for patients undergoing LVRS as compared with those undergoing medical management alone at three, six, 12, and 29 months

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (random) 95% CI</th>
<th>Weight %</th>
<th>RR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geddes, 2000</td>
<td>4/24</td>
<td>1/24</td>
<td>25.68</td>
<td>4.00</td>
<td>[0.48, 33.22]</td>
</tr>
<tr>
<td>Goldstein, 2003</td>
<td>2/28</td>
<td>0/27</td>
<td>15.67</td>
<td>4.83</td>
<td>[0.24, 96.16]</td>
</tr>
<tr>
<td>NETT, 2003</td>
<td>48/608</td>
<td>8/610</td>
<td>58.65</td>
<td>6.02</td>
<td>[2.87, 12.62]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>660</td>
<td>661</td>
<td>100.00</td>
<td>5.71</td>
<td>[2.89, 11.26]</td>
</tr>
<tr>
<td>Total events:</td>
<td>660</td>
<td>661</td>
<td>100.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2=0.14$, df=2 (p=0.93), I²=0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $Z=5.02$ (p&lt;0.00001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 6 months              |               |             |                     |          |                     |
| Geddes, 2000          | 4/24          | 1/24        | 18.51               | 4.00     | [0.48, 33.22]       |
| Pompe, 2000           | 2/30          | 1/30        | 16.19               | 4.19     | [0.24, 20.90]       |
| Goldstein, 2003       | 2/28          | 1/27        | 16.19               | 1.69     | [0.24, 20.05]       |
| CLVR, 2004            | 5/31          | 4/29        | 32.48               | 1.71     | [0.35, 9.39]        |
| OBEST, 2004           | 2/24          | 1/11        | 16.67               | 0.92     | [0.05, 9.07]        |
| Subtotal (95% CI)      | 137           | 121         | 100.00              | 1.56     | [0.68, 3.56]        |
| Total events:         | 137           | 121         | 100.00              |          |                     |
| Test for heterogeneity: $\chi^2=1.28$, df=4 (p=0.87), I²=0% |
| Test for overall effect: $Z=1.05$ (p=0.30) |

| 12 months             |               |             |                     |          |                     |
| Geddes, 2000          | 5/24          | 2/24        | 59.03               | 2.50     | [0.54, 11.45]       |
| Goldstein, 2003       | 4/28          | 1/27        | 40.97               | 3.86     | [0.46, 32.35]       |
| Subtotal (95% CI)      | 52            | 51          | 100.00              | 2.90     | [0.83, 10.10]       |
| Total events:         | 52            | 51          | 100.00              |          |                     |
| Test for heterogeneity: $\chi^2=0.11$, df=1 (p=0.75), I²=0% |
| Test for overall effect: $Z=1.67$ (p=0.09) |

| 29 months             |               |             |                     |          |                     |
| NETT, 2003            | 157/608       | 160/610     | 100.00              | 0.98     | [0.81, 1.19]        |
| Subtotal (95% CI)      | 608           | 610         | 100.00              | 0.98     | [0.81, 1.19]        |
| Total events:         | 157           | 160         | 100.00              |          |                     |
| Test for heterogeneity: not applicable |
| Test for overall effect: $Z=0.16$ (p=0.87) |
Pulmonary function was measured by forced expiratory volume in one second (FEV\textsubscript{1}), forced vital capacity, residual volume, and total lung capacity. Compared with medical management, LVRS significantly improved FEV\textsubscript{1}, whether it was measured in litres (L) or as a percentage of predicted value. For instance, the FEV\textsubscript{1} (L) status at three and six months of follow-up was WMD (95% CI)=0.19 (0.04, 0.34) and 0.26 (0.16, 0.37) respectively for LVRS compared with medical management. At nine and 12 months, the difference was no longer statistically significant. LVRS patients also did better than those under medical management when assessed using other measures of pulmonary function, although not all comparisons reached statistical significance.

Likewise, exercise function improved more with LVRS than medical management. Data on blood gases were also reported, but the association between that outcome and others, such as QoL, exercise tolerance, and mortality remains controversial.

c) Economic Analysis
The NETT included a prospective economic analysis\textsuperscript{,22} which excluded high risk patients. The cost-effectiveness ratio for LVRS compared with medical management was US$190,000 per quality-adjusted life-year (QALY) at three years and US$53,000 per QALY at 10 years. For patients with upper-lobe emphysema and low exercise capacity, the ratios were US$98,000 per QALY and US$21,000 per QALY respectively. These estimates are based on assumptions about long-term outcomes, which have substantial uncertainty.

d) Limitations
There were limitations to the LVRS versus medical management results. Not all RCTs reported all outcomes at all time points, thereby reducing power. There were differences in study design, patient selection criteria, and outcomes, though the overall findings were similar. Investigators used different QoL measurement instruments, making it difficult to compare results across trials. The RCTs were all done in large hospitals and academic centres, so the results may not be generalizable to smaller hospitals. The patient selection criteria were restrictive, so the results may not be generalizable to all patients with emphysema.

Comparison of Different LVRS Techniques
A total of 25 potentially relevant reports were retrieved. There were six about RCTs and 19 about cohort studies. Two RCTs were excluded, because they reported on the same trial. The four reports that remained described four unique RCTs. Seven cohort studies were excluded, because they were irrelevant or duplicates. The 12 reports that remained described 10 unique cohort studies. Of the four RCTs, three\textsuperscript{25-27} compared LVRS with or without buttressing, and one compared\textsuperscript{28} laser versus staple procedures. Of the 12 cohort studies, one\textsuperscript{29} compared unilateral VATS, bilateral VATS, and MS. Four\textsuperscript{30-33} compared unilateral VATS and bilateral VATS. Two\textsuperscript{34,35} compared staged versus simultaneous LVRS, and five\textsuperscript{36-40} compared MS and VATS.
a) Trial and Patient Characteristics

All four RCTs reported complications of surgery, and two reported pulmonary function data. The number of patients ranged from 60 to 123, and their mean age ranged from 44 to 69 years. The quality of each RCT was low, varying between one and two out of five (Jadad five-point scale). Allocation concealment was unclear in all these reports.

For the cohort studies comparing unilateral and bilateral procedures, the number of patients ranged from 41 to 682. The two cohort studies comparing staged and simultaneous procedures had 50 and 59 patients respectively, and the number of patients in the cohort studies comparing MS and VATS ranged from 30 to 511. The quality of the cohort studies was fair, with scores varying between seven and eight out of 15 (Hailey et al. scale).

b) Data Analysis and Synthesis

The length of hospital stay, as reported in one of three RCTs that compared surgery with buttressing (using bovine pericardium) and without buttressing, was significantly shorter in the group with buttressing. The other trial that reported these data showed similar hospital stays for both groups. The duration of air leaks appeared to be less with buttressing than without, but this difference was statistically significant in only one RCT.

In the one RCT comparing laser versus staple, the number of patients having delayed pneumothorax was significantly higher in the laser group. Significant advantages were seen in pulmonary function at six months by the staple procedure, and QoL was also better.

A comparison of unilateral and bilateral procedures resulted in information of minimal significance. One cohort study found mortality in the unilateral group higher at one year (17% compared with 2.5% for bilateral) due to respiratory failure; two other studies did not make this observation. One cohort study found some functional improvements and better QoL in the bilateral VATS group versus the unilateral VATS.

Two studies comparing staged surgery with simultaneous surgery found more sustained benefits in the staged groups, although long-term survival did not differ between groups. The six cohort studies looking at MS versus VATS had inconsistent results, with the evidence not favouring one technique over the other.

c) Economic Analysis

In the NETT, the total cost six months after surgery was significantly less (p=0.005) in the VATS group compared with the MS group (US$51,053±US$4,502 versus US$61,481±US$3,189).

d) Limitations

There were limitations in comparing the results from different LVRS techniques. Studies were done at large hospitals and academic centres, so the results may not be generalizable to all health-care settings. Patient selection criteria were restrictive, so they may not be generalizable to all patients. The studies were of low to modest quality, and most of the cohort studies were retrospective evaluations, so results need to be viewed with caution.
5 Conclusions

LVRS improves QoL, pulmonary function, and exercise tolerance in patients with severe emphysema. These benefits come at a price of increased short-term mortality. LVRS offers no reduction in overall mortality when compared with medical management. Patients with FEV$_1$ (%predicted) $\leq$ 20% and either homogeneous emphysema on computed tomography or DLCO (%predicted) $\leq$ 20 are at high risk of death when undergoing LVRS. Compared with medical management, LVRS offers a reduced risk of death in patients with upper-lobe emphysema and low baseline exercise capacity. Data on the risks associated with LVRS are poorly documented. Limited evidence from low quality RCTs suggest that buttressing the staple lines may provide better results than no buttressing, and that the stapling procedure may be better than the laser resection method. The studies comparing unilateral versus bilateral procedures, staged versus simultaneous, or MS versus VATS were non-randomized. The evidence from these studies is inconsistent, so it is impossible to conclude whether one procedure is better than another. Uncertainty will continue unless appropriate RCTs are undertaken.
6 References


