SURVIVAL AFTER UNILATERAL VERSUS BILATERAL LUNG VOLUME REDUCTION SURGERY FOR EMPHYSEMA

D. L. Serna, MD[a]
M. Brenner, MD[a]
K. E. Osann, PhD
R. J. McKenna, Jr, MD[b]
J. C. Chen, MD[a]
R. J. Fischel, MD, PhD[b]
B. U. Jones, MD
A. F. Gelb, MD[c]
A. F. Wilson, MD, PhD[a]

Objective: **Bilateral staple lung volume reduction surgery (LVRS) immediately improves pulmonary function and dyspnea symptoms in patients with advanced heterogeneous emphysema to a greater degree than do unilateral procedures. However, the long-term outcome after these surgical procedures needs to be critically evaluated. We compare 2-year survival of patients who underwent unilateral versus bilateral video-assisted LVRS in a large cohort treated by a single surgical group.** ***Methods:*** **The cases of all 260 patients who underwent video-assisted thoracoscopic stapled LVRS from April 1994 to March 1996 were analyzed to compare results after unilateral versus bilateral procedures. Overall survival was calculated by Kaplan-Meier methods; Cox proportional hazard methods were used to adjust for patient heterogeneity and baseline differences between groups.** ***Results:*** **Overall survival at 2 years was 86.4% (95% CI 80.9%-91.8%) after bilateral LVRS versus 72.6% (95% CI 64.2%-81.2%) after unilateral LVRS (*P* = .001 for overall survival comparison). Improved survival after bilateral LVRS was seen among high- and low-risk subgroups as well. Average follow-up time was 28.5 months (range, 6 days to 46.6 months) for the bilateral LVRS group and 29.3 months (range, 6 days to 45.0 months) for the unilateral LVRS patients.** ***Conclusions:*** **Comparison of unilateral versus bilateral thoracoscopic LVRS procedures for the treatment of emphysema reveals that bilateral LVRS by video-assisted thoracoscopy resulted in better overall survival at 2-year follow-up than did unilateral LVRS. This survival study, together with other studies demonstrating improved lung function after bilateral LVRS, suggests that bilateral surgery appears to be the procedure of choice for patients undergoing LVRS for most eligible patients with severe heterogeneous emphysema. (J Thorac Cardiovasc Surg 1999;118:1101-9)**

Multiple studies have demonstrated that lung volume reduction surgery (LVRS) provides immediate improvement of pulmonary function and dyspnea symptoms in selected patients with severe heterogeneous emphysema. However, limited data exist regarding long-term outcome after LVRS. Our group and others, have shown that bilateral LVRS produces greater short-term improvement in FEV_1 than do unilateral staple or Nd:YAG volume reduction procedures.[1,2] Therefore, we have adopted bilateral thoracoscopic staple LVRS as our standard approach to bilateral heterogeneous, severe emphysema. However, the ultimate value of bilateral versus unilateral LVRS will depend on the long-term results.

Longer term survival outcomes after unilateral and bilateral LVRS procedures have not been reported. The purpose of this study was to compare 2-year mortality between bilateral and unilateral thoracoscopic LVRS in a large group of patients operated on by a single group of thoracic surgeons at one medical center.

From Divisions of Pulmonary Medicine, Cardiothoracic Surgery, and Beckman Laser Institute,[a] and UC Irvine Medical Center, Orange, and Chapman Lung Center,[b] Orange and Lakewood Regional Medical Center,[c] Lakewood, Calif.

Supported in part by DOE Grant DE-F603-91ER61227, ALA Grant CI-030-N, CTRDRP Grant 6RT-0158, ACS Faculty Grant.

Presented as a poster at the American College of Chest Physicians, 1998, Toronto, Ontario, Canada.

Received for publication Oct 15, 1998; revisions requested Feb 5, 1999; revisions received Aug 1, 1999; accepted for publication Aug 17, 1999.

Address for reprints: Matt Brenner, MD, Pulmonary and Critical Care Medicine Division, UC Irvine Medical Center, Orange, CA 92668 (E-mail: mbrenner@bli.uci.edu).

0022-5223/99 $8.00 + 0 **12/1/102290**

Table I. *Means and standard error of the mean for baseline characteristics of all study patients*

Characteristic	*Bilateral VATS**	*Unilateral VATS**	P *value*
No.	159	110	
Age	67.14 ± 6.73	68.39 ± 7.51	.16
FVC	2.00 ± 0.73	2.11 ± 0.71	.17
FEV_1	0.64 ± 0.25	0.70 ± 0.29	.13
RV	4.54 ± 1.41	4.80 ± 1.21	.13
TLC	7.15 ± 1.74	7.54 ± 1.42	.08
RAW	5.37 ± 2.22	4.91 ± 1.93	.12
RV/TLC	0.67 ± 0.10	0.72 ± 0.30	.10
DLCO	5.31 ± 2.84	4.75 ± 2.63	.07
Po_2†	64.80 ± 12.43	60.40 ± 12.30	.008
Pco_2	43.17 ± 7.33	44.81 ± 9.17	.01

FVC, Forced vital capacity; *FEV_1,* forced expiratory volume in 1 second; *RV,* residual volume; *TLC,* total lung capacity; *RAW,* airway resistance; *DLCO,* diffusing capacity for carbon monoxide.

* The pulmonary function tests are plethysmographic. Values are expressed as mean ± SD.

† Significant value between unilateral and bilateral VATS, $P \leq .05$.

Methods

Methods for patient selection, preoperative analysis, surgical procedures, and follow-up studies for patients undergoing bilateral and unilateral thoracoscopic staple LVRS in this clinical program have been previously described.[1,2]

All patients who underwent unilateral or bilateral thoracoscopic staple LVRS at Chapman Medical Center from April 1994 to March 1996 were included in this evaluation. Baseline characteristics of all study patients appear in Table I. Patients underwent baseline complete pulmonary function testing, including: spirometry, gas exchange measures (room air arterial blood gas measurement, DLCO), plethysmography, and gas dilution lung volumes. Maximum inspiratory and expiratory flow volume curves and thoracic gas volume were measured in a plethysmograph (Collins/Cybermedic Classic TCI and Body Plethysmograph; Warren E. Collins Inc, Braintree, Mass) and compared with predicted values, as previously described.[1,3] All patients underwent LVRS at Chapman Medical Center by one or both of 2 thoracic surgeons in the research group (R.J.M., R.J.F.). No procedures were performed at any other center in this protocol.

Repeated pulmonary function studies were requested from patients 3 months postoperatively, at 6 months, and at approximately 6-month intervals thereafter. Whenever possible, repeated spirometry was performed at least once at Chapman Medical Center within 3 months of surgery, but subsequent spirometry data were obtained from the referring site. Informed consent for surgery and preoperative evaluation was obtained from all patients. Despite maximal medical management, all patients were markedly symptomatic. Chest radiographs showed hyperexpansion of the thorax, with flattening or inversion of the diaphragms.

Contraindications to surgery included current cigarette smoking, age greater than 80 years, severe cardiac disease (congestive heart failure, significant coronary or valvular disease), history of cancer within the last 5 years, ventilator dependency, or prior thoracic surgery. Relative contraindications included age older than 75 years, severe anxiety, severe depression, or CO_2 retention with resting $PaCO_2$ higher than 55 mm Hg.[1,3]

To be accepted for the procedure, the patient had to have a pattern of emphysema, seen on computed tomography (CT), that was severe and heterogeneous. Radionuclide lung perfusion scans were also used to confirm the heterogeneous pattern of emphysema.[1,3]

Thoracoscopic LVRS operative methods. Operative procedures for thoracoscopic staple LVRS have been described previously.[1,2] All patients underwent video-assisted thoracic surgery while under paralyzed (pipecuronium) general anesthesia (isoflurane), with use of a left-sided double-lumen tube (Mallincrodt Anesthesia, St Louis, Mo).

Procedures were performed by one surgical group (R.J.M., R.J.F., M.B.) with the patient in the lateral decubitus position. The trocar and thoracoscope were placed through the 10th intercostal space in the posterior axillary line. Three additional 1- to 2-cm incisions were made for standard instruments. Patients undergoing bilateral thoracoscopic procedures were turned to the contralateral decubitus position for separate sterile preparation and draping after the procedure on the initial side was completed.

Preoperative lung CT scans and ventilation-perfusion ($\dot{V}/\dot{Q}$) scans were used to identify areas of dysfunctional or degenerated lung targeted for resection with the staples.[1,2] Ring forceps were used to manipulate the lung into a 60-mm endoscopic stapler (ELC 60; Ethicon, Cincinnati, Ohio) with bovine pericardium (Peristrips; Biovascular, Saint Paul, Minn) or bovine collagen matrix (Instat; Johnson and Johnson, New Brunswick, NJ) used to buttress the staples. The staples were fired an average of 15 times for bilateral operations. Typically, approximately half of the upper lobe was resected in patients with upper lobe disease.

Survival. Survival status was assessed for all patients by contacting them directly or their referring physicians between March and June 1998. The latest date of known survival was recorded, and the date and cause of death (if known) were recorded for patients who had died. Six patients had undergone a second LVRS procedure. These patients' records were coded for their first surgical procedure with all available follow-up in accordance with "intent-to-treat" methods. Patients with survival beyond Feb 28, 1998, were censored as of Feb 28, 1998, for purposes of survival analysis.

Response assessment. To be included in the follow-up evaluation analyses of pulmonary function in this study, patients were required to have follow-up pulmonary function testing at 2 years ± 6 months after surgery. To be included in the follow-up evaluation analyses of mortality in this study, patients were required to have had their surgical procedure between the period of April 1994 and March 1996. All study patients had known mortality or survival information.

Statistical analysis. Baseline characteristics for patients undergoing unilateral or bilateral surgery are described in

terms of means and standard error of the mean. Comparison of differences between patients before and after surgery is determined by 2-tailed paired *t* tests. Differences between surgery groups at baseline are tested by 2-tailed *t* tests for continuous variables or chi-square tests for categorical variables. Overall survival is calculated by using the Kaplan-Meier survival analysis. Differences between survival curves for unilateral and bilateral surgery are tested using the log-rank test. To examine the influence of potential confounders and control for baseline differences in pulmonary function, we used stratified Kaplan-Meier methods. Patients were stratified into 2 groups by baseline characteristics, using the cut points forced expiratory volume in 1 second (FEV_1; 0.50 L/s), PaO_2 (55 mm Hg), age (70 years), forced vital capacity (FVC; 1.5 L), total lung capacity (TLC; 8.5 L), residual volume (RV; 5.5 L), and surgery date (eg, May 1, 1995). Cut points for FEV_1, PaO_2, and age were chosen according to an earlier published definition of high-risk subgroups.[4] Cut points for FVC, TLC, and RV were arbitrarily defined as the limit of the highest risk quartile after finding that the cutoffs for FEV_1 and PaO_2 approximated the lower limits of the highest risk quartile. Differences between the bilateral and unilateral surgery groups after stratification was taken into account were tested with the log-rank test.

In addition, we used Cox proportional hazards methods to test the significance of differences between surgery groups after simultaneously adjusting for baseline differences between patients. To adjust for patient heterogeneity and baseline differences between the surgical groups, we calculated a propensity score to be included as a covariant in the Cox regression analysis.[5] The propensity score, calculated by logistic regression with "surgery type" used as the dependent variable, represents the likelihood for a patient with specified baseline values to have unilateral, versus bilateral, surgery. Independent variables included in the estimation of propensity scores are age, sex, FEV_1, PaO_2, FVC, TLC, RV, and surgery date. For 33 patients with missing data, data were imputed by regressing that variable against all variables with acceptable values for that individual in a stepwise procedure. Three patients had insufficient data for imputation. Covariables included in the Cox regression analysis are propensity score, age, sex, FEV_1, PaO_2, FVC, TLC, RV, and surgery date. Analyses were conducted by using the Systat 7.0 for Windows and BMDP 7.0 statistical software packages (SPSS Inc, Chicago, Ill).

Rehabilitation. Patients did not receive preoperative rehabilitation at Chapman Medical Center before undergoing LVRS. All patients underwent a regimen of pulmonary rehabilitation at Chapman Medical Center immediately following hospital discharge after surgery. The rehabilitation consists of a 10-day outpatient regimen involving a multidisciplinary approach with nursing, respiratory, dietary, nutritional, psychosocial, occupational, and physical therapy. Patient education, physical exercise (walking, flexibility, and strengthening), self-monitoring, breathing retraining, and bronchial hygiene instruction are included.

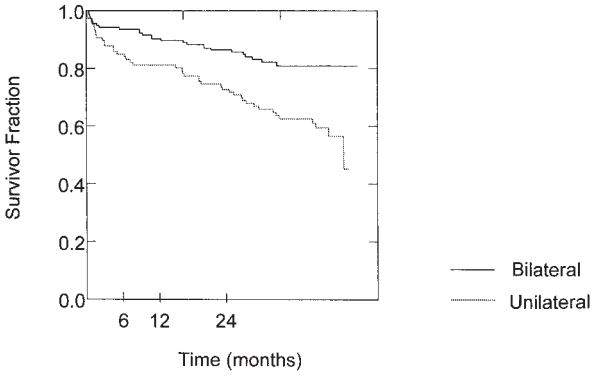


Fig 1. Overall Kaplan-Meier survival analysis 2 years after surgery, unilateral versus bilateral LVRS.

Results

Composite results in all patients. A total of 260 patients underwent LVRS procedures in this program during the analysis interval: 106 patients underwent unilateral thoracoscopic staple LVRS and 154 patients bilateral thoracoscopic staple LVRS. In addition, 6 patients had a second LVRS procedure. Four patients initially underwent unilateral LVRS followed by a second unilateral surgery. One patient underwent bilateral LVRS after an initial unilateral procedure. One patient underwent bilateral surgery followed by a second bilateral LVRS. Patients who underwent a second LVRS procedure were analyzed according to the initial intent-to-treat and were classified by the first surgery only.

Unilateral thoracoscopic staple LVRS–treated patients. Overall survival at 1 and 2 years was 81.1% (95% CI 73.6%-88.6%) and 72.6% (95% CI 64.2%-81.2%), respectively, after unilateral thoracoscopic LVRS (Fig 1, Table II).

Bilateral thoracoscopic staple LVRS–treated patients. Overall survival at 1 and 2 years was 90.3% (95% CI 85.6%-94.9%) and 86.4% (95% CI 80.9%-91.8%), respectively, after bilateral thoracoscopic LVRS (P = .001 for overall survival comparison between unilateral and thoracoscopic LVRS).

Average follow-up time was 28.5 months (range, 6 days to 46.6 months) for the bilateral LVRS group and 29.3 months (range, 6 days to 45.0 months) for the unilateral patients. During this period, 27% (29/106) of unilaterally treated study patients died of respiratory failure (Table III). In comparison, 6% (10/154) of bilaterally treated patients died of respiratory failure.

Risk subgroup analysis. Previously identified risk factors for poor 2-year survival after bilateral LVRS[6] (age > 70 years, $PaO_2 \leq 55$ mm Hg, $FEV_1 \leq 0.5$) were

Table II. *Overall survival*

	6 mo 182 d	*12 mo 365 d*	*18 mo 547 d*	*24 mo 730 d*	*36 mo 1095 d*
Unilateral LVRS					
Cumulative survival	0.85	0.81	0.77	0.73	0.63
95% CI	0.78-0.92	0.74-0.89	0.69-0.85	0.64-0.81	0.53-0.72
Cumulative deaths	16	20	24	29	39
Remaining at risk	90	86	82	77	48
Bilateral LVRS					
Cumulative survival	0.94	0.9	0.88	0.86	0.81
95% CI	0.90-0.97	0.86-0.95	0.83-0.93	0.81-0.92	0.74-0.88
Cumulative deaths	10	15	18	21	27
Remaining at risk	144	139	136	123	22

Table III. *Mortality of all patients*

	Unilaterally treated patients (%)			*Bilaterally treated patients (%)*		
Cause of death	*<30 d*	*>30 d*	*Overall*	*<30 d*	*>30 d*	*Overall*
Respiratory failure	3	26	29	2	8	10
Pneumonia	0	2	2	0	3	3
Pneumonitis	0	0	0	0	1	1
Pulmonary embolism	0	0	0	0	1	1
Pulmonary bleb rupture	1	1	2	0	0	0
Cardiac arrest or MI	1	3	4	1	3	4
Congestive heart failure	0	1	1	0	1	1
AAA	0	1	1	0	1	1
Acute abodomen	0	0	0	1	0	1
Cancer	0	1	1	0	1	1
Colitis	0	1	1	0	0	0
Unspecified infection	0	0	0	0	1	1
Amyotrophic lateral sclerosis	0	0	0	0	1	1
Head trauma	0	0	0	0	1	1
Unknown	0	1	1	0	1	1

MI, Myocardial infarction; *AAA*, abdominal aortic aneurysm.

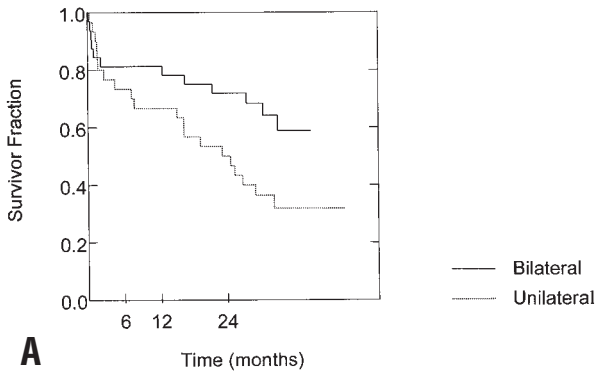
Table IV. *$Pa_{O_2} \leq 55$ mm Hg (torr)*

	6 mo 182 d	*12 mo 365 d*	*18 mo 547 d*	*24 mo 730 d*	*36 mo 1095 d*
Unilateral LVRS					
Cumulative survival	0.73	0.67	0.57	0.5	0.32
95% CI	0.58-0.89	0.50-0.84	0.39-0.74	0.32-0.68	0.15-0.49
Cumulative deaths	8	10	13	15	20
Remaining at risk	22	20	17	15	5
Bilateral LVRS					
Cumulative survival	0.81	0.81	0.75	0.72	0.59
95% CI	0.68-0.95	0.68-0.95	0.60-0.90	0.56-0.88	0.40-0.77
Cumulative deaths	6	6	8	9	12
Remaining at risk	26	26	24	23	3

examined for their effects on outcome in unilateral, compared with bilateral, LVRS patients.

Thirty-two percent (30/94) of patients who underwent unilateral LVRS had baseline hypoxemia defined as $Pa_{O_2} \leq 55$ mm Hg, compared with 21% (32/149) of patients who underwent bilateral LVRS. When stratified by baseline Pa_{O_2}, survival was better for bilateral LVRS patients (log-rank test, $P = .02$; Fig 2, Tables IV and V).

Forty-three percent (45/104) of patients who underwent unilateral LVRS were more than 70 years of age, compared with 32% (50/154) of bilateral LVRS



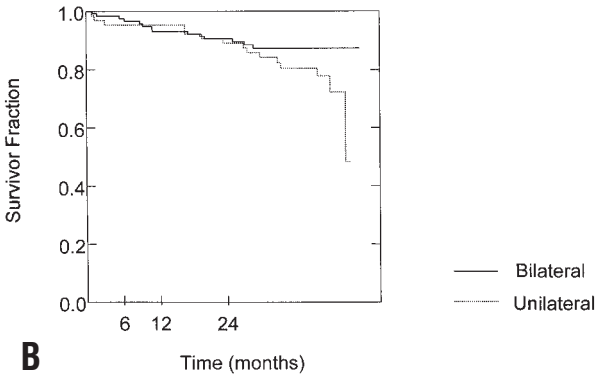
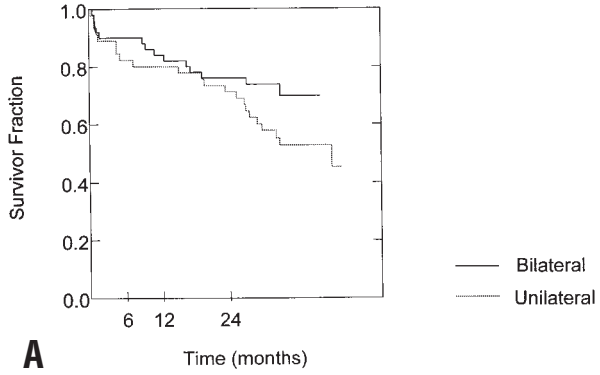


Fig 2. A, Risk subgroup analysis, all study patients with Pa_{O_2} ≤ 55 mm Hg, unilateral versus bilateral LVRS. **B,** Risk subgroup analysis, all study patients with Pa_{O_2} > 55 mm Hg, unilateral versus bilateral LVRS.



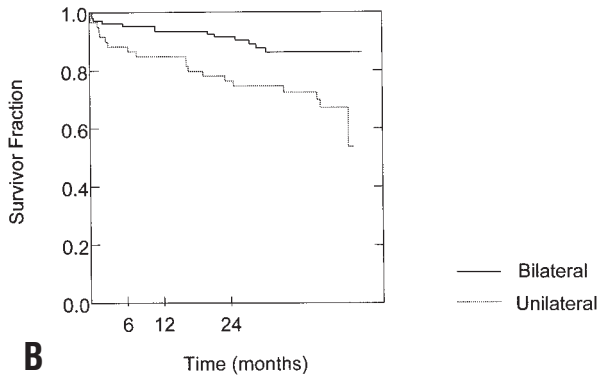


Fig 3. A, Risk subgroup analysis, all study patients over 70 years old at time of surgery, unilateral versus bilateral LVRS. **B,** Risk subgroup analysis, all study patients 70 years old or younger at time of surgery, unilateral versus bilateral LVRS.

Table V. *Pa_{O_2} > 55 mm Hg (torr)*

	6 mo 182 d	*12 mo 365 d*	*18 mo 547 d*	*24 mo 730 d*	*36 mo 1095 d*
Unilateral LVRS					
Cumulative survival	0.95	0.94	0.92	0.89	0.8
95% CI	0.90-1.00	0.88-1.00	0.86-0.99	0.81-0.97	0.70-0.90
Cumulative deaths	3	4	5	7	12
Remaining at risk	61	60	59	57	39
Bilateral LVRS					
Cumulative survival	0.97	0.93	0.92	0.91	0.87
95% CI	0.95-1.00	0.88-0.98	0.87-0.97	0.85-0.96	0.81-0.94
Cumulative deaths	3	8	9	11	14
Remaining at risk	113	108	107	95	18

patients. Stratified Kaplan-Meier analysis showed a significant difference in survival after stratifying for age, with better survival for bilateral LVRS patients (P = .007, Fig 3, Tables VI and VII).

Twenty-four percent (24/102) of bilateral LVRS had preoperative FEV_1 under 0.5 L/s, compared with 32% (49/154) of patients who underwent bilateral LVRS. After stratification for baseline FEV_1, patients who underwent bilateral LVRS had significantly better survival than did patients who had unilateral LVRS (P = .003, Fig 4, Tables VIII and IX).

For gender subgroup (female, male) analysis, bilateral surgery demonstrated better survival compared with unilateral (P = .004). For TLC subgroup analysis (>8.5 L, ≤8.5 L), bilateral surgery demonstrated better survival than unilateral LVRS (P = .01). When patients

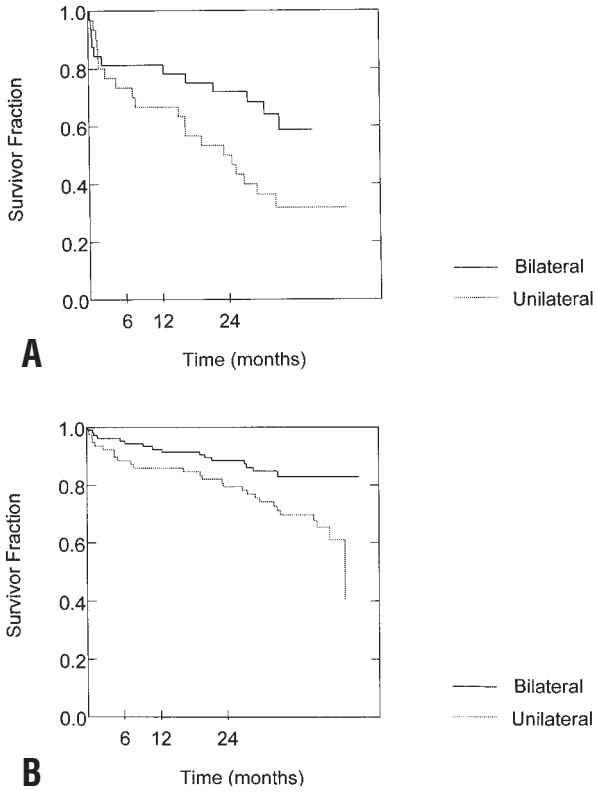


Fig 4. A, Risk subgroup analysis, all study patients with $FEV_1 \leq 0.5$ L/s, unilateral versus bilateral LVRS. **B,** Risk subgroup analysis, all study patients with $FEV_1 > 0.5$, unilateral versus bilateral LVRS.

were stratified by baseline RV (>5.5 L, ≤5.5 L), patients who received bilateral LVRS again had better survival than patients who received unilateral surgery ($P = .005$). For the date of surgery (after May 1, 1995), stratified Kaplan-Meier analysis showed a significant advantage for bilateral surgery ($P = .002$).

In an attempt to simultaneously control for patient heterogeneity and any baseline differences between the two surgery groups, we analyzed data using the Cox regression analysis. After adjusting for all covariables (propensity score, age, gender, FEV_1, Pao_2, FVC, TLC, RV, and surgery date) in a proportional hazards model, the hazard ratio for unilateral LVRS compared with bilateral surgery was 2.00 ($P = .05$, 95% CI 1.02-3.92). No significant interactions existed between surgery type and the other risk factors in the model.

Baseline characteristics and lung function studies. Baseline characteristics revealed statistically significant differences between patients who underwent unilateral and patients who underwent bilateral procedures in Pao_2 (Table I). In general, patients who underwent unilateral procedures did not have more severe disease than those who underwent bilateral procedures.

Lung function. Follow-up pulmonary function results are available on 108 patients (40% of total population) at 2 years ± 6 months after the date of the operation. Sixty-nine of these patients had bilateral thoracoscopic staple LVRS, whereas 39 had unilateral thoracoscopic staple LVRS.

Two years after unilateral LVRS, mean improvement in FEV_1 was 77 mL, while mean improvement in FVC was 301 mL above preoperative levels. Mean FEV_1 was 731 mL preoperatively and rose to 808 mL 2 years after the operation. Mean FVC was 2.232 L preoperatively and rose to 2.533 L 2 years after the operation. Average follow-up time after unilateral LVRS until pulmonary function testing was 24.6 months.

Two years after bilateral LVRS, mean improvement in FEV_1 was 274 mL, while mean improvement in FVC was 711 mL above preoperative levels. Mean FEV_1 was 666 mL preoperatively and rose to 940 mL 2 years after the operation. Mean FVC was 2.040 L preoperatively and rose to 2.751 L 2 years after the operation. Average follow-up time after bilateral LVRS until pulmonary function testing was 23.2 months.

Discussion

Bilateral staple LVRS has been shown in numerous studies to immediately improve objective pulmonary function and improve subjective dyspnea.[1,3,4,7-12] Bilateral staple LVRS appears superior to unilateral staple LVRS in achieving these benefits in short-term follow-up, with similar operative morbidity and mortality.[7-11,13-20] Longer term outcome information is needed before definitive conclusions can be drawn regarding the overall value of unilateral versus bilateral LVRS in severe emphysema patients.

This study shows significant and substantially greater survival at an average of more than 2 years' follow-up of patients who underwent bilateral, compared with unilateral, LVRS. Two-year mortality was 13.6% for bilateral LVRS patients and 27.4% for the unilaterally treated patients ($P = .001$). There are a number of possible reasons for this apparently greater survival after bilateral procedures. Pulmonary function improvements are greater after bilateral LVRS, compared with unilateral procedures.[1,7-10,17] The effects of greater improvements in oxygenation, lung, diaphragmatic, chest wall, dynamic hyperinflation, and respiratory muscle function,[2,11,21-25] or all of the above, may contribute to superior survival after bilateral LVRS (Table II).

FEV_1 has been shown to correlate with survival in patients with emphysema in previous studies.[21,22] Patients undergoing bilateral staple LVRS demonstrate

Table VI. *Age > 70 years*

	6 mo 182 d	*12 mo 365 d*	*18 mo 547 d*	*24 mo 730 d*	*36 mo 1095 d*
Unilateral LVRS					
Cumulative survival	0.82	0.80	0.78	0.71	0.53
95% CI	0.71-0.93	0.68-0.92	0.66-0.90	0.58-0.84	0.38-0.68
Cumulative deaths	8	9	10	13	21
Remaining at risk	37	36	35	32	17
Bilateral LVRS					
Cumulative survival	0.9	0.84	0.78	0.76	0.7
95% CI	0.82-0.98	0.74-0.94	0.67-0.90	0.64-0.88	0.56-0.84
Cumulative deaths	5	8	11	12	14
Remaining at risk	45	42	39	37	5

Table VII. *Age ≤ 70 years*

	6 mo 182 d	*12 mo 365 d*	*18 mo 547 d*	*24 mo 730 d*	*36 mo 1095 d*
Unilateral LVRS					
Cumulative survival	0.88	0.85	0.8	0.76	0.72
95% CI	0.80-0.96	0.76-0.94	0.69-0.90	0.65-0.87	0.61-0.84
Cumulative deaths	7	9	12	14	16
Remaining at risk	52	50	47	45	31
Bilateral LVRS					
Cumulative survival	0.96	0.93	0.92	0.91	0.86
95% CI	0.91-0.99	0.88-0.98	0.87-0.97	0.86-0.97	0.79-0.93
Cumulative deaths	5	7	8	9	13
Remaining at risk	99	97	96	86	17

Table VIII. *FEV_1 ≤ 0.5 L/s*

	6 mo 182 d	*12 mo 365 d*	*18 mo 547 d*	*24 mo 730 d*	*36 mo 1095 d*
Unilateral LVRS					
Cumulative survival	0.83	0.79	0.67	0.63	0.5
95% CI	0.68-0.98	0.63-0.95	0.48-0.86	0.43-0.82	0.30-0.70
Cumulative deaths	4	5	8	9	12
Remaining at risk	20	19	16	15	9
Bilateral LVRS					
Cumulative survival	0.90	0.86	0.82	0.82	0.76
95% CI	0.81-0.98	0.76-0.96	0.71-0.93	0.71-0.93	0.64-0.89
Cumulative deaths	5	7	9	9	11
Remaining at risk	44	42	40	37	6

Table IX. *FEV_1 > 0.5 L/s*

	6 mo 182 d	*12 mo 365 d*	*18 mo 547 d*	*24 mo 730 d*	*36 mo 1095 d*
Unilateral LVRS					
Cumulative survival	0.88	0.86	0.85	0.79	0.7
95% CI	0.81-0.96	0.78-0.94	0.77-0.93	0.71-0.88	0.59-0.80
Cumulative deaths	9	11	12	16	23
Remaining at risk	69	67	66	62	39
Bilateral LVRS					
Cumulative survival	0.95	0.92	0.91	0.86	0.83
95% CI	0.91-0.99	0.87-0.96	0.86-0.97	0.83-0.95	0.75-0.91
Cumulative deaths	5	8	9	12	16
Remaining at risk	100	97	96	86	16

superior sustained improvements in FEV_1 and FVC at 2-year follow-up that may explain the improved overall survival. In previous analyses of bilateral LVRS patients, we found that patients with greatest short-term improvement in pulmonary function tests have better long-term survival.[6] In the current study, FEV_1 for these patients was 274 mL above baseline, compared with only 77 mL above baseline in the unilateral LVRS patients 2 years after bilateral LVRS. These findings are limited by the fact that less than half of the study population had complete follow-up spirometry at 2 years. Therefore, these values may not be truly representative of the total study population. Nonetheless, the differences in overall survival between unilateral and bilateral LVRS patients are seen both in the short-term and the long-term. This may reflect improved ability to survive the acute morbidity of surgery, as well as the longer term pulmonary function benefits of more extensive resection.

The patients who underwent unilateral procedures were not randomized. Therefore, it is a theoretical possibility that preoperative patient selection characteristics could have favored patients undergoing bilateral surgery and thus explain superior long-term survival after bilateral LVRS. Nevertheless, we do not think procedure choice was based on the preoperative level of overall comorbidity. Further, the majority of the unilateral surgeries were performed early in our experience with LVRS. Unilateral LVRS were performed most commonly later in our experience for patients with clear unilateral disease. When patients were stratified by covariables known to be associated with survival and data were analyzed by stratified Kaplan-Meier analysis and log-rank tests, differences between bilateral and unilateral LVRS remained significant. Also, the consistent pattern shown in the univariate analyses strongly supports the survival advantage associated with bilateral surgery in this group of patients.

Overall 2-year survival in bilateral LVRS patients in this series (86%) is similar, but not identical to 2-year survival we recently reported in patients who underwent bilateral staple LVRS at this center (81%).[6] The slight differences in reported survival arise from exclusion in the current study of patients who underwent median sternotomy and exclusion of patients who underwent surgery less than 2 years ago.

Overall longer term survival has not been previously reported comparing unilateral with bilateral LVRS procedures. Short-term lung function response results favor bilateral procedures but do not necessarily predict long-term response. Such information is important since the upcoming NIH-sponsored National Emphysema Treatment Trial examines only bilateral procedures, assuming they are superior to unilateral procedures overall. The current study suggests that long-term survival outcome also favors bilateral LVRS.

Thus far, there has been only 1 study to demonstrate overall survival benefit from LVRS compared with conventional medical management.[26] The current study does not have a medical control arm for direct comparison of LVRS survival effects. However, we believe this study provides further, albeit indirect, evidence to suggest that bilateral LVRS may improve overall survival by the following reasoning. If findings from this study are confirmed in other centers, there are at least 2 possible interpretations why bilateral LVRS may be associated with significantly improved survival, compared with unilateral procedures: (1) bilateral procedures improve overall survival, or (2) both procedures reduce survival, but bilateral procedures cause less survival deterioration than unilateral procedures. While the latter explanation is possible, it is unlikely that more extensive bilateral procedures would cause less damage than more limited unilateral procedures if both are detrimental. Thus, the most likely explanation for the significantly greater bilateral LVRS outcome is due to overall improvement in survival from bilateral LVRS. Thus, while these data are suggestive of overall survival benefits after bilateral LVRS, a controlled study would be needed for definitive proof.

In summary, bilateral staple LVRS appears to be superior to unilateral staple LVRS for the treatment of severe heterogeneous emphysema and can be accomplished safely by using a video-assisted approach. While prior studies have documented the superior acute palliative effects of bilateral staple LVRS over unilateral staple, the present study documents superior survival 2 years after bilateral staple LVRS.

REFERENCES

1. McKenna RJ Jr, Brenner M, Fischel RJ, Gelb AF. Should lung volume reduction for emphysema be unilateral or bilateral? J Thorac Cardiovasc Surg 1996;112:1331-8; discussion 1338-9.
2. Gelb AF, Zamel N, McKenna RJ Jr, Brenner M. Mechanism of short-term improvement in lung function after emphysema resection. Am J Respir Crit Care Med 1996;154:945-51.
3. Cooper JD, Patterson GA. Lung-volume reduction surgery for severe emphysema. Chest Surg Clin N Am 1995;5:815-31.
4. Argenziano M, Moazami N, Thomashow B, Jellen PA, Gorenstein LA, Rose EA, et al. Extended indications for lung volume reduction surgery in advanced emphysema. Ann Thorac Surg 1996;62:1588-97.
5. Rosenbaum P, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika 1983;70:41-55.
6. Brenner MB, McKenna RJ, Chen JC, Osann K, Powell L, Gelb

AF, et al. Survival following bilateral staple lung volume reduction surgery for emphysema. Chest 1999;115:390-6.

7. Cooper JD, Patterson GA, Sundaresan RS, Trulock EP, Yusen RD, Pohl MS, et al. Results of 150 consecutive bilateral lung volume reduction procedures in patients with severe emphysema [see comments]. J Thorac Cardiovasc Surg 1996;112:1319-29; discussion 1329-30.
8. Keenan RJ, Landreneau RJ, Sciurba FC, Ferson PF, Holbert JM, Brown ML, et al. Unilateral thoracoscopic surgical approach for diffuse emphysema. J Thorac Cardiovasc Surg 1996;111:308-15; discussion 315-6.
9. McKenna RJ Jr, Brenner M, Gelb AF, Mullin M, Singh N, Peters H, et al. A randomized, prospective trial of stapled lung reduction versus laser bullectomy for diffuse emphysema [see comments]. J Thorac Cardiovasc Surg 1996;111:317-21; discussion 322
10. Naunheim KS, Keller CA, Krucylak PE, Singh A, Ruppel G, Osterloh JF. Unilateral video-assisted thoracic surgical lung reduction [see comments]. Ann Thorac Surg 1996;61:1092-8.
11. Sciurba FC, Rogers RM, Keenan RJ, Slivka WA, Gorcsan J III, Ferson PF, et al. Improvement in pulmonary function and elastic recoil after lung-reduction surgery for diffuse emphysema [see comments]. N Engl J Med 1996;334:1095-9.
12. Sciurba FC. Early and long-term functional outcomes following lung volume reduction surgery. Clin Chest Med 1997;18:259-76.
13. Brenner M, Yusen R, McKenna R Jr, Sciurba F, Gelb AF, Fischel R, et al. Lung volume reduction surgery for emphysema. Chest 1996;110:205-18.
14. Brenner M, McKenna RJ, Gelb AF, Fischel RJ, Yoong B, Huh J, et al. Dyspnea response following bilateral thoracoscopic staple lung volume reduction surgery. Chest 1997;112:916-23.
15. Brenner M, McKenna R Jr, Gelb A, Osann K, Schein MJ, Panzera J, et al. Objective predictors of response for staple versus laser emphysematous lung reduction. Am J Respir Crit Care Med 1997;155:1295-301.
16. Hazelrigg S, Boley T, Henkle J, Lawyer C, Johnstone D, Naunheim K, et al. Thoracoscopic laser bullectomy: a prospective study with three-month results. J Thorac Cardiovasc Surg 1996;112:319-26; discussion 326-7.
17. Kotloff RM, Tino G, Bavaria JE, Palevsky HI, Hansen-Flaschen J, Wahl PM, et al. Bilateral lung volume reduction surgery for advanced emphysema. A comparison of median sternotomy and thoracoscopic approaches. Chest 1996;110:1399-406.
18. Little AG, Swain JA, Nino JJ, Prabhu RD, Schlachter MD, Barcia TC. Reduction pneumonoplasty for emphysema. Early results. Ann Surg 1995;222:365-71; discussion 371-4.
19. Yusen RD, Trulock EP, Pohl MS, Biggar DG. Results of lung volume reduction surgery in patients with emphysema. The Washington University Emphysema Surgery Group. Semin Thorac Cardiovasc Surg 1996;8:99-109.
20. Cooper JD, Trulock EP, Triantafillou AN, Patterson GA, Pohl MS, Deloney PA, et al. Bilateral pneumectomy (volume reduction) for chronic obstructive pulmonary disease. J Thorac Cardiovasc Surg 1995;109:106-16; discussion 116-9.
21. Martinez FJ, de Oca MM, Whyte RI, Stetz J, Gay SE, Celli BR. Lung-volume reduction improves dyspnea, dynamic hyperinflation, and respiratory muscle function. Am J Respir Crit Care Med 1997;155:1984-90.
22. Benditt JO, Lewis S, Wood DE, Klima L, Albert RK. Lung volume reduction surgery improves maximal O2 consumption, maximal minute ventilation, O2 pulse, and dead space-to-tidal volume ratio during leg cycle ergometry. Am J Respir Crit Care Med 1997;156(Pt 1):561-6.
23. Tschernko EM, Wisser W, Hofer S, Kocher A, Watzinger U, Kritzinger M, et al. The influence of lung volume reduction surgery on ventilatory mechanics in patients suffering from severe chronic obstructive pulmonary disease. Anesth Analg 1996;83:996-1001.
24. Bloch KE, Li Y, Zhang J, Bingisser R, Kaplan V, Weder W, et al. Effect of surgical lung volume reduction on breathing patterns in severe pulmonary emphysema. Am J Respir Crit Care Med 1997;156(Pt 1):553-60.
25. O'Donnell DE, Webb KA, Bertley JC, Chau LK, Conlan AA. Mechanisms of relief of exertional breathlessness following unilateral bullectomy and lung volume reduction surgery in emphysema. Chest 1996;110:18-27.
26. Meyers BF, Yusen RD, Lefrak SS, Patterson GA, Pohl MS, Richardson VJ, Cooper JD. Outcome of Medicare patients with emphysema selected for, but denied, a lung volume reduction operation. Ann Thorac Surg 1998;66:331-6.