Long-term outcome of staged versus one-stage bilateral thoracoscopic reduction pneumoplasty

Eugenio Pompeo*, Tommaso Claudio Mineo for the Pulmonary Emphysema Research Group
Department of Thoracic Surgery, Tor Vergata University, Policlinico Tor Vergata, Via Oxford 81, 00133 Rome, Italy

Received 15 September 2001; received in revised form 21 December 2001; accepted 8 January 2002

Abstract

Objective: In a prospective non-randomized study, we tested the hypothesis that unilateral reduction pneumoplasty followed by completion of bilateral treatment at the reappearance of symptoms might result in more sustained improvements and better survival than one-stage bilateral treatment. Method: Fifty-nine patients undergoing bilateral thoracoscopic reduction pneumoplasty as a one-stage (n = 33) or staged (n = 26) procedure were evaluated on. The main indication for staged reduction pneumoplasty was symptom deterioration after unilateral treatment for asymmetric emphysema. Complete clinical assessment was carried out preoperatively and every 6 months postoperatively.

Results: The mean length of follow-up was 34 ± 15 months. Interval time between operations in the staged group averaged 15.2 months. There was no inter-group difference in baseline data. Peak improvements in forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC) and residual volume (RV) was significantly greater following one-stage bilateral reduction pneumoplasty. In particular, ΔFEV₁ was 0.33 ± 0.2 l in the staged group and 0.43 ± 0.2 l in the one-stage group (P = 0.007). At 48 months, FEV₁, RV and 6-min-walking-test (6MWT) were still significantly improved only in the staged group. Four-year survival was 70% in the staged group and 81% in the one-stage group (Cox–Mantel test, P = not significant).

Conclusion: Durable physiological improvements and satisfactory survival were achieved in this study for up to 4 years following either staged or one-stage bilateral reduction pneumoplasty using thoracoscopic technique. However, while peak improvements in FEV₁, FVC and RV were significantly greater following one-stage bilateral reduction, long-term improvements in FVC and 6MWT were more stable following a staged procedure. We speculate that sequential unilateral reduction pneumoplasty may reduce the mechanical stress in the lung leading to less steep postoperative deterioration of respiratory function. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Reduction pneumoplasty; Lung volume reduction surgery; Pulmonary emphysema; Thoracoscopy

1. Introduction

Reduction pneumoplasty is continuing to be actively investigated as a palliative surgical therapy for patients with end-stage emphysema [1]. Randomized studies have showed that the operation is superior to maximized medical therapy including respiratory rehabilitation for improving lung function, exercise capacity and subjective dyspnea for up to 1 year [2–4].

A range of techniques and surgical approaches are currently available for reduction pneumoplasty. It can be performed as an open or thoracoscopic procedure, unilaterally or bilaterally, and lung tissue can be excised using stapling resection or plication, laser ablation or combined techniques [5]. Current consensus is that the best technique is simultaneous bilateral stapling via median sternotomy or video-assisted thoracoscopy that produces greater functional improvement than unilateral treatment [6,7]. However, the finding that functional deterioration following bilateral reduction pneumoplasty can be steeper than that of unilateral treatment [8], called into question the optimal strategy for obtaining the most durable benefit and led to hypothesize merits for a staged unilateral approach. To date, only one study has compared staged unilateral reduction pneumoplasty versus simultaneous bilateral treatment [9]. In this comparative analysis, similar complication rates and early outcomes were found although the combination of two hospitalizations for staged procedures was longer than the stay of one-stage procedures. These results led the authors to conclude that staged reduction pneumoplasty do not offer any measurable advantages over a single hospitalization and bilateral procedure. Unfortunately, the 3-month interval between operations in the staged group negated the possi-
bility to verify whether unilateral reduction pneumoplasty followed by completion of contra-lateral treatment at the reappearance of symptoms might result in more durable benefit than simultaneous bilateral treatment.

In this prospective, non-randomized study, we analyze the long-term outcome and survival of one-stage versus staged bilateral thorascoscopic reduction pneumoplasty. In contrast with the study of Hazelrigg and coworkers [9], we preferred to delay the completion of staged bilateral treatment until the clinical benefit achieved with the first operation was lost or was considered unsatisfactory.

2. Material and methods

Between October 1995 and October 2000, 117 patients underwent thorascoscopic reduction pneumoplasty at our Institution. Among these, 59 patients undergoing bilateral reduction either as a one-stage (N = 33) or as a staged (N = 26) procedure were included in this study. Written informed consent was obtained from all patients once they were informed about the risks and potential benefits of each surgical approach. Patients selected for the operation had emphysema graded radiologically as diffuse and severe. All patients suffered of significant functional disability despite maximized medical therapy that consisted of antibiotics, inhaled and oral bronchodilators including short-acting and long-acting βₐ-agonists, ipratropium bromide, corticosteroids, and repeated attempts at physical conditioning. Eligibility criteria for operation have been described previously [4] and included post-bronchodilator forced expiratory volume in 1 s (FEV₁) less than 40% predicted, residual volume (RV) more than 180% predicted, and emphysema with heterogeneous distribution documented by high resolution computed tomography. No patient had giant bullae, clinically dominant bronchitis, bronchiectasis, asthma or systolic pulmonary artery pressure >55 mmHg.

All patients were former smokers and had quit smoking at least 4 months before the operation; no patient had homozygous α₁ antitrypsin deficiency.

Indications for unilateral and bilateral treatment, which were applied at our Institution are illustrated in Table 1.

2.1. Surgical technique

The operation was directed at reducing about 25% of the lung volume by excising functionally useless and hyperinflated lung tissue. Reduction pneumoplasty was routinely carried out by means of video-assisted thorascoscopic surgery. Extrapleural dissection was selectively carried out in patients with dense adhesions. Staple resection of target areas was performed excising a single strip of lung tissue. Suture lines were initially buttressed with bovine pericardium whereas more recently no buttress was employed on a routine basis. Patients were extubated immediately after the operation and transferred to the recovery room.

Table 1

<table>
<thead>
<tr>
<th>Indications for unilateral and staged or one-stage bilateral reduction pneumoplasty that have been prospectively applied</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unilateral reduction pneumoplasty</strong></td>
</tr>
<tr>
<td>Asymmetric emphysema</td>
</tr>
<tr>
<td>Age &gt;70 years</td>
</tr>
<tr>
<td>Associated comorbidity</td>
</tr>
<tr>
<td>Major air leak at the completion of the first reduction in planned bilateral operations</td>
</tr>
<tr>
<td><strong>Staged bilateral reduction pneumoplasty</strong></td>
</tr>
<tr>
<td>Functional deterioration after unilateral reduction</td>
</tr>
<tr>
<td>Patient unsatisfied with the clinical improvement achieved following the first reduction</td>
</tr>
<tr>
<td><strong>One-stage bilateral reduction pneumoplasty</strong></td>
</tr>
<tr>
<td>Heterogeneous and symmetric emphysema</td>
</tr>
</tbody>
</table>

2.2. Pulmonary evaluation

Timed spirometry, plethysmography and single breath diffusing capacity for carbon monoxide were routinely carried out. Reference spirometric values were those of the European Respiratory Society [10]. Exercise tolerance was assessed by the 6-min walk test (6MWT) with standardized encouragement and an oxygen supply titrated to maintain oxygen saturation above 90%. Dyspnea was rated according to the modified Medical Research Council score.

2.3. Radiologic evaluation

Inspiratory and expiratory digital chest radiographs were performed to evaluate the degree of thoracic distention and diaphragmatic excursion. High resolution computed tomography (CT) and spiral CT of the chest were performed to evaluate emphysema morphology and volumes, respectively. Single photon emission computed tomography (SPECT) perfusion imaging was also routinely carried out. Radiologic morphology of emphysema was assessed according to a previously validated visual scoring system [11]. Briefly, in each lung the severity of emphysema (SE) was estimated in six CT layers and the individual lung score (SEᵢ) was summed up to give a global score (possible scores from 12 to 48). Also, the asymmetric ratio of emphysema between the lungs was expressed by the ratio: higher SEᵢ/lower SEᵢ scores. Finally, the difference between the median SE score in the three worst sections and the three best sections was calculated to express the degree of heterogeneity.

2.4. Pulmonary rehabilitation

Patients were encouraged to participate in a preoperative outpatient pulmonary rehabilitation program with the goals of optimizing exercise endurance and pulmonary hygiene. Rehabilitation was then continued postoperatively for up to 12 weeks either on an outpatient basis or as a home-based supervised program. Subsequently, a maintenance program was not carried out on a routine basis.
2.5. Outcome assessment

Complete clinical and functional assessment was carried out postoperatively every 6 months. The postoperative measurements obtained between 3 and 6 months after surgery were taken into account to calculate the peak improvements in respiratory function and exercise capacity indexes.

2.6. Statistics

Group descriptive statistics are presented as mean ± SD. The Wilcoxon or the Mann–Whitney tests were used respectively for paired and unpaired data. Frequencies were compared with a χ²-test or Fisher’s Exact test when appropriate.

3. Results

Staged bilateral reduction pneumoplasty was carried out due to the loss of benefit achieved following unilateral treatment (15 patients), initial clinical result judged unsatisfactory by the patient himself (6 patients), and completion of bilateral treatment interrupted after the first reduction due to major air leak (5 patients). Staged bilateral reductions represented the 31% rate (26 out of 84 unilateral reductions) of the total number of unilateral reductions carried out during the study period.

Operative mortality regarded one patient in the one-stage group and none in the staged group. Non-fatal complications occurred in 13 patients in the one-stage group and in 14 patients in the staged group (9 after the first reduction and 5 after the second reduction) with no statistically significant difference. Conversely, due to the two hospitalizations required for staged bilateral procedures, the overall inhospital stay was longer in the staged group (11.7 ± 4.5 days versus 18.4 ± 4.3 days, P < 0.01).

Paired preoperative and 12, 24, 36, and 48 postoperative data were available for 24, 21, 14 and 8 patients, respectively, in the staged group; and in 26, 15, 6, and 4 patients, respectively, in the one-stage group. The mean follow-up time was 40 ± 18 months in the staged group and 29 ± 17 months in the one-stage group. There was no difference in demographics and baseline data amongst the two groups (Table 2). Assessment of radiologic morphology of emphysema revealed no difference between the staged and one-stage groups in severity of emphysema (31 ± 7 versus 34 ± 8, P = not significant) and degree of heterogeneity (1.15 ± 0.8 versus 1.25 ± 0.7, P = not significant) while a significant difference was found in the asymmetric ratio of emphysema (1.17 ± 0.2 versus 1.0 ± 0.07, P = 0.01). In the staged group, the mean interval between operations was 15.2 months. Specifically, in 13 patients the second reduction was carried out within 12 months after the first reduction whereas in the other 13, it was performed between 20 and 50 months (Fig. 1).

Table 2
Preoperative characteristics of the two study groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Staged group</th>
<th>One-stage group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>59.8 ± 8</td>
<td>60.2 ± 10</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>22.2 ± 3</td>
<td>22.8 ± 4</td>
<td>NS</td>
</tr>
<tr>
<td>O₂ use (patients)</td>
<td>10</td>
<td>16</td>
<td>NS</td>
</tr>
<tr>
<td>DI (score)</td>
<td>3.1 ± 0.7</td>
<td>3.4 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁ (l)</td>
<td>0.84 ± 0.3</td>
<td>0.83 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁ (% predicted)</td>
<td>29 ± 10</td>
<td>28 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.40 ± 0.7</td>
<td>2.35 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>FVC (% predicted)</td>
<td>65 ± 19</td>
<td>64 ± 18</td>
<td>NS</td>
</tr>
<tr>
<td>RV (l)</td>
<td>5.2 ± 0.7</td>
<td>5.4 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>RV (% predicted)</td>
<td>238 ± 39</td>
<td>247 ± 44</td>
<td>NS</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>69 ± 9</td>
<td>70 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>41 ± 4</td>
<td>41 ± 3</td>
<td>NS</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>373 ± 50</td>
<td>372 ± 69</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Legenda: BMI = body mass index; DI = dyspnea index; FEV₁ = forced expiratory volume in 1 s; FVC = forced vital capacity; RV = residual volume; PaO₂ = arterial oxygen tension; PaCO₂ = arterial carbon dioxide tension; 6MWT = six-min walking test; and NS = not significant.
4. Discussion

Prospective long-term studies, beyond 2 years after reduction pneumoplasty are very limited [12–14]. Flaherty and coworkers [14] evaluated long-term outcome of 89 patients undergoing one-stage bilateral reduction pneumoplasty. They found that at 36 months, FEV1, 6MWT and transitional dyspnea index were still significantly improved and an absolute FEV1 improvement of more than 0.2 l was observed in 29% of the patients. Gelb and coworkers [13], reported that among 26 patients undergoing one-stage bilateral thoracoscopic reduction pneumoplasty, increase above baseline for FEV1 of more than 0.2 l and/or for FVC of more than 0.4 l occurred at 3 and 5 years in 35 and 8% of all patients while decrease in subjective dyspnea of more than one grade, in 46 and 15%, respectively.

This prospective study, with no patient lost to follow-up, demonstrates that durable clinical and significant physiological improvement was achieved following either staged or one-stage bilateral reduction pneumoplasty using thoracoscopic technique. The main finding of our study is that while peak improvements in FEV1, FVC and RV was significantly greater following one-stage bilateral reduction, long-term improvements in FVC and 6MWT were more stable following a staged procedure. Also, despite in our series, FEV1, RV and subjective dyspnea, were still significantly improved at 36 months in both groups, a FEV1 improvement of more than 0.2 l occurred in 57% of patients in the staged group and only in 17% of patients in the one-stage group. This result seems in accordance with the finding of Brenner and coworkers [8] who found that FEV1 deterioration averaged 255 ml/year after bilateral reduction pneumoplasty and 107 ml/year after unilateral treatment. Such different behavior may be due to increased mechanical stress in the lung following simultaneous bilateral treatment and leading to steeper functional deterioration than following sequential unilateral reduction.

Data regarding outcome of each procedure in staged reduction pneumoplasty is scarce. Kotloff and coworkers [15] have found in seven patients undergoing staged bilateral reduction pneumoplasty that while peak improvements in FEV1, FVC and RV was significantly greater following one-stage bilateral reduction, long-term improvements in FVC and 6MWT were more stable following a staged procedure. Also, despite in our series, FEV1, RV and subjective dyspnea, were still significantly improved at 36 months in both groups, a FEV1 improvement of more than 0.2 l occurred in 57% of patients in the staged group and only in 17% of patients in the one-stage group.

<table>
<thead>
<tr>
<th>12-month result</th>
<th>Intergroup</th>
<th>36-month result</th>
<th>Intergroup</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Staged group</td>
<td>One-stage group</td>
<td>P value</td>
</tr>
<tr>
<td>DI (score)</td>
<td>2.0 ± 1.0*</td>
<td>2.0 ± 0.6*</td>
<td>0.9</td>
</tr>
<tr>
<td>FEV1 (l)</td>
<td>1.08 ± 0.4*</td>
<td>1.22 ± 0.5*</td>
<td>0.2</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.57 ± 0.6**</td>
<td>2.75 ± 0.6***</td>
<td>0.4</td>
</tr>
<tr>
<td>RV (l)</td>
<td>4.5 ± 0.8*</td>
<td>4.0 ± 1.0*</td>
<td>0.1</td>
</tr>
<tr>
<td>PaO2 (mmHg)</td>
<td>72 ± 6**</td>
<td>74 ± 7**</td>
<td>0.5</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>40 ± 3.1</td>
<td>41 ± 4.2</td>
<td>0.5</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>474 ± 89*</td>
<td>478 ± 81*</td>
<td>0.8</td>
</tr>
<tr>
<td>O2 independence (%)</td>
<td>57</td>
<td>54</td>
<td>0.7</td>
</tr>
</tbody>
</table>

* Preoperative versus postoperative result:*P < 0.0001; **P < 0.006; and ***P < 0.05.
eral reduction that the contribution of each procedure to the net improvement in FEV$_1$ was highly variable with only one patient realizing marked incremental increases following both procedures. Also they found that peak improvement in FEV$_1$ was 0.14 l after the first procedure and 0.13 after the second. Identical incremental improvements in FEV$_1$ have been reported by Hazelrigg and coworkers [9] in 50 patients undergoing staged reduction pneumoplasty with a 3–4 months interval between the operations. In our study, peak improvement in FEV$_1$ was significantly greater after the first reduction. This discrepant result may be due to differences in emphysema morphology or to the preponderance amongst first-stage operations of right-sided reductions, which in our experience are followed by greater improvements in FEV$_1$ than left-sided reductions.

Our staged group data confirm prior reports of significant improvements in 6MWT distance for up to 3 years [14]. The lack of significance of the mean improvement of 53 m observed at 36 months may be due to the limited cohort that completed the 36 months follow-up in that group. Also, it is worth of noting that overall, the number of patients who required the completion of a bilateral treatment constituted a minority (31%) of those who underwent a unilateral procedure initially. Even considering that among these latter patients, seven died, three declined to undergo a contralateral reduction despite an initial unsatisfactory result, and eight still have a relatively short follow-up, this feature suggests that, in 40 patients, a unilateral RP produced improvements, which remained sustained for up to 4 years.

One of the open issues on reduction pneumoplasty is whether it offers any survival advantage over medical treatment. In patients with chronic obstructive pulmonary disease of the emphysematous type with a FEV$_1$ of less than 0.75 l or 30%, predicted mortality is 40–50% at 3 years [16]. Differently, after reduction pneumoplasty better survival has been recently reported. Yusen and coworkers [17] noted

![Fig. 2. Changes in FEV$_1$ (A); and RV (B) in the study groups.](image1)

![Fig. 3. Changes in 6MWT (A); and dyspnea index (B) in the study groups.](image2)

![Fig. 4. Actuarial survival in the study groups (Cox-Mantel test, P = not significant).](image3)
a 3–5 years actuarial survival of 82, 72 and 62%, respectively, in 192 patients undergoing one-stage bilateral reduction pneumoplasty via median sternotomy. In a multi-institutional study, Naunheim and coworkers [12] reported 1–3 years survival of 90, 81 and 74% in 343 patients undergoing bilateral reduction pneumoplasty, and of 86, 75 and 69% in 330 patients undergoing unilateral treatment. They concluded that contrary to previous reports survival after bilateral reduction pneumoplasty was not superior to that of unilateral procedure. On the other hand, Butler and associates [18] raised a note of caution regarding the reliability of reported survival data on reduction pneumoplasty. In fact, they noted that since in most studies 5–60% of patients failed to return for follow-up, interpretation of data collected in longitudinal analyzes can be biased leading to substantial underestimation of mortality. In our study with no patient lost to follow-up, 4 years survival rate observed in the staged and one-stage group was 70 and 81%, respectively. Interestingly, these figures, did not differ significantly and are similar to those reported in the aforementioned studies.

We acknowledge some limitations in this study. Firstly, the diverse timing for the completion of bilateral treatment in the staged group, renders impossible a perfectly matched transversal comparison of outcome data. Secondly, patients were not randomly assigned to either a staged or one-stage bilateral reduction pneumoplasty and one of the morphologic indexes of emphysema, i.e. the asymmetric ratio of emphysema, differs significantly amongst the groups. However, using each patient as their own control does not systematically overestimate the magnitude of the effects of treatment as compared with those in randomized, controlled trials on the same topic [19]. Also, no difference existed in age, body mass index and baseline functional data indicating that the two groups were reasonably well matched with respect to degree of functional impairment. Finally, in this study we focused on physiologic outcome parameters and subjective dyspnea index without scrutinize quality of life that has been considered as a further primary outcome measure of reduction pneumoplasty. Significant improvements in both physical and psychosocial domains assessed by quality of life questionnaires have been reported to occur in association with improvements in respiratory function and exercise capacity [20,21]. In a randomized study, we have recently shown that improvements in quality of life following reduction pneumoplasty were greater than those following comprehensive respiratory rehabilitation [22]. Hence, we are now completing the collection of follow-up data on quality of life and we plan to provide in a forthcoming study further insights on the comparative quality of life responses of staged versus one-stage bilateral reductions.

In conclusion, durable physiological improvements and satisfactory survival were achieved in this study for up to 4 years following either staged or one-stage bilateral reduction pneumoplasty using thoracoscopic technique. However, while peak improvements in FEV\(_1\), FVC and RV were significantly greater following one-stage bilateral reduction, long-term improvements in FVC and 6MWT were more stable following a staged procedure.

We speculate that sequential unilateral reduction pneumoplasty can reduce the mechanical stress in the lung leading to less steep postoperative deterioration of respiratory function.

**Acknowledgements**

This study was supported by grant COFIN #9906274194–06 of the Ministero dell’Università e della Ricerca Scientifica e Tecnologica.

**References**


Appendix A. Pulmonary Emphysema Research Group (PERG)

Università Tor Vergata, Roma: Tommaso Claudio Mineo, MD (Principal Investigator and Coordinator); Eugenio Pompeo, MD; Vincenzo Ambrogi, MD; Benedetto Cristino, MD; Alessandro P Sabato, MD; Mario Dauri, MD; Mauro Polzoni, MD; Franco Turani, MD; Gian Luigi Serciaomi, MD; Cesidio Cipriani, MD; Paolo Rossi, MD; Lucia Senis, MD, Paola Rogliani, MD.

Ospedale ‘Cartoni’ Rocca Priora: Giuseppe Matteucci, MD; Filippo De Padova, MD.

Università ‘La Sapienza’, Roma: Italo Nofrioni, BS; Andrea Fabbri, MD. Istituto Nazionale della Nutrizione, Roma: Angela Polito, PhD. Ministero della Sanità: Natalia Magliocchetti, BS.

Ospedale Civile di Frascati: Luigi Casella, MD.

Ospedale S. Giuseppe, Marino: Franz Finocchio Torel, MD.

Ospedale ‘Calai’, Gualdo Tadino: Marcello Paci.

Ospedale Civile di Aognone: Nicola Iavicoli, MD.

Ospedale Civile di Lecce: Corrado Sorrenti, MD; Gaetano Greco, MD. Ospedale Forlanini, Roma: Salvatore Mariotta, MD.

Ospedale S. Eugenio, Roma: Gaetano Aiello, MD; Paola Codato, MD; Giudo Sciarra, MD; Nello Giovannone, MD; Gianpaolo Giovannone, MD.

Appendix B. Conference discussion

Dr G. Friedel (Gerlingen, Germany): How do you make the decision at what time you perform the second operation?

Dr Pompeo: As you have seen, there is not only one criterion. In a subgroup of the patients we reoperated on due to the loss of the benefit achieved, and normally we look at FEV1 in this respect, but there is also a subgroup of patients who received a second operation due to their specific request despite the maintenance of a certain significant benefit after a unilateral procedure. Finally, in a third subgroup, as I showed, the operation was performed as a completion of a planned bilateral operation, and I must say that we normally perform a one-stage bilateral operation in patients with heterogeneous bilateral emphysema.

Dr G. Friedel (Gerlingen, Germany): How do you make the decision at what time you perform the second operation?