Sequential VATS lung volume reduction surgery: prolongation of benefits derived after the initial operation

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Abstract

Objective: Sequential lung volume reduction (LVR) is thought to provide additional and prolonged benefit compared with unilateral LVR. We tested this hypothesis by reviewing physiological, subjective and survival outcome data on patients who underwent sequential or unilateral LVR.

Methods: LVR was performed as a unilateral video-assisted thoracoscopic surgery (VATS) procedure, with bilateral reduction being undertaken in a staged manner. Pulmonary function data were collected prospectively. A telephone survey of patients and general practitioners was used to determine quality of life and survival.

Results: Fifty patients underwent LVR. Twenty-one patients had staged reduction of the contra-lateral lung at a median interval of 9 months. Pre-operatively, patients undergoing sequential LVR were not significantly different from patients undergoing unilateral LVR: forced expiratory volume in 1 s (FEV1) 23% predicted vs. 27% predicted, Kco 40% vs. 45%, total lung capacity (TLC) 124% vs. 121%, residual volume (RV) 217% vs. 214%, health score 34.5 vs. 30.8. After single-side LVR, both groups demonstrated equivalent and significant improvement in spirometric and subjective health scores: FEV1 +15% (P = 0.01), TLC +5% (P = 0.03), health score +80% (P < 0.01). Patients undergoing sequential reduction demonstrated no further significant improvements using either an intragroup comparison with their pre-second operation values or an intergroup comparison with the unilateral LVR patients. However, sequential LVR appeared to prolong the benefits experienced after the initial surgery by 1 year. Overall, 12 patients (24%) died during follow-up with no survival difference between the two groups (P = 0.65).

Conclusion: Sequential LVR is a safe strategy. Undertaking LVR to the second side does not further improve spirometric or subjective performance but does prolong the benefits achieved with the initial reduction. © 2003 Elsevier Science B.V. All rights reserved.

Keywords: Lung volume reduction; Video assisted thoracoscopic surgery

1. Introduction

Emphysema is a growing problem in the western world. It accounts for 18 deaths per 100 000 in England and Wales (National Statistics, Department of Health) and consumes a substantial amount of health resources due to the chronic progressive nature of this disease. Patients with end-stage emphysema have a distressingly poor quality of life due to disabling dyspnoea despite being on maximal medical therapy. Traditionally, lung transplantation was the surgical treatment of choice but the shortage of donors made its widespread uptake impractical. It is against this background that lung volume reduction emerged as a safe and effective method of symptomatic palliation and clinical improvement in a carefully selected group of patients.

Most centres favour the use of bilateral lung volume reduction (LVR) over unilateral LVR as the procedure of choice due to greater improvements in physiological status post surgery and also a reportedly lower long term mortality rate [1–3]. However, it has also been reported that the enhanced improvements in spirometric measurements following bilateral lung volume reduction surgery is associated with a more rapid rate of decline when compared with unilateral surgery [4,5]. Sequential video-assisted LVR surgery might therefore produce a more sustained improvement with less surgical trauma. The option of operating on the contra-lateral side when the physiological parameters begin to decline towards pre-operative levels remains appealing to many surgeons. On the other hand, many...
patients with severe chronic obstructive pulmonary disease (COPD) have a mortality of 50% at approximately 4 years [6,7], suggesting that unilateral surgery might suffice for many patients.

We adopted a policy of sequential video-assisted thoracoscopic surgery (VATS) unilateral lung volume reduction surgery for all our patients in the first instance. We hypothesized that sequential reduction would produce significant cumulative benefits and improvements to the patients’ spirometry, dyspnoea, health status and possibly mortality. Before proceeding to staged surgery on the contra-lateral side, patients underwent a period of stabilization, optimization and intense rehabilitation after the initial surgery to gain maximum benefit from their initial operation.

2. Methods

Over an 8-year period from 1994 to 2001, a total of 71 VAT lung volume reduction surgery operations were carried out on 50 patients. All these patients were severely incapacitated by emphysema despite being on maximal medical therapy. Patients underwent physiological, functional and anatomical assessment with regards to their suitability for surgery. Tests performed included spirometry, gas transfer, lung volumes, chest X-ray, electrocardiography, ECG, computed tomography (CT) scan, VQ scan, 6-min shuttle walking test, arterial blood gas and baseline bloods.

Selection criteria were rigorously applied and include Medical Research Council (MRC) dyspnoea index of grade 3 or 4, forced expiratory volume in 1 s (FEV\textsubscript{1}) < 40% of predicted, residual volume (RV) > 150%, total lung capacity (TLC) > 115%, FEV\textsubscript{1}/forced vital capacity (FVC) ratio < 50%. Patients also had to demonstrate anatomical areas suitable for surgical resection on high-resolution CT scan and perfusion/ventilation scintigraphy. Targets areas were identified as those with severe emphysema and ventilation/perfusion mismatch.

Patients were excluded if they had a PaCO\textsubscript{2} > 7 kPa, FEV\textsubscript{1} < 20% of predicted, single giant bullae, cor pulmonale (systolic pa > 50 mmHg), malignancy, multi-system disease and 6-minine shuttle walk distance < 100 m.

All the patients selected had severe emphysematous disease that were suitable for bilateral surgical reduction. However a policy of sequential reduction was adopted to limit the initial surgical insult as these patients are often frail and have significant co-morbidities. The side that had the worse ventilation/perfusion mismatch and anatomical destruction was operated on first. The timing of surgery on the contra-lateral side was determined by a combination of factors such as the patients’ recovery after initial surgery, the improvements made after a period of intense rehabilitation and the patients’ desire for an additional operation

All the lung volume reduction surgery was undertaken with the assistance of a video thoracoscope. Linear stapling devices (GIA endo-stapler) were employed to resect the functionless area of lung. Butress material (bovine pericardium) was tried in the early cases to decrease the incidence of air leak. However they were abandoned in the latter cases, as they did not appear to make any significant difference to the duration of air leak.

Post-operatively, patients were followed up at approximately 4, 8, 12 and 18 months in the outpatient department. They underwent spirometry, lung volumes and gas transfer testing. An audit nurse and medical student also carried out telephone surveys with regards to their perception of dyspnoea (MRC dyspnoea index; Appendix A) and quality of life at various time intervals. The patients were asked to give a subjective quality of life score ranging from 0 to 100, with 0 being the worst possible quality of life.

Data were analysed using non-parametric methods. Interval group differences between the unilateral and sequential reduction groups were analyzed using the Wilcoxon signed-rank test. Intra-group differences were analyzed using the Wilcoxon signed-rank test. Kaplan–Meier analysis with log rank comparison was used to compare mortality between the two groups. A P-value of 0.05 or less was considered to indicate a statistically significant difference.

3. Results

Fifty patients underwent LVR. Twenty-one patients had staged reduction of the contra-lateral lung at a median interval of 9 months. Pre-operatively, patients with sequential LVR showed similar characteristics to patients with unilateral LVR: FEV\textsubscript{1} 25% predicted vs. 24% predicted (P = 0.53), KC\textsubscript{o} 40% vs. 45% (P = 0.43), TLC 120% vs. 121% (P = 0.98), RV 217% vs. 214% (P = 0.72), health score 34.5 vs. 30.8 (P = 0.9), MRC 3.7 vs. 3.8 (P = 0.50) (Table 1).

Post surgery, these patients generally did well. They had

Table 1

<table>
<thead>
<tr>
<th>Statistical Parameter</th>
<th>Unilateral (n = 29)</th>
<th>Sequential (n = 21)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.2 (± 7.3)</td>
<td>60.0 (± 6.7)</td>
<td>0.111</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>13:16</td>
<td>6:15</td>
<td></td>
</tr>
<tr>
<td>FEV\textsubscript{1}</td>
<td>0.72 (± 0.27)</td>
<td>0.66 (± 0.23)</td>
<td>0.532</td>
</tr>
<tr>
<td>FVC</td>
<td>2.41 (± 0.83)</td>
<td>2.17 (± 0.68)</td>
<td>0.179</td>
</tr>
<tr>
<td>RV</td>
<td>4.50 (± 1.38)</td>
<td>4.65 (± 1.72)</td>
<td>0.723</td>
</tr>
<tr>
<td>TLC</td>
<td>7.13 (± 1.75)</td>
<td>7.16 (± 2.22)</td>
<td>0.982</td>
</tr>
<tr>
<td>KC\textsubscript{o}</td>
<td>0.66 (± 0.24)</td>
<td>0.60 (± 0.27)</td>
<td>0.431</td>
</tr>
<tr>
<td>Health score</td>
<td>30.8 (± 18.1)</td>
<td>34.5 (± 17.5)</td>
<td>0.900</td>
</tr>
<tr>
<td>MRC dyspnoea index</td>
<td>3.8 (± 0.42)</td>
<td>3.7 (± 0.48)</td>
<td>0.495</td>
</tr>
</tbody>
</table>

FEV\textsubscript{1}, forced expiratory volume in 1 s; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity; KC\textsubscript{o}, CO gas transfer coefficient; MRC, Medical Research Council.
an average air leak of 13 days (SD 10.2), and average high-dependency unit stay of 41 h (SD 26.6). Only two out of 71 procedures (2.8%) required post-operative ventilation. Mean hospital stay was 18 days (SD 14).

After the first surgery, both groups demonstrated similar improvements to their spirometric and subjective health scores which were significant on univariate testing: FEV\textsubscript{1} +15% predicted ($P < 0.01$), TLC −5% ($P = 0.02$), health score +80% ($P < 0.01$), MRC −17% ($P < 0.01$). When corrected for multiple comparisons, the effect on TLC disappeared but the effect on the other parameters remained significant at the 5% level (Table 2).

Patients undergoing sequential reduction demonstrated small but not statistically significant improvements using either an intra-group comparison with their pre-second operation values or an inter-group comparison with the unilateral LVR patients. However, there appeared to be a ‘lengthening’ of the curve by approximately 1 year with bilateral reduction before declines in physiological and subjective benefits occurred. (Fig. 1a,b).

There was no 30-day mortality. However, there were two deaths (4%) at days 43 and 64. The causes of death were due to ruptured right hemi-diaphragm in one case and primary respiratory failure in the other. Overall, 12 patients (24%) died during follow up with no survival difference between the two groups (Fig. 2; $P = 0.65$; Kaplan–Meier with log-rank comparison).

### Table 2

<table>
<thead>
<tr>
<th>Intra-group comparison following second operation in sequential reduction</th>
<th>1st op.</th>
<th>2nd op.</th>
<th>Change</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV\textsubscript{1}</td>
<td>0.79</td>
<td>0.83</td>
<td>+5.1%</td>
<td>0.39</td>
</tr>
<tr>
<td>TLC</td>
<td>6.94</td>
<td>6.8</td>
<td>−2.1%</td>
<td>0.89</td>
</tr>
<tr>
<td>MRC dyspnoea index</td>
<td>2.89</td>
<td>2.99</td>
<td>+3.5%</td>
<td>0.56</td>
</tr>
<tr>
<td>Health score</td>
<td>62</td>
<td>63</td>
<td>+1.6%</td>
<td>0.92</td>
</tr>
</tbody>
</table>

4. Discussion

It has been nearly a decade since the concept of LVR...
surgery for the treatment of COPD was re-introduced by Cooper. Since then, there has been an explosion of interest in the potential benefits of LVR surgery and many institutions have published their results in the literature. There are a few prospective randomized trials under way at the present moment and the pulmonary community is awaiting with abated breath the results of the landmark NETT (National Emphysema Treatment Trial) study which is scheduled for completion at the end of 2002. However, the debate still goes on a number of key issues which have not been addressed in these studies.

Firstly, there is still significant controversy about the relative roles of unilateral, sequential and bilateral lung volume reduction surgery. Many papers [3,14–16] have advocated bilateral lung volume reduction surgery as the treatment of choice, due to its perceived greater short term improvements in spirometry, lung volumes, dyspnoea, quality of life and survival. However, the role of sequential unilateral reduction remains unclear as there is a paucity of data in the literature. The questions that we would like answered are whether (1) sequential reduction produces cumulative benefits, (2) whether it retards the decline in physiologic parameters gained after the initial operation, and (3) whether it results in survival benefits.

Our data confirms the findings of others [1,3] in terms of spirometric improvements after unilateral LVR. We achieved a 15% improvement in FEV₁ after unilateral reduction with no 30-day mortality, minimal intensive therapy unit requirements and an average hospital stay of 18 days, mainly from prolonged air leak. However, the small improvements in FEV₁ resulted in a disproportionately large increase of 80% in the patients’ subjective quality of life score. Therefore, it is conceivable that operations aimed at maximal increase in spirometric measurements might not always correlate with a proportional increase in quality of life [9,10].

The group of patients that underwent sequential lung volume reduction on the contra-lateral side did not result in statistically significant improvements in terms of spirometry, dyspnea and quality of life. However, we noted that sequential reduction appeared to slow the decline in spirometry, dyspnea, and quality of life for almost a year as compared to the unilateral reduction group. It has been previously reported [4] that the rate of decline in FEV₁ after unilateral reduction is in the region of 100 ml/year and that the point of maximal improvement appear to be 3–6 months post initial surgery. This is in keeping with our findings. The rate of decline appears to gather speed after 1 year, with most patients returning to baseline levels at approximately 2–3 years [11,12]. Therefore, it would be logical for the timing of sequential reduction to be at the point of maximal improvements (i.e. at approximately 1 year) to attempt to retard the decline in objective physiological parameters and subjective health measures.

There was no demonstrable difference in mortality between the two groups, although the two late in-hospital deaths were from patients having their first lung volume reduction. The mortality rate of 22% at 4 years is in keeping with previous reports [13]. Therefore it would seem that a policy of sequential reduction would not result in any additional risks to the patients.

In conclusion, instead of the traditional unilateral versus bilateral lung volume reduction argument, staged sequential reduction may have the potential advantages of providing physiological and subjective improvements with slower rates of decline and therefore more long-lasting benefits. We therefore recommend that a randomized prospective study into the role of sequential LVR surgery versus bilateral LVR surgery in the treatment of COPD be carried out. It may well be that some of the patients found to be at high risk of mortality from the NETT study [8] might benefit from a less aggressive initial surgical approach and that these patients might then also potentially benefit from LVR that would otherwise be denied to them.

References


Appendix A. MRC Dyspnoea Index

Grade 1 Troubled by shortness of breath when hurrying on the level or walking up a slight hill
Grade 2 Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level
Grade 3 Stops for breath after walking about 100 yards or after a few minutes on the level
Grade 4 Too breathless to leave the house or breathless when dressing or undressing

Appendix B. Conference discussion

Professor K. Moghissi (Goole, UK): Can I ask you something for clarification. The title, when you say, ‘Staged bilateral VATS lung volume reduction: do we really need to do the second side?’ do you mean if you did the operation by VATS or by any method?

Dr Soon: Well, I think it’s probably only feasible with VATS to carry out staged LVRS.

Dr K. Al-Kattan (Riyadh, Saudi Arabia): We learned with experience that those patients have a transient benefit time and then end up with eitherredo volume reduction or transplant. Why did you choose 9 months, because if you look at the curve you drew, it’s not the time when they started to deteriorate. If you are going to do sequential, based on this, I would rather follow those patients for as long as they maintain their pulmonary function with a satisfactory, good quality of life, and then when the curve started to relate, then I would introduce the other side. So was that 9 months a random figure in the beginning or are you trying to now sort of look into it?

Dr Soon: Most papers in the literature have reported patients that had significant benefit by 4–6 months post-operation and this benefit starts to decline after a year. So our rationale is that we’re hoping to extend this period of maximum benefit after the first operation, and that’s why the median interval was 9 months, so to prolong the maximum benefits derived after operation rather than to wait for it to decline.

Dr Al-Kattan: Now, after seeing the curve, do you want to keep it 9 months or maybe keep it as long as it’s maintained?

Dr Soon: We note from the unilateral curve that it starts to decline after a year. So between 9 months to a year, that would be the time of maximum improvement anyway.

Dr E. Pompeo (Rome, Italy): Did you look at the cost-to-benefit ratio when comparing unilateral and bilateral treatment? The second question, did you apply different selection criteria for the sequential bilateral group and the unilateral group? I mean was the decision to operate bilaterally made at the beginning or afterwards?

Dr Soon: We are looking at that right now actually. There will be a paper coming.

Dr S. Guth (Mainz, Germany): If you do a unilateral procedure, which side do you prefer?

Dr Soon: Well, that is dependent on a combination of CT scan and ventilation/perfusion scanning. We will do the worst side first. So the lung that has the worst ventilation/perfusion scan and the lung that is most emphysematous on the CT scan, we will operate on that side first.

Dr Guth: Is it easy for you to decide which side is the worst?

Dr Soon: Sometimes it’s not easy. Sometimes they might appear to be pretty similar and you just have to go with your gut feeling.

Dr P. Macchiarini (Hannover, Germany): I do have some comments. It seems to me that you are comparing two different things. Patients who need only one side are different than patients who need two sides. I can accept that the patients who are looked into have the second side operation following the first one, but do you think that you should first of all compare within the group of patients that have, for instance, a profile of one single lung disease and compare it to the second lung disease?

Second, I would really like to see in your paper that you eventually do functional testing as well, not only asking the patients, because this is something that is very subjective, and if you ask the patient the same question the day after, they will probably tell you something else. So for scientific accuracy, I really urge you to use very specific questions concerning functional evaluation of the patients as well, or maybe you have.

Dr Soon: The subjective health score was just an overall view of how the patients performed after the operation. It’s just a global assessment of how they are getting on in life after their initial operation.

With regards to your first question, the patients that underwent sequential lung volume reduction as compared to the unilateral lung volume reduction had the same demographics. There was no significant difference in their pre-operative spirometry, their dyspnoea index, or their health score.