Eur Respir J 1999; 13: 1170–1176
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European Respiratory Journal
ISSN 0903-1936

SERIES 'LUNG VOLUME REDUCTION SURGERY'
Edited by E. Russi and W. Weder
Number 3 in this Series

Short- and long-term functional results after lung volume reduction surgery for severe emphysema

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Short- and long-term functional results after lung volume reduction surgery for severe emphysema. H. Teschler, A.B. Thompson, G. Stamatis. ©ERS Journals Ltd 1999.
ABSTRACT: Lung volume reduction surgery (LVRS) has emerged as a surgical therapeutic intervention for advanced emphysema. Designed for the relief of dyspnoea, LVRS has been demonstrated to be efficacious in a subset of carefully selected patients. Short-term improvements in dyspnoea are accompanied by improvements in forced expiratory volume in one second ranging 13–96%. Lung volumes likewise improve, with lessening of trapped gas, residual volume, and total lung capacity. Improvements in functional status and quality-of-life measures parallel the improvements in dyspnoea and lung function. One preliminary study suggests that life expectancy after 3 yrs may be improved following LVRS.

Many questions regarding lung volume reduction surgery in terms of operative technique, selection of patients, and outcome remain to be answered. Data are available which begin to address some of these issues. Bilateral procedures have greater short-term improvements than unilateral procedures, but the rate of loss of function following the surgery may also be greater. Stapled resection of lung tissue has been demonstrated to be superior to laser ablation. In a majority of reports, outcome is superior in patients with heterogeneous distribution of their emphysema, and patients with α_1-proteinase inhibitor deficiency emphysema do less well than patients with smoker's emphysema.
Eur Respir J 1999; 13: 1170–1176.

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Keywords: Emphysema
lung volume reduction surgery
outcome
results

Received: November 16 1998
Accepted after revision November 23 1998

Supported in part by LVA Rheinprovinz and AFPR.

Chronic obstructive pulmonary disease (COPD) is characterized by expiratory flow limitation and includes a spectrum of chronic bronchitis and emphysema. Emphysema is a progressive, debilitating disease associated with high rates of morbidity and mortality. Based on recent international treatment guidelines, standard management of emphysema is limited to medical treatment, which targets airway inflammation and bronchospasm, but does not address the underlying pathophysiology [1]. Two surgical procedures are also accepted as standard care for carefully selected emphysema patients, namely bullectomy and lung transplantation. Bullectomy is limited to patients with giant bullous emphysema in an otherwise nonemphysematous lung, and lung transplantation is limited by the restricted availability of suitable donor organs, recipient age, and medical comorbidities and contra-indications for immunosuppression [2–4]. Thus, alternative therapeutic options have been sought. To this end, lung volume reduction surgery (LVRS) was reintroduced by COOPER *et al.* [5] in 1995 as a possible treatment modality for patients with advanced emphysema. This technique was initially described by BRANTIGAN and coworkers [6, 7] in the late 1950s, but did not gain general acceptance mainly because of a 16–25% operative mortality rate.

The modified technique of LVRS described by COOPER and coworkers [5, 8, 9] involves bilateral wedge resection of the most affected portions of nonbullous emphysema of both lungs (surgical "targets"), aiming to reduce lung volume by 20–30%. Multiple nonsegmental resections are performed after median sternotomy using linear staplers and reinforcing the staple lines with bovine pericardial strips [9]. The results at six months follow-up for the first 101, highly selected patients demonstrated a 51% improvement in forced expiratory volume in one second (FEV_1), as well as significant subjective improvements in dyspnoea, 6-min walk distance (6MWD), and quality of life (QoL) [5, 8]. The encouraging results demonstrating short-term palliative benefit led to rapid acceptance of this contemporary version of LVRS. A review of the literature demonstrates that the number of surgeries performed at different centres has grown exponentially both in the USA and Europe, despite numerous unanswered questions.

Previous articles in this Series: No. 1. E. Marchand, G. Gayan-Ramirez, P. De Leyn, M. Decramer. Physiological basis of improvement after lung volume reduction surgery for severe emphysema: where are we? *Eur Respir J* 1999; 13: 686–698. **No. 2.** W. Klepetko. Surgical aspects and techniques of lung volume reduction surgery for severe emphysema. *Eur Respir J* 1999; 13: 919–925.

The aim of this review is to summarize the published short- and long-term functional outcomes after LVRS, with special emphasis on changes in pulmonary function, blood gases, exercise capacity, dyspnoea, quality of life, and survival [10–44]. Attention will focus on the procedure (bilateral *versus* unilateral, laser ablation *versus* surgical stapling, video-assisted thoracoscopy (VAT) *versus* median sternotomy), the distribution of emphysema (upper *versus* lower lobe, homogeneous *versus* heterogeneous), the aetiology of emphysema (cigarette smoking *versus* α_1-proteinase inhibitor (A1PI) deficiency), and preliminary data concerning the impact of LVRS upon survival.

Bilateral *versus* unilateral LVRS

Both bilateral and unilateral resections have been used for LVRS [8, 10–43]. As summarized in tables 1 and 2, short-term functional outcomes after either unilateral or bilateral LVRS suggest that substantial improvements in advanced emphysema can be obtained.

Overall, the bilateral approach, compared to the unilateral procedure, tends to produce a greater magnitude of short-term functional outcome as reflected by a greater increase in FEV1, reduction of total lung capacity (TLC) and residual volume (RV), improvement in dyspnoea, improvement in exercise tolerance, and enhancement in QoL. On average, the improvement in the FEV1 following a bilateral procedure was 52% *versus* 28% following a unilateral procedure. Quality of life, as assessed by the Short Form (SF)-36 questionnaire was evaluated by COOPER *et al.* [8]. Six months after the surgery, 78% of the patients reported a marked improvement in QoL and 20% a moderate improvement. At the same time, 6MWD had improved by 56.7 m and remained constant up to 1 yr after surgery. Less favourable data have been reported for patients after unilateral LVRS (table 1).

Two studies directly compared unilateral to bilateral procedures [23, 26]. Neither study randomized patients to the treatment arms and different surgeons performed the procedures, limiting the strength of their conclusions. However, similar trends in outcomes are suggested. KOTLOFF *et al.* [23] reported a significant difference in FEV1, FVC, RV, and 6MWD after both unilateral and bilateral stapled LVRS. Interestingly, the magnitude of improvement following unilateral LVRS exceeded the results from bilateral stapled LVRS by more than half, suggesting that functional outcome after the unilateral procedure was disproportionate to the amount of tissue resected. The findings of BRENNER *et al.* [12], while using different surgical techniques, supported the results of KOTLOFF *et al.* [23]. The postoperative and 6 month improvements were greater for patients who underwent bilateral stapled LVRS, but the improvement seen following unilateral procedures was more than half the magnitude.

Longer-term studies have suggested that the gains in functional capacity following LVRS are not entirely stable. BRENNER *et al.* [12] calculated that over a period of 16 months, the rate of annual decline in FEV1 was significantly greater for the bilateral (0.255±0.057 $L \cdot yr^{-1}$ (mean± SEM)) than for the unilateral (0.074±0.034 $L \cdot yr^{-1}$) staple LVRS procedures.

The greater incremental improvement, but more rapid rate of decline, in patients after bilateral staple LVRS, raises an important question regarding optimal procedures. A possible approach which would take advantage of the disproportionate improvement in lung function and slower rate of decline following unilateral LVRS would be a two stage unilateral procedure in which a second, contralateral resection is performed following significant deterioration in symptoms. Future randomized, controlled studies would be necessary before adopting this approach which dictates a second major surgery.

Laser ablation *versus* stapled resection

Results to date, summarized in table 1, suggest that stapled resection *versus* laser ablation leads to superior functional outcome. In the studies with the best design [25], the improvement in FEV1 following unilateral laser ablation was 13% compared to 33% for unilateral stapled resection. Furthermore, the rate of decline in lung function following laser ablation is greater, leading to return to

Table 1. – Short-term functional outcome following unilateral lung volume reduction surgery (LVRS) using various surgical techniques

First author	[Ref.]	ΔFEV1 %	ΔVC %	ΔRV %	ΔTLC %	P_{a,O_2} mmHg	Δ6MWD m	Patients n[#]	Technique	Method
WAKABAYASHI	[37]	+30	-	-	-	-	-	22	Unilat. VAT	Laser
LITTLE	[24]	+18	+29	-11	-14	+4	-	22/55	Unilat. VAT	Laser
HAZELRIGG	[19]	+16	+14	-14	-7	+2	+58	91/141	Unilat. VAT	Laser
MCKENNA	[25]	+13	+6	-	-	-	-	26/30	Unilat. VAT	Laser
Eugene	[16]	+34	+24	-12	-20	-	-	28/28	Unilat. VAT	Laser+resection
WAKABAYASHI	[36]	+31	+21	-13	-5	+1	-	96/500	Unilat. VAT	Laser+resection
KEENAN	[20]	+27	+19	-16	-6	+1	+33	40/57	Unilat. VAT	Resection
MCKENNA	[26]	+33	+21	-	-	-	-	36/40	Unilat. VAT	Resection
MAUNHEIM	[29]	+35	+15	-33	-	+8	-	25/50	Unilat. VAT	Resection
KELLER	[21]	+31	+23	-14	-1	+9	+41	25/25	Unilat. VAT	Resection
TESCHLER	[35]	+33	-	-28	-	+5	-	12/14	Unilat. open	Resection
ARGENZIANO	[10]	+28	+29	-	-	-	+95	21/64	Unilat. open	Resection
KOTLOFF	[23]	+23	-16	-17	-	-	+45	32/32	Unilat. VAT*	Resection

FEV1: forced expiratory volume in one second; VC: vital capacity; RV: residual volume; TLC: total lung capacity; P_{a,O_2}: arterial oxygen tension; 6MWD: 6-min walk distance; Unilat.: unilateral; VAT: video-assisted thoracoscopy. #: data presented as follow-up/total number of patients; *: two by median sternotomy, 30 by VAT; Δ: different post - pre LVRS. (1 mmHg=0.133 kPa.)

Table 2. – Short-term functional outcome following bilateral lung volume reduction surgery (LVRS) using various surgical techniques

First author	[Ref.]	ΔFEV1 %	ΔVC %	ΔRV %	ΔTLC %	P_{a,O_2} mmHg	Δ6MWD m	Patients n#	Technique	Method
McKenna	[26]	+57	+12	-	-	-	-	70/79	Bilat. VAT	Resection
Keenan	[20]	+41	+17	-32	-17	+7	+41	17/35	Bilat. VAT	Resection
Bingisser	[11]	+37	-	-24	-	-	-	20/20	Bilat. VAT	Resection
Kotloff	[22]	+41	+25	-23	-	-	+83	26/40	Bilat. VAT	Resection
Stammberger	[34]	+47	+18	-25	-8	+3	+137*	42/42	Bilat. VAT	Resection
Argenziano	[10]	+70	+48	-	-	-	+289	45/68	Bilat. thoracoscopy	Resection
Cooper	[8]	+51	+26	-28	-14	+8	+56	101/137	Sternotomy	Resection
Miller	[28]	+96	+86	-	-	+8	+246	40/53	Sternotomy	Resection
Demertzis	[15]	+32	-	-27	-	-	-	-	Sternotomy	Resection
Daniel	[14]	+49	+23	-30	-14	+6	-	17/26	Sternotomy	Resection
Kotloff	[23]	+34	-18	-27	-	-	+59	86/88	Sternotomy or VATS	Resection
Stamatis	[44]	+58	-	-23	-15	+7	+220	72/74	Sternotomy or thoracoscopy	Resection

Bilat.: bilateral; For other definitions see footnote to table 1. #: data presented as follow-up/total number of patients; *: 12-min walk distance; Δ: different post - pre LVRS. (1 mmHg=0.133 kPa.)

baseline values by 12 months, and there was a rapid deterioration of the small initial improvements in dyspnoea score and 6MWD [16, 19, 24, 25, 36, 37].

VAT *versus* median sternotomy

VAT has been suggested as an alternative approach to sternotomy or thoracotomy for LVRS [38, 39]. The smaller incisions involved with VAT may lead to a more desirable cosmetic result and less postoperative pain. Functional results from studies employing VAT or open procedures are summarized in tables 1 and 2.

Keenan *et al.* [20] reported the 3 month follow-up data of 57 patients undergoing unilateral thoracoscopic stapled resection. The mean improvement in FEV1 was 27%. Sixty-three per cent of these patients showed an improvement in FEV1 >20%, but resting arterial oxygen tension (P_{a,O_2}) did not change. This magnitude of change was confirmed by several authors who reported changes in FEV1 using the unilateral approach ranging 27–35% [21, 26, 29]. A recent publication by Weder *et al.* [38], using a bilateral thoracoscopic LVRS procedure, reported in 20 patients a mean improvement of FEV1 by 42% and a mean improvement in 12-min walking distance of 40% after 3 months. A direct comparison of bilateral LVRS *via* median sternotomy and VAT was performed by Kotloff *et al.* [22] and Stamatis [44]. Functional outcomes with the two techniques were quite similar. There was no difference between the two groups in mean postoperative FEV1, forced vital capacity (FVC), RV, or 6MWD, or in the magnitude of change in these parameters at 3 months over preoperative measures. However, total in-hospital mortality was less (2.5%) for the VAT group compared to the sternotomy patients (13.8%). Although the 6 month postoperative improvement is usually superior for patients who undergo bilateral stapled LVRS, controversy still exists as to whether or not the long-term rate of decline in FEV1 is greater for median sternotomy *versus* VAT lung volume reduction [12].

The use of buttressing materials has been promoted by some investigators for decreasing the incidence of prolonged air leak after stapled LVRS [9]. Others, however, have challenged the need for expensive buttressing material. Stammberger *et al.* [33, 34] performed bilateral LVRS by VAT without buttressing material. These investigators reported no increase in prolonged air leaks when compared with data from other investigators. Their patients demonstrated a 43% gain in FEV1, which persisted for at least 1 yr. Similar improvements were reported for vital capacity, RV, TLC, and the 12-min walking distance.

Distribution of emphysema: homogeneous *versus* heterogeneous

Analysis of the group mean improvements in lung function data, walking distance, and dyspnoea score demonstrates large standard deviations for all studies, implying that at least a fraction of patients derived no benefits from LVRS. Almost 30% of patients reported by Cooper and coworkers [5, 8] and Keenan *et al.* [20] had an FEV1 change of <25% and up to 15% of patients had postoperative FEV1 values lower than the preoperative values. These results reflect limitations of the generally accepted selection criteria for LVRS. In this regard, an important issue of controversy remains whether LVRS should be performed in patients with severe emphysema characterized by homogeneous *versus* heterogeneous lung involvement.

Recently, several groups have reported that even patients with a comparatively homogeneous type of diffuse emphysema, without distinct target areas, experience short-term improvements from LVRS [28, 31, 40]. Despite the recent documentation in short-term benefits, the question of the anticipated duration of improvement of LVRS in patients with homogeneous emphysema has yet to be answered. It seems that in homogeneous emphysema, lung function peaks between 3 and 6 months after LVRS and thereafter rapidly begins to decline [40], while in patients with heterogeneous emphysema and target zones chiefly in the upper lobes, the functional status remains stable for at least 1 yr and possibly 2 yrs after surgery [9, 33, 42, 43].

These findings are consistent with the author's observations in 12 patients with homogeneous emphysema. In this series (unpublished data), the increase in FEV1 6-months after bilateral LVRS in patients with homogeneous emphysema was 27% as compared to 42% in patients with markedly heterogeneous emphysema largely of the upper lobes. The average annual decline in FEV_1 of this group was 0.28 $L \cdot yr^{-1}$ compared to 0.11 $L \cdot yr^{-1}$. Ten of the 12 patients returned to baseline within 12 months of follow-up. Based on these short-term functional results, the presence of a homogeneous pattern of destruction throughout the lung is now considered to be a contra-indication for LVRS by many groups.

α_1-Proteinase inhibitor emphysema

The most striking feature of A1PI emphysema is the predominant destruction of the lower lung zones which is seen in over 90% of those cases with an abnormal chest radiograph. This is in contrast to the upper zone or more uniformly distributed emphysematous destruction of the lung commonly observed in smoker's emphysema.

NAUNHEIM *et al.* [29] were the first to include patients with A1PI emphysema in their report, but results of this subset were not separated out. A report by CASSINA *et al.* [43] confirms significant differences in subjective and objective benefits from LVRS in subjects with A1PI emphysema compared to smoker's emphysema. Twelve consecutive patients with advanced A1PI emphysema and 18 patients with smoker's emphysema underwent bilateral LVRS. Prior to surgery, there was no statistically significant difference between the groups in regard to 6MWD, dyspnoea score and pulmonary function data except for FEV_1 (24 *versus* 31% predicted; $p<0.05$). In both groups, LVRS produced a significant short-term improvement in dyspnoea, 6MWD, pulmonary function, and respiratory mechanics. While the functional status in the smoker's group remained significantly improved over a follow-up period of 2 yrs, the benefits were short-lived in the A1PI group (fig. 1). Despite weekly A1PI replacement therapy and continued intermittent pulmonary rehabilitation, all functional measures in the A1PI group returned to baseline between 6 and 12 months postoperatively and showed further deterioration at 24 months except for the 6MWD. The observed discrepancy in terms of duration of improvement between spirometric and exercise capacity has also been described in patients undergoing resection of large bullae [2].

These findings are in agreement with data of 18 patients included in a recent study by COOPER *et al.* [8], in whom the most severe areas of destruction were located in the lower lobes. Eleven patients had A1PI emphysema, and seven did not. In these 18 patients, the mean improvement in FEV_1 was 27% and the reduction in RV 28%. These values were significantly less than for the overall series.

One explanation for the rapid functional deterioration following LVRS for A1PI emphysema could be a technical problem related to the reduction of lung volume. However, inadequate resection of lung parenchyma seems unlikely because the short-term results 3 months after surgery were satisfactory and of a similar degree to those in the smoker's group [43]. An impairment of the function of the diaphragm in the zone of apposition may be caused by progressive adhesions between the diaphragm and chest wall, possibly induced by resection of the basal lung zones adjacent to both the diaphragm and chest wall. Other possibilities are related to intrinsic differences in the lungs

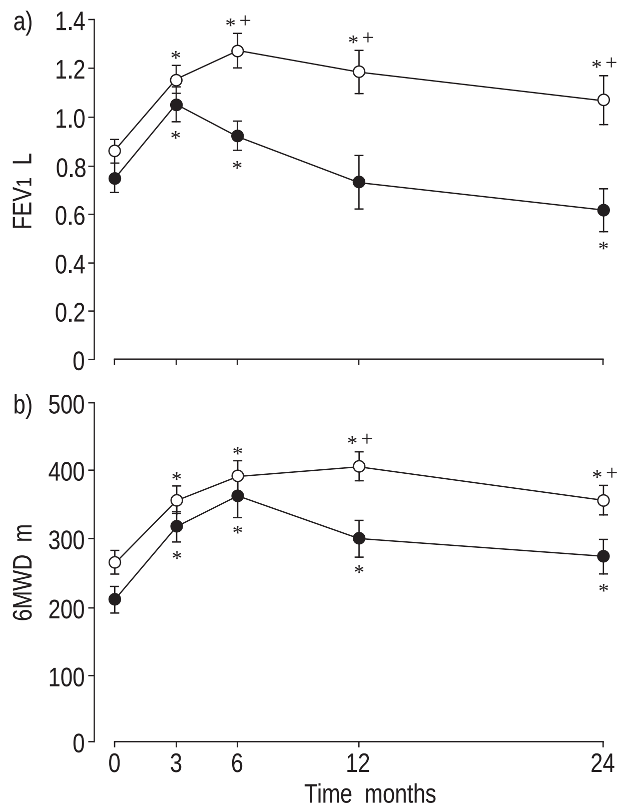

Fig. 1. – Forced expiratory volume in one second (FEV_1; a) and 6-min walk distance (6MWD; b) before and 3, 6, 12 and 24 months following bilateral lung volume reduction surgery in 12 patients with α_1-proteinase inhibitor (A1PI) emphysema (●) and 18 patients with smokers' emphysema (○). Data presented as mean±SEM. *: $p<0.05$ from baseline; $^+$: $p<0.05$ between A1PI and smokers' emphysema group. (Reproduced from [43] with permission.)

of A1PI patients. It is possible that following surgery the emphysema progresses more rapidly in A1PI patients. Moreover, there may be differences in the architecture of the connective tissue stroma in panacinar *versus* centriacinar emphysema which leads to more rapid loss of elastic recoil following LVRS.

Routine evaluation for LVRS should include consideration of the anatomical distribution of surgical targets [5, 8]. Current functional outcome data indicate that bilateral LVRS should not be undertaken in patients with A1PI emphysema who are suitable candidates for lung transplantation, for which long-term clinical outcomes are well documented [4, 29, 43]. Whether bilateral lower lobe resection might be a better surgical technique in patients with advanced A1PI emphysema, even as a temporary measure, to delay the need for transplantation, needs to be determined and requires carefully designed studies in the future.

Long-term results

The observed functional improvements seem to peak at 3–6 months following surgery and are in most studies maintained for at least 12 months. Ultimately, the value of the procedure will be judged based on long-term outcomes which are limited at the present time [13, 17, 18, 30, 33, 42, 43] (table 3).

Table 3. – Long-term outcome following lung volume reduction surgery using various surgical approaches

				Follow-up months			
Parameter	[Ref.]	Pre	Post	12	18	24	36
FEV_1 L	[33]	0.79	1.14	1.09	1.03	1.00	-
	[41]	0.83	-	1.28	-	1.27	1.04
	[13]	0.63	0.93	0.90	0.91	-	-
	[17]	0.72	1.19	1.02	0.93	0.88	-
	[30]	0.59	0.90	0.75	0.97	0.85	0.80
FEV_1 % pred	[33]	28	41	39	37	36	-
	[41]	29	-	44	-	40	36
	[13]	32	31	40	29	-	-
	[17]	33	31	40	29	-	-
	[30]	18	27	23	26	23	22
RV L	[33]	5.46	3.86	4.19	4.21	4.42	-
	[41]	5.70	-	4.25	-	4.24	4.24
	[13]	4.77	3.47	3.46	3.30	-	-
	[17]	6.00	4.4	4.7	5.2	4.9	-
	[30]	-	-	-	-	-	-
6MWD m	[33]*	500	701	705	631	623	-
	[41]	369	-	453	-	444	430
	[13]	251	387	362	398	-	-
	[17]	-	-	-	-	-	-
	[30]	-	-	-	-	-	-
P_{a,O_2} mmHg	[33]	66	71	67	62	65	-
	[41]	63	-	74	-	71	67
	[13]	-	-	-	-	-	-
	[17]	63	-	73	-	60	-
	[30]	54	61	63	58	50	56

Surgical procedures used by STAMMBERGER *et al.* [33] = bilateral video-assisted thoracoscopy (VAT), YUSEN *et al.* [41] and CORDOVA *et al.* [13] = bilateral *via* median sternotomy, GELB *et al.* [17] = sequential bilateral VAT, ROUÉ *et al.* [30] = retrospective study including unilateral right (n=7) or left (n=4) and bilateral *via* sternotomy (n=8) or thoracotomy (n=11). For definitions see footnote to table 1. *: 12-min walk distance. (1 mmHg=0.133 kPa.)

Preliminary data with 3-yr follow-up are beginning to be reported. In an abstract, YUSEN and coworkers [41, 42] reported on a subset of 25 patients from a series of COOPER [5]. Previously, they had noted a downward trend in the FEV_1 and oxygenation during the second year of surgery [41]. These trends continued during the third year. In contrast, the improvement in RV was maintained. Functional status was also maintained as reflected by a minimal change in the 6MWD. Similar findings were reported by STAMMBERGER *et al.* [33], who found during a 2-yr follow-up period maximal functional gain 3 months after bilateral VAT. Thereafter, pulmonary function slowly declined but relevant clinical and functional improvements lasted for the 2-yr observation period. A recent report by CORDOVA *et al.* [13] also suggests that after bilateral LVRS *via* median sternotomy in selected patients with advanced emphysema, improvements in lung function, exercise performance, and QoL at 3 months follow-up can be maintained for at least 12–18 months after surgery. A recent report of CASSINA *et al.* [43] included follow-up data of 18 patients with smoker's emphysema. After bilateral LVRS lung function, respiratory mechanics, as well as 6MWD and dyspnoea score remained improved for at least 1 yr (fig. 1). Trends towards decline in function and performance were seen within the following year after surgery, although most measures in the smoker's group were still significantly improved within 2 yrs compared to baseline. This is in agreement with findings by GELB *et al.* [17] who, in a 2-yr follow-up study with 12 highly selected patients, documented a variable clinical and physiological improvement in lung elastic recoil and expiratory airflow limitation. ROUÉ and colleagues [30] published their long-term retrospective results in 13 patients with severe emphysema, who underwent a modified LVRS. At 6 months, >90% of the patients had a >20% improvement above preoperative FEV_1 values and significant improvements in dyspnoea scores. After 3-yrs follow-up, those proportions were reduced to 24 and 31%, respectively. Substantial improvements in P_{a,O_2} both at rest and during exercise, particularly following bilateral LVRS, have been reported early after the operation [5, 8]. However, only limited long-term information is available on oxygen requirements. It seems, however, that only a small number of patients requiring supplemental oxygen before LVRS no longer require this at 18 months after surgery.

Caution in the interpretation and extension of these limited data is required because of the lack of control groups and the relatively small number of patients included or the high proportion of subjects lost during follow-up. In addition, highly significant group mean changes in FEV_1 or other functional outcome measures may not tell the whole story. Group mean improvements in outcome variables imply, however, that at least a fraction of patients did better after LVRS. Distribution histograms would identify whether some patients did extraordinarily well with regard to changes in functional parameters, whereas others have derived no benefit at all or may have progressively worsened with the passage of time. Future long-term studies would undoubtedly be strengthened by reporting individual outcomes as well as means.

There has been limited data published concerning the impact of LVRS upon survival. The procedure of LVRS is associated with a significant risk of mortality. Across all published reports there are no consistent differences in the mortality rates comparing bilateral VAT or thoracotomy to median sternotomy among different institutions. The published early and late mortality ranges are 0–7% and 3–17%, respectively [5, 8, 11–42]. The average mortality rate of unilateral LVRS procedures is not substantially different. A recent study by MEYERS *et al.* [27] compared survival in patients who underwent LVRS to that of patients who were screened for the operation, found to be good candidates, but who were denied the operation when Medicare stopped payment for LVRS. The 3 yr survival for the patients who received LVRS (n=65) was 82% while for the group who did not receive LVRS (n=22), the survival was 64%. This difference, however, did not reach statistical significance.

Open questions

Current short- and medium-term results of bilateral LVRS confirm an important, albeit palliative, role for this procedure especially in highly selected patients with heterogeneous smoker's emphysema with large target zones in the upper lobes of both lungs. It has been shown that lung function improves during the first few months following LVRS and appears to peak at ~6 months following surgery in the majority of patients. The short-term functional benefits following bilateral staple LVRS performed by either median sternotomy or VAT are clearly superior to improvements following unilateral and laser procedures. However, further studies will be needed to address the important observation that greater incremental improvement after bilateral LVRS may be associated with a higher rate of functional decline. This raises the question as to whether sequential unilateral procedures could potentially be more beneficial over a long period of time. Further randomized, controlled studies would clearly be necessary to answer these controversial topics.

Other questions remain unanswered regarding the impact of various treatment modalities on long-term functional results. How impaired must a patient be before they can be considered a candidate for lung volume reduction surgery? Does lung volume reduction surgery affect long-term mortality? How much care and rehabilitation do patients need after discharge from the hospital? Is repeated pulmonary rehabilitation and a regularly performed exercise training at home or in hospital of crucial importance to sustain or even maximize the initial functional and subjective benefits of lung volume reduction surgery over the long-term? Why do some patients experience favourable early results of lung volume reduction surgery but months later suddenly have a severe progression of their chronic obstructive lung disease? Is this restricted to those who start smoking again or develop recurrent acute bronchitis? Is it possible to prevent this deterioration by continuous education and smoking cessation programmes, vigorous physiotherapy, optimization of the medical treatment regimen for bronchospasm, airway inflammation, or lower respiratory tract infection?

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