The long-term health status improvements seen after lung volume reduction surgery

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Abstract

Objectives: To correlate the long-term changes in respiratory physiology, body mass index (BMI) and health status after lung volume reduction surgery (LVRS). Patients/methods: From 1995 to 2002 77 patients; 48 male: 29 female, median age 59 (41–72) years, have undergone LVRS (simultaneous bilateral in 27; staged bilateral in 3; unilateral in 47). FEV1, total lung capacity (TLC), residual volume (RV) and RV/TLC ratio were measured preoperatively and at 3 months, 6 months, 1 year, 2 years, 3 years and 4 years post surgery. At the same time interval health status was assessed by Euroquol and Short Form 36 (SF 36) questionnaires. Seventeen patients have died within 4 years of their operation (30 day mortality 5%). Results: The changes in FEV1 are only significantly improved for 1 year post LVRS, while the improvements in TLC and RV remain significant up to 3 years postoperatively. The improvements in BMI also persist for 3 years. The best scores in Euroquol and SF 36 are obtained 6 months after LVRS but are only significantly improved up to 1 year. Conclusion: The physiological effects of volume LVRS are lasting but initial improvements in health status decline more rapidly.

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1. Introduction

Since Cooper reported his first experience with lung volume reduction in 1995, several groups have reported on the long-term benefits of lung volume reduction surgery (LVRS) in respect of sustained improvements in pulmonary physiology [1–3].

FEV1 is the usual outcome measure in studies of chronic obstructive pulmonary disease (COPD), including studies involving LVRS. It is used in the evaluation of treatment of individual patients, as well as in trials of new treatments. FEV1 is also used to classify the severity of COPD, as it correlates with morbidity and mortality [4].

Health status assessment is becoming more important, in health economic studies and in clinical research to assess new treatment options. Health status has also found to be independently associated with morbidity and mortality [4]. The use of health status questionnaires in individual patient management needs further assessment and may be too time consuming [5].

Improvements in health status after LVRS have been reported to last at least 2 years [6]. When compared with a randomized control group, who underwent continued medical treatment, these changes were significant for at least 12 months post LVRS. [7]. Information about the subsequent decline in health status is however limited. We therefore wanted to assess the long-term results of LVRS in terms of health status and correlate these with changes in respiratory function.

2. Patients and methods

2.1. Selection criteria

Patients had to have significant symptomatic dysfunction judged by the MRC dyspnoea scale as grades 3–5. Spirometric inclusion criteria consisted of an FEV1 of 15–40% of predicted; residual volume (RV) in excess of 200% of predicted; total lung capacity (TLC) greater than 120% of predicted and a RV:TLC ratio over 60%.

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Anatomical criteria included the presence of heterogeneous emphysema with target areas of severe emphysema on computed tomography scan. Physiological heterogeneity was assessed on radionuclide scintigraphy. This was quantitated by calculating the so-called ’Q score’ as determined by the ratio of perfusion in the target zone to the total lung perfusion. Patients with target areas in either upper or lower lobes were included.

All patients underwent preoperative pulmonary rehabilitation. Exercise tolerance was assessed using the shuttle walk test. This is a standardized and externally paced field walking test conducted on a 10 m course [8]. Patients who, after rehabilitation, could not complete a distance of 150 m in a shuttle walk test did not proceed to operation.

Before surgery but after rehabilitation patients completed Short Form 36 (SF 36) and Euroquol questionnaires. The SF 36 is a generic health status questionnaire in which 36 questions covers eight health domains; physical functioning, social functioning, role limitations due to physical problems, mental health, energy/vitality, pain and general health status. For each domain scores are transformed to range from 0 (worst possible health status) to 100 (best possible health status). The Euroquol is also a generic questionnaire consisting of five dimensions; mobility, self-care, usual activities, pain and discomfort, anxiety and depression. The scoring of these dimensions can be transformed into a single index of health status (the highest score the best possible health status).

2.2. Surgical approach

At the start of the series all operations were performed bilaterally via median sternotomy. Subsequently one of the surgeons adopted a policy of bilateral video-assisted thoracoscopic surgery (VATS) and latterly a policy of staged unilateral VATS [9]. All operations entailed stapled resection of functionless areas of lung using bovine pericardial buttresses (Peri Strips, Bio-Vascular, MN).

2.3. Postoperative follow-up

Patients were reviewed in out-patient clinics at 3, 6, 12 months after surgery and then annually. At each visit, patients underwent detailed spirometry and plethysmography and their weight was recorded. They also completed SF 36 and Euroquol health status questionnaires.

2.4. Statistical analysis

The relationships between preoperative and postoperative variables were assessed using the paired or unpaired Student’s t-test and the Wilcoxon test. A $P < 0.05$ was considered to indicate a statistically significant difference.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Postoperative follow-up of patients</th>
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<tbody>
<tr>
<td></td>
<td>Follow-up</td>
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<tr>
<td>3 months</td>
<td>63</td>
</tr>
<tr>
<td>6 months</td>
<td>62</td>
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<tr>
<td>1 year</td>
<td>57</td>
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<td>2 years</td>
<td>41</td>
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<tr>
<td>3 years</td>
<td>31</td>
</tr>
<tr>
<td>4 years</td>
<td>18</td>
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</table>

3. Results

3.1. Preoperative characteristics

From 1995 to 2002 77 patients underwent LVRS. Median age was 59 (41–72) years. There were 48 male and 29 female patients. 27 patients underwent simultaneous bilateral LVRS, eight by VATS and 19 by median sternotomy. Forty-seven patients had unilateral VATS and three patients had staged bilateral VATS.

Ten patients were α1-antitrypsin deficient. None of the patients were lost to follow-up but in some patients we were not able to obtain PFT and health status questionnaires (Table 1). This was due to some patients not having left hospital since their original operation. At subsequent time intervals patients who lived geographically distant did not attend all yearly appointments. However details were obtained from the local pulmonologists.

3.2. Perioperative changes in respiratory physiology

Table 2 shows the preoperative pulmonary physiology. FEV1 remained above preoperative values for at least 4 years post LVRS but these changes were statistically significant only up till 1 year after surgery (Fig. 1). The changes in TLC and RV were also improved compared to preoperative values for 4 years and these changes were significant for 3 years (Fig. 1).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Preoperative pulmonary function</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% predicted mean (SD)</td>
</tr>
<tr>
<td>FEV1</td>
<td>28 (10)</td>
</tr>
<tr>
<td>TLC</td>
<td>144 (18)</td>
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<tr>
<td>RV</td>
<td>259 (58)</td>
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<tr>
<td>RV/TLC ratio</td>
<td>64 (9) %</td>
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<tr>
<td>DLCO</td>
<td>44 (13)</td>
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<tr>
<td>PaO2</td>
<td>9.0 (1.1) kPa</td>
</tr>
<tr>
<td>PaCO2</td>
<td>5.1 (0.7) kPa</td>
</tr>
</tbody>
</table>
3.3. Perioperative changes in health status

SF 36 questionnaire (Fig. 2).

In four domains the changes were improved for 2 years, in three domains for 1 year. Significant changes were found in seven domains at 6 months. The scores in the pain domain never reached preoperative values with significant worsening of the scores at 3 months.

There were weak but statistically significant correlations between the changes in RV/TLC ratio and changes in the domains of social functioning, mental health and energy/vitality ($r = -0.3, P < 0.05$) at 3 month. At 1 year correlations were found between changes in RV and RV/TLC ratio and changes in the domain of role limitation due to emotional problems ($r = -0.4, P < 0.05$). At 2 years there were correlations between RV and social functioning ($r = -0.7, P < 0.05$) and between RV/TLC ratio and social functioning ($r = -0.8, P < 0.05$) and mental health ($r = -0.9, P < 0.05$). At 3 years correlations were found between RV/TLC ratio and general health perception ($r = -0.9, P < 0.05$).

Euroquol questionnaire (Fig. 2).

Similarly, improved scores were seen lasting up till 2 years post LVRS, but these changes were only statistically significant up till 1 year.

At 3 months, when the maximum physiological benefits are obtained, no correlation was found with the changes in Euroquol score. At 6 months, when the best EQ scores are obtained, also no correlation was found. At 1, 2, and 3 years a statistically significant correlation was found between EQ score and RV/TLC ratio (at 1 year $r = -0.05, P = 0.02$, at 2 years $r = -0.7, P = 0.02$ and at 3 years $r = -0.9, P = 0.04$).
3.4. Perioperative changes in body mass index (BMI)

Mean preoperative BMI was 22 kg/m². Postoperative significant improvements were seen from 6 months to 3 years (Fig. 3).

4. Discussion

4.1. Changes in respiratory physiology

In evaluating the outcome of LVRS changes in FEV₁ are consistently reported. However, we found that FEV₁ was only significantly improved for 1 year. Nevertheless, the values remain better than preoperative values for at least 4 years, while without surgery a steady decline could have been expected [2]. Obviously, there is a lack of long-term results of a control group, despite the report of randomized controlled studies comparing LVRS with conservative treatment [7].

Several studies have found that after unilateral LVRS the subsequent decline in FEV₁ was smaller than after bilateral LVRS [9,10]. As we initially performed bilateral surgery it may be that, as we get a longer follow-up of patients who have undergone a unilateral procedure, the changes in FEV₁ may remain significantly elevated for a longer period. We found that the initial improvements were not significantly different between unilateral or bilateral LVRS.

The observed deterioration may also be influenced by the number of patients with α₁-antitrypsin deficiency. Comparing a group of α₁-antitrypsin deficient patients with a group with smokers-related emphysema, Cassina found that in the group of α₁-antitrypsin deficient patients the functional results returned to preoperative values 6–12 months post surgery [11]. This was in contrast to the smokers-related emphysema group where improvements were seen to last at least 2 years.

Although we do not operate on patients who are actively smoking some patients resume smoking after surgery. We have not formally assessed the number of these patients but this may also have an influence on the subsequent rate of decline in pulmonary function.

More extensive physiological measurements have been performed in trying to explain the results seen after LVRS.

Firstly there seems to be an improvement in lung and chest wall mechanics. Fessler theorized, and subsequently confirmed this theory after a study of patients who underwent LVRS, that impairment of airflow is due primarily to a mismatch between the size of the lung and the chest wall, with RV/TLC ratio being the primary determinant of this. LVRS would result in an improvement of this mismatch [12].

Several studies have concentrated on the changes seen in the respiratory muscles, in particular the diaphragm [13]. There may also be an indirect influence of LVRS on other muscles. Nutritional depletion has been reported in one third of patients with stable COPD [14]. In addition to the ineffective function of respiratory muscles due to hyperinflation, loss of fat free mass result in respiratory muscle dysfunction. In contrast, we and several other surgical series have reported an increase in weight after LVRS which could be due to increased muscle mass [15,16].

Finally, improvement in ventilation/perfusion mismatch has been suggested after LVRS. Albert reviewed the results of LVRS studies with regards of PaO₂ and PCO₂ changes [17]. Although some studies reported an increase in pO₂ other studies failed to find a significant change. Similarly, although some studies showed a decrease in pCO₂, other studies failed to reveal any changes in pCO₂. In Albert’s own study a considerable variation of the postoperative arterial blood gasses was found. In addition these changes did not show any correlation with the postoperative changes in FEV₁, TLC, RV or DLCO. We do not routinely measure arterial blood gasses postoperatively but in a preliminary study of nine patients (unpublished, Jean Peters) we found that those patients who were on home oxygen preoperatively used 86% less oxygen 6 months postoperatively.

4.2. Changes in health status

Patients with severe COPD have a worse health status than patients with milder forms of COPD [18]. However, it is well known that there is a poor correlation between respiratory physiology and health status [5]. Moy did find significant correlations between FEV₁ and the domains of social functioning, energy and physical functioning at 6 months; in our study no such correlations were found [19]. At 3 months a weak correlation was found between FEV₁ and physical functioning (r = 0.3, P = 0.01). On the other hand, if we had measured more extensively various physiological changes we might have found some stronger correlation between health status and respiratory physiology. Especially in the initial period after surgery we found no or weak correlations, this may be due to the different time course of changes in health status and respiratory physiology. Although the best improvements in respiratory physiology occur at 3 months, the delayed peak in health status occurs after 6 months. This may not be surprising; it has been shown that after a thoracotomy for lung cancer the health status in these patients needs 6 months to return to baseline values [20].

The improvements in health status do not seem to last as long as the changes in hyperinflation. We use generic health status questionnaires. These tend to be less sensitive to changes than disease-specific questionnaires. Harper reviewed the use of generic and disease-specific questionnaires in COPD patients [5]. In particular the Euroqol score was not very responsive to minor changes in health status. The chronic respiratory questionnaire (CRQ) on the other hand was found to be very responsive to changes. It may well be had we used something like the CRQ, we might have found a longer lasting benefit. We used generic
questionnaire rather than a disease-specific instrument so that we could measure the impact of LVRS on the wider aspects of health status.

As with the changes in pulmonary physiology, the patients might have experienced a continued deterioration in health status if no surgery was performed. In a 3-year follow-up of COPD patients Spencer found a linear rate of deterioration in all components of the SF 36 [18]. However the patients in this group had a better FEV$_1$ of 50% predicted than our surgical group of patients. It may be that the rate of decline in health status score might have slowed down; the SF 36 in patients with severe COPD tends to have a floor or ceiling effect in the domains of role limitation, while 35% of patients in Harper’s study scored in the lowest decile in the physical functioning domain. This would limit the ability to measure changes from baseline [5].

4.3. What determines the changes in health status after LVRS?

There is a wide variation both in the initial improvement of health status as in the subsequent decline. Although there was a significant change in the mean values of the Euroquol and SF 36 scores there is a wide variation with 20 patients not showing any improvement in Euroquol. One factor is that generic questionnaires also measure the impact of pain on health status: we found a third of patients had a worsening pain score 3 and 6 months postop [21].

Leyenson found a correlation between the degree of hyperinflation and the improvement in SIP score 3 months after LVRS [22]. However, as with our study this correlation was weak ($r = 0.45$). They found this correlated with the reduced requirements of systemic steroids and with reduced need for daily oxygen requirement, although the latter was not statistically significant.

Some patients require repeated admissions after surgery. Most frequently this is related to an exacerbation of COPD. In addition three patients were readmitted with empyema due to a persistent apical space, related to the operated lung. This may be of influence on the rate of decline in health status.

Smoking cessation does not seem to influence the change in health status. Although it has been found to reduce the decline in FEV$_1$ in patients with emphysema [23], Spencer did not found a difference in the decline in health status between patients who has stopped smoking and those who had continued smoking [18].

Some patients have a repeat course in pulmonary rehabilitation. This was either soon after surgery for those patients who did badly after surgery, in terms of a prolonged hospital stay and/or no health status benefits, or after several years for those patients who experienced a gradual decline in their health status. It is known that pulmonary rehabilitation improves health status without any changes in respiratory physiology [24].

4.4. Mortality

Since the start of our LVRS programme 17 patients out of 77 patients operated have died within 4 years of their operation (Table 1). Our overall 30-day mortality is 5%, but since we started with our unilateral VATS approach operative mortality in this group has been reduced to 2%. There are only limited numbers of prospective randomized trials of LVRS versus non-surgical treatment that do not report on long-term follow-up [7]. The surgical group did have a higher mortality but the selection criteria were subsequently modified to exclude patients who could not complete a 150 m shuttle walk distance or who had a KCO less than 30% of the predicted value. We have similar exclusion criteria. In Meyers’s 2-year follow-up study comparing patients who underwent LVRS with those patients who were selected for surgery but subsequently denied by Medicare, it was found that the non-surgical group had a lower survival rate of 64% compared to the surgical group (82%) [25].

5. Conclusion

Physiological improvements after LVRS are maintained for at least 4 years. Health status benefits, as assessed by SF 36 and Euroquol, tail off earlier. However, one should bear in mind that generic health status questionnaires are not as sensitive as disease-specific questionnaires. Although we have no comparison with a control group, in carefully selected patients surgery is likely to be better than conservative treatment.
References


