Four-Year Results After Lung Volume Reduction Surgery for Emphysema

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OBJECTIVES: While the short-term results of lung volume reduction surgery are known, follow-up over several years has not often been described. The purpose of the present study was to describe results in terms of functional improvement, dyspnea, quality of life, and mortality over a 4-year period in patients with advanced emphysema.

PATIENTS AND METHODS: Fourteen successive patients were enrolled between 1996 and 2000 and studied prospectively for 4 years. All patients served as their own controls and initially received pulmonary rehabilitation and medication. Preoperative data were used as baseline and were compared to postoperative data over 4 years. The data analyzed were: functional improvement (forced expiratory volume in 1 second [FEV_1]), quality of life, dyspnea, and patient loss due to death or referral to a lung transplantation program.

RESULTS: Patients with advanced emphysema (mean FEV_1 [SD]: 22.8% [11%] of predicted) were studied. Postoperative mortality was 14%. Overall mortality (postoperative plus deaths due to respiratory insufficiency) was 28% at 1 year and 35% at 4 years. Two patients died of cancer and 5 were referred for transplantation. At 3 months, FEV_1 had improved more than 15% in 9 patients (64%); the improvement was maintained in 43% of patients at 1 year and 7% at 4 years. Improvement in dyspnea paralleled improvement in FEV_1. Overall, at 3 months mean FEV_1 had improved 41.9% (68%), transitional dyspnea index 2.7 (3), and quality of life questionnaire score 1 (0.9). Thus, improvements were considerable, but there was great variation. Preoperative mean decrease in FEV_1 was 50 (32) mL/y, and postoperative decrease 194 (70) mL/y.

CONCLUSIONS: With the inclusion criteria used, there was considerable variation in the results. Significant overall functional improvement was maintained in 50% of the patients 1 year following surgery and in 7% 4 years after surgery. Given such results, together with a surgical mortality rate of 14% and overall mortality of 28% in the first year, we believe that the criteria for using lung reduction surgery should be revised.

Key words: *Lung volume reduction. Emphysema surgery. Dyspnea. Quality of Life. Survival.*

Resultados a los 4 años de la cirugía de reducción de volumen en el enfisema

OBJETIVOS: Aunque se conocen los resultados de la cirugía de reducción de volumen a corto plazo, son pocas las series que describen el seguimiento durante varios años. El propósito de este estudio es describir los resultados, en relación con la mejoría funcional, disnea, calidad de vida y mortalidad, a lo largo de 4 años en pacientes con enfisema avanzado.

PACIENTES Y MÉTODOS: Se ha estudiado de forma prospectiva a 14 pacientes incluidos sucesivamente entre los años 1996 y 2000, y seguidos a lo largo de 4 años. Cada paciente fue su propio control y recibió inicialmente tratamiento rehabilitador y farmacológico. Se utilizaron los datos preoperatorios como basales y se compararon con los postoperatorios a lo largo de 4 años. Los datos analizados fueron: mejoría mecánica —volumen espiratorio forzado en el primer segundo (FEV_1)—, calidad de vida, disnea y pérdida del paciente, tanto por fallecimiento como por remitirlo a un programa de trasplante pulmonar.

RESULTADOS: Se incluyó a pacientes con enfisema avanzado (FEV_1: 22,8 ± 11%). La mortalidad postoperatoria fue del 14% y, unida a la originada por la insuficiencia respiratoria, del 28 y el 35% al año y a los 4 años, respectivamente. Dos pacientes murieron por cáncer y 5 se remitieron a trasplante. A los 3 meses, 9 pacientes (64%) habían mejorado más del 15% el FEV_1 y esta mejoría se mantuvo en el 43% al año y en el 7% a los 4 años. La mejoría de la disnea fue paralela a la mejoría del FEV_1. Globalmente, a los 3 meses el FEV_1 había mejorado un 41,9 ± 68%, el índice transicional de disnea un 2,7 ± 3 y la calidad de vida 1 ± 0,9, es decir, mejorías importantes pero con mucha dispersión. La caída del FEV_1 prequirúrgica fue de 50 ± 32 ml/año, y la posquirúrgica de 194 ± 70 ml/año.

CONCLUSIONES: Con los criterios de inclusión seguidos, hay una importante variabilidad en los resultados y, globalmente, se mantiene una mejoría funcional significativa en el 50% de los pacientes al año de la cirugía y del 7% a los 4 años. Estos hechos, unidos a una mortalidad operatoria del 14% y global del 28% en el primer año, hacen que se tengan que revisar los criterios de indicación de esta cirugía.

Palabras clave: *Neumorreducción. Cirugía del enfisema. Disnea. Calidad de vida. Supervivencia.*

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Introduction

Emphysema is a progressive disabling disease which, together with other types of chronic obstructive pulmonary disease, is the fourth cause of death in Spain. Until now, only preventive therapies, such as smoking cessation and lung transplantation in the final stages of the disease, have had a significant effect on outcome. Despite intensive medical treatment, patients with emphysema present progressive dyspnea, exercise limitation, and increased morbidity and mortality.[1] Lung volume reduction surgery (LVRS) has been proposed as a palliative treatment for severe emphysema.[2] The majority of studies published to date have reported short-term results, and only those of Gelb et al,[3] the National Emphysema Treatment Trial (NETT) research group,[4,5] and, more recently, Yusen et al,[6] have analyzed 4- or 5-year outcomes. In Spain, no long-term results have been published to date, suggesting that this type of surgery has not been widely accepted.

In the Hospital General Universitario, Valencia, Spain, a LVRS program was begun in 1996 and 14 patients had undergone surgery by the year 2000. The objective of this study was to describe the overall results of the program after 4 years, analyzing lung function, dyspnea, quality of life, and especially survival.

Patients and Methods

Design

Fourteen consecutive patients were enrolled between 1996 and 2000 and studied prospectively for 4 years. All patients served as their own controls after receiving pulmonary rehabilitation and medication. Preoperative data were used as baseline values and were compared with postoperative data over a 4-year period. The data analyzed were functional improvement (forced expiratory volume in 1 second [FEV_1]), quality of life, dyspnea, and patient loss due either to death or to referral for lung transplantation.

Population

The study population consisted of patients from various public health areas of the city of Valencia, corresponding to a population of 500 000 inhabitants. After signing informed consent, they underwent surgery performed by the same surgical team in a tertiary university hospital (Department of Thoracic Surgery, Hospital General Universitario, Valencia).

The criteria for inclusion were *a)* clinical, radiographic, and functional diagnosis of emphysema; *b)* breathlessness at rest or with minimal effort interfering significantly with patient's life; *c)* post-bronchodilator FEV_1 35% or less, residual volume 140% or more, and total lung capacity (determined by body plethysmography) 120% or more; *d)* moderate or severe hyperinflation shown on chest x-ray[7]; *e)* heterogeneity in the regional distribution of emphysema determined by ventilation/perfusion or computed tomography scan[8]; *f)* willingness to participate in the preoperative pulmonary rehabilitation program; and *g)* abstinence from smoking for at least 6 months.

Exclusion criteria were: *a)* age over 80 years; *b)* smoking in the previous 6 months; *c)* pulmonary hypertension (pulmonary artery systolic pressure ≥45 mm Hg and mean pulmonary artery pressure ≥35 mm Hg); *d)* severe respiratory insufficiency ($PaCO_2$ ≥55 mm Hg at rest and on room air), persisting for 1 month after treatment in a clinically stable patient; *e)* marked obesity (body mass index [BMI]≥32) or malnutrition (BMI ≤18); *f)* absence of clearly identifiable emphysematous regions; *g)* unstable heart disease; *h)* other serious diseases such as uncontrolled cancer, severe cirrhosis, advanced renal or cardiac insufficiency; *i)* respirator dependence; *j)* chronic bronchitis, bronchiectasis, or asthma; and *k)* bullous emphysema.

Surgical Techniques

After 3 months of medication and intensive pulmonary rehabilitation, patients underwent unilateral LVRS via lateral thoracotomy or bilateral LVRS via median sternotomy, according to previously described techniques.[9] Between 20% and 30% of each lung was resected and a Gore Seamguard suture (W.L. Gore and Associates, Flagstaff, AZ, USA) was used to prevent leakage.

Lung Function Tests and Quality of Life and Dyspnea Questionnaires

Lung function—including lung volumes and expiratory flows—was studied (Master Lab, Erich Jaeger, Inc, Würzburg, Germany) in accordance with American Thoracic Society guidelines.[10] Arterial blood gases were determined at rest and on room air (Chiron Diagnostic Corporation, East Walpole, MA, USA). Dyspnea was quantified on the Mahler scale[11] and quality of life according to the chronic lung disease questionnaire developed by Guyatt et al[12] and translated into Spanish by Güell et al.[13]

Surgery was considered to have been of immediate benefit to the patient when FEV_1 measured 3 months after surgery had improved more than 15% compared to immediate preoperative values.

Follow-up

All patients were followed for at least 4 years, or until death or inclusion on a waiting list for transplantation.

Results

Over a 4-year period, 14 (24%) of the patients requesting LVRS were accepted. The most frequent reasons for ruling out the procedure, accounting for 31% of exclusions, were concomitant diseases (especially chronic bronchitis and bronchiectasis), or more than 12% reversibility of the degree of obstruction with β-blockers; pachypleuritis accounted for 20% of exclusions; hyperinflation or insufficient heterogeneity, 12%; and low level of functional impairment, 12%. All patients undergoing LVRS received pulmonary rehabilitation and medication for at least 3 months before surgery, and no significant changes in FEV_1, severity of dyspnea, or quality of life were observed. LVRS was performed on a single lung via lateral

TABLE 1
Baseline (Preoperative) Values for All Patients, in Order of Date of Surgery*

Patients	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Date of surgery	July 1996	Sept. 1996	Oct. 1996	Oct. 1996	Feb. 1997	May. 1997	June 1997	Oct. 1997	Nov. 1997	Dec. 1997	Feb. 1999	June 1999	Jan. 2000	June 2000
Age, years	76	66	71	62	54	78	51	60	50	53	65	55	55	59
FEV_1	534 (23%)	450 (21%)	819 (31%)	523 (28%)	855 (25%)	625 (24%)	690 (21%)	580 (18%)	640 (19%)	542 (18%)	915 (34%)	514 (17%)	540 (19%)	520 (22%)
DH	S	S	S	M	M	S	M	S	M	S	S	S	S	S
Heterogeneity	S	M	S	M	M	S	M	M	S	S	M	S	S	M
PaO_2	55	51	94	53	62	56	54	63	86	63	66	75	53	65
$PaCO_2$	47	46	29	48	42	46	39	38	39	43	36	40	42	38
Surgery	U	U	U	U	U	U	U	U	B	U	U	B	U	B
BMI	27.4	18.5	22	18.3	29.5	20.02	27.4	18.1	21.1	21.8	23.4	26.1	19	25.8
BDI	4	1	4	0	4	2	3	2	2	3	3	3	2	4
QOL	6.9	3.4	6	3.2	7.5	4.6	6.9	3.7	5.1	5.6	7.1	7.8	6.2	6.9

*FEV_1 indicates forced expiratory volume in 1 second; DH, degree of hyperinflation; S, severe; M, moderate; U, unilateral; B, bilateral; BMI, body mass index; BDI, baseline dyspnea index; QOL, quality of life questionnaire score.

TABLE 2
Changes in Forced Expiratory Volume in 1 Second (FEV_1), Transitional Dyspnea Index, and Increase in Quality of Life 3 Months After Surgery in Patients With More Than 15% Improvement in FEV_1*

Patients	1	2	3	5	7	10	11	12	13
Increase in FEV_1%	42	63	28	21	18	43	16	259	90
TDI	+3	+2	+3	+6	+9	+3	+3	+6	+2
Increase in QOL	1.51	0.83	1.50	1.77	1.80	1.71	1.68	2.01	2.1

*TDI indicates transitional dyspnea index; QOL, quality of life questionnaire score.

TABLE 3
Changes in Forced Expiratory Volume in 1 Second (FEV_1), Transitional Dyspnea Index, and Increases in Quality of Life at 3 Months Following Surgery in Patients With Less Than 15% Improvement in FEV_1*

Patients	4†	6	8	9	14†
Increase in FEV_1%	–	9	–2	–3	–
TDI	–	+1	–1	–2	–
Increase in QOL	–	0.55	0.1	–1.53	–

*TDI indicates transitional dyspnea index; QOL, quality of life questionnaire score.
†Patients 4 and 14 died in the postoperative period.

thoracotomy in 11 patients and on both lungs via median sternotomy in 3 patients. Except in 1 patient with α_1-antitrypsin deficiency, the targeted regions were in the upper lobes. All patients are either currently being followed in our hospital or were followed until death or referral for lung transplantation.

Table 1 shows age, severity of emphysema, baseline FEV_1 and arterial blood gas values, dyspnea and quality of life scores, and the type of surgery each patient underwent in chronological order. The considerable degree of functional impairment in our patients was noteworthy, with a mean (SD) preoperative FEV_1 of 624(0.2) mL (22.8% [11%] of predicted). Five patients with FEV_1 less than 20% of predicted, classified as belonging to a high-risk group by the NETT researchers,[14] were included. It is also noteworthy that the 3 bilateral procedures were performed mainly at the end of the study period.

Of the 14 patients, 9 had experienced functional improvement at 3 months (increase in FEV_1 >15%) and 5 either showed a less than 15% increase in FEV_1, a decrease in FEV_1, or died less than 3 months after surgery. Tables 2 and 3 show variations in FEV_1, in dyspnea, and in quality of life in the 2 groups of patients. There was considerable variation in outcomes, from improvement of up to 259% in FEV_1 to worsening; from improvements in the transitional dyspnea index score (TDI) of +6 to worsening of –2; and finally, from improvements of up to 2.01 points in quality of life to worsening of 1.53 points or death. These data reflect how unpredictable the outcome of surgery was in our series.

Figure 1 shows FEV_1 values as percent of predicted, at baseline, and over the 4-year period (or until death or inclusion on a waiting list for transplantation) for the 9 patients who responded to surgery. It is noteworthy that within 6 months, all of them (with the exception of patient 12) began to show a more or less rapid decline in FEV_1, reaching preoperative values in a maximum of 2 years.

Figure 2 shows curves for survival and maintenance of improvements in FEV_1 and dyspnea. The survival curve refers to patients who are still alive and have not been referred for lung transplantation. The maintenance of improvement in dyspnea refers to a TDI above 1, and in FEV_1 to an increase of more than 15%. The slopes of the curves for maintenance of improvements in FEV_1 and in dyspnea are very similar, and reached 50% at 9

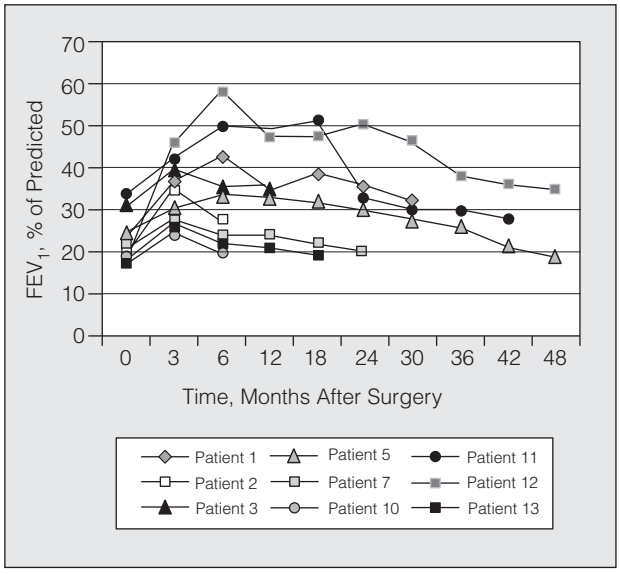

Figure 1. Changes in forced expiratory volume in 1 second (FEV_1) over the 4-year period in those patients with more than a 15% improvement in FEV_1 at 3 months.

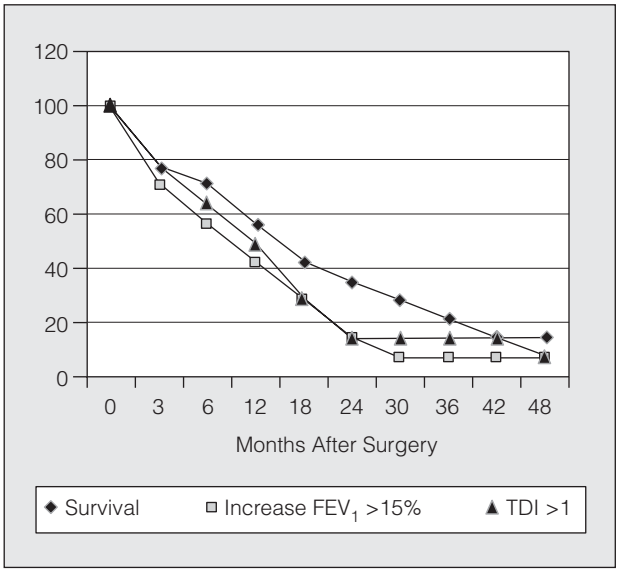

Figure 2. Percent of patients who survived and were not referred to a lung transplantation program, and percent of patients who maintained a 15% improvement in forced expiratory volume in 1 second (FEV_1) compared to preoperative values and a transitional dyspnea index (TDI) greater than 1.

months. Postoperative mortality (within the first 2 months after surgery) was 14% (2 patients), as was mortality in the first year (excluding postoperative mortality). Two patients (14%) were referred to a lung transplantation program during the first year after surgery, and 1 patient (7%) was referred at 2.5 years. Two patients died of lung cancer (1 year and 2 years after surgery, respectively) and another died in the fourth year. Functional improvement after surgery was more than 15% at 3 months (in 64% of patients), 6 months (in 50%), 12 months (in 43%), 18 months (in 28%), 30 months (in 14%), and 48 months (in 7%) compared to preoperative values. The decrease in the percentage of patients with a TDI above 1 followed a curve that was practically identical to that of the percentage of patients with a decrease in functional improvement.

For 4 patients data on lung function over the 2 years preceding surgery were available, and we were able to follow them for a period ranging from 6 months to 4 years. The preoperative decrease in FEV_1 was 50(32) mL/y, and the postoperative decrease, 194(70) mL/y (Figure 3).

According to our data, LVRS in our series led to significant functional improvement (increase in FEV_1 more than 15%) in 43% of patients at 1 year, in 14% at 2 years, and in only 7% at 4 years after surgery.

Discussion

This prospective study, with no patients lost to follow up, showed that LVRS for emphysema led to functional improvement in 43% of patients at 1 year and in only 7% at 4 years. All patients had advanced emphysema and had previously received intensive medical treatment and pulmonary rehabilitation, with no improvement. Those patients for whom preoperative lung function data were available showed a progressive decrease in FEV_1 of 50 mL/y, and consequently their prognosis was poor. Baseline data for all patients showed considerable functional impairment, with FEV_1 of 624(0.2) mL (22.8% [11%] of reference), severe dyspnea (baseline dyspnea index of 2.6), and quality of life impairment (score of 5.2).

The aim of LVRS is to alleviate symptoms (mainly dyspnea) and improve quality of life for patients with severe emphysema. By resecting nonfunctioning and hyperinflated regions of the lung, lung volume is reduced and the mechanical status of the chest wall and the respiratory muscles improved. Lung conductance and elasticity are also improved, as well as ventilation of the rest of the lung. The mechanisms by which lung

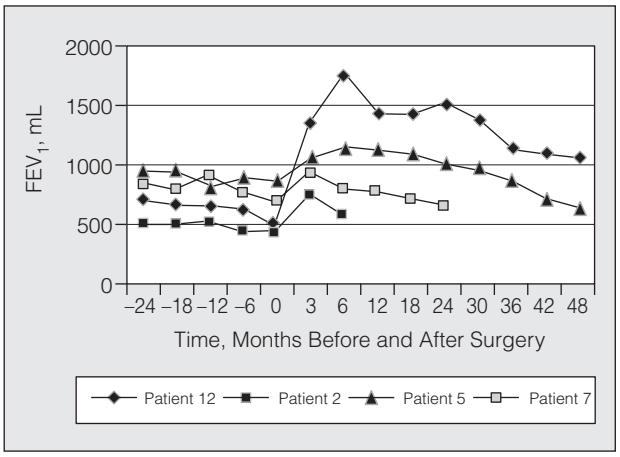

Figure 3. Forced expiratory volume in 1 second (FEV_1) in 4 patients for whom preoperative values were available.

function improves are *a)* improved elastic recoil;[15] *b)* decreased ventilation-perfusion mismatch;[16] *c)* greater respiratory muscle efficiency;[17] and *d)* improved hemodynamic status.[18]

The immediate results of this type of surgery vary according to the technique used and the population studied.[9,16] In general, postoperative mortality is reported to be 0% to 18%; increase in FEV_1, 15% to 85%; improvement in the 6-minute walk test, 15% to 104%; improvement in PaO_2, 5 to15 mm Hg, increase in lung compliance, 1.3 to 1.8 cm H_2O/L; and improvement in lung volumes (decrease in functional residual capacity, total lung capacity, and residual volume), approximately 15%.[19] While the results of the randomized prospective studies of Criner et al[20] and Geddes et al[21] contributed important data for the evaluation of this procedure, it was findings of the NETT that have given us our current outlook on LVRS.[4] In that trial, 608 patients who underwent surgery were compared to 610 who received medical treatment. Surgery was found to increase survival and the likelihood of functional improvement only in the group of patients with predominantly upper-lobe emphysema and low exercise capacity. The assessment of the cost-effectiveness of LVRS for that subgroup was left open to analysis of how well benefit is maintained over time.

In Spain, little has been published on LVRS, as the procedure has not found wide acceptance. With the exception of isolated cases[22] or the initial results of studies with a limited number of patients,[23] there have been no publications reporting first-hand experience, let alone original conclusions.

Although the patients in our series came from various public health areas providing care for 500 000 inhabitants of the city of Valencia, the number who underwent surgery was small due to the strict inclusion criteria. Only 24% of those who had applied to participate in our study were included. The criteria for inclusion in our series were those currently recommended by the majority of authors and pneumology associations at the start of the program (1996).[24] Thus, some patients with very advanced emphysema (FEV_1 ≤20%) were included. One patient (patient 9), whose emphysema was located chiefly in the lower lobes due to α_1-antitrypsin deficiency, progressed poorly and is included in the group of those not responding to surgery. Later, in 1998[25] and 1999,[26] studies were published advising against the use of LVRS in such patients. On the whole, given the advanced stage of the disease in our patients, with a mean baseline FEV_1 of 22.8% (11%), the results obtained were similar to those published by other authors.[27-29] We obtained changes in FEV_1 of 41.9% (68%), in TDI of 2.7(3), and in quality of life questionnaire score of 1(0.9). While overall results were positive, the wide variation is worthy of note. Operative mortality was 14%: 2 patients died before discharge from hospital, the first at 1 month, and the other at 2 months.

Based on the data for the first 12 patients of the series,[30] we found that patients who showed no functional improvement (Table 3) differed from those who did (Table 2) only in the severity of dyspnea, the degree of quality of life impairment, and poorer nutritional status. In other words, the greater the degree of subjective impairment (dyspnea, quality of life questionnaire score) or the poorer the nutritional status, the worse the outcome of surgery. The possible effect of decreased carbon monoxide diffusion was not studied as data were not available for all patients, due to technical difficulties (patient inability to maintain apnea or insufficient vital capacity for evaluation by the single-breath method). In general, the patients with more severe dyspnea, worse quality of life scores, and poorer nutritional status were those with more advanced emphysema, and such factors also increased surgical risk (especially nutritional status). The similarity in changes of quality of life and dyspnea scores may be explained, at least in part, by the inclusion of dyspnea as one of the parameters on the quality of life scale used. As the patients in our series generally had advanced emphysema, such data would probably be useful for establishing lower limits of viability of surgery. The NETT results, defining a group of patients at high risk of death following this type of surgery, seem to point in this direction.[14] Mortality in that study was 16% in patients with advanced emphysema (defined as FEV_1 ≤20% and a carbon monoxide diffusing capacity ≤20%), and for this reason LVRS was not advised for such patients.

All but one of the patients who had experienced functional improvement at 3 months (Figure 1) showed a mean progressive decline in FEV_1 of 194 mL/y beginning in the sixth month, reaching preoperative value in a maximum of 2 years. These results are similar to those described in other series[3] and show how short-lived the benefits of this type of surgery are. For this reason, the NETT authors[5] concluded that the cost-effectiveness of this type of surgery depends on the maintenance of benefits, even for the group with the most favorable prognosis. The more rapid decrease in FEV_1 after surgery compared to the decline before surgery is a phenomenon that has already been described.[31] It coincides with our results and can be attributed to the enlargement of the lung parenchyma remaining in the chest wall.

The survival rate in our series (Figure 2) was lower than in others,[3] but it must be remembered that our series included 2 patients who died of cancer and 5 who were referred for lung transplantation because LVRS failed. Excluding these patients, the mortality rate due to the procedure and/or respiratory insufficiency would have been 28% in the first year and 35% in the fourth. This rate is somewhat higher than in other series and is attributable to the advanced stage of the disease in our patients. Functional improvement (in FEV_1 and dyspnea) was significant in 43% of the patients at 2 years and only in 7% at 4 years, although again our

results would have been similar to those of other published studies if they had not included those patients who died of cancer.

The excellent results recently reported by Cooper et al[2] are surprising. They obtained an operative mortality rate of 4.5%, with a 93% survival rate at 1 year and 63% at 5 years, with improvements in FEV_1 (58%), dyspnea (74%), and quality of life scores (69%) 5 years after surgery. The difference compared to our series can only be explained by the more moderate functional impairment of the patients (FEV_1 of 710 mL: 25%), the use of bilateral LVRS in the majority of cases, and the greater experience of the surgical team. However, we did not see an improvement in outcomes over the course of our treatment of the 14 patients in our series; such improvement would be expected, even though it was towards the end of our study that the bilateral lung reduction procedures were performed, if we were to argue that a learning effect were relevant.

The outcomes of surgery were poor and short-lived in our series of patients with advanced emphysema who were admitted using inclusion criteria in use at the beginning of our study Only 43% maintained functional improvement at 1 year and mortality was significant at 28% in the first year. For that reason, indications for this procedure should be limited to those recommended on the basis of the aforementioned NETT findings.

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