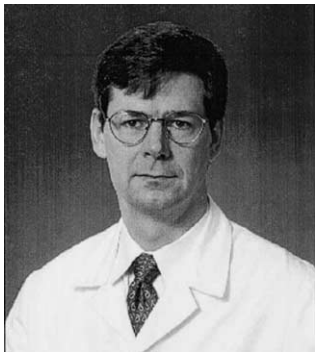
Results of lung volume reduction surgery in patients meeting a National Emphysema Treatment Trial high-risk criterion

Bryan F. Meyers, MD,[a,d] Roger D. Yusen, MD, MPH,[b,c,d] Tracey J. Guthrie, RN, BSN,[a,d] G. Alexander Patterson, MD,[a,d] Stephen S. Lefrak, MD,[c,d] Gail E. Davis, RN,[a,d] and Joel D. Cooper, MD[a,d]



Dr Meyers

See related editorial on page 631.

From the Division of Cardiothoracic Surgery, Department of Surgery,[a] the Division of Pulmonary and Critical Care Medicine and the Division of General Medical Sciences,[b] and the Department of Internal Medicine,[c] Washington University School of Medicine, St Louis, Mo, and the Jacqueline Maritz Lung Center at Barnes-Jewish Hospital,[d] St Louis, Mo.

Read at the Eighty-third Annual Meeting of The American Association for Thoracic Surgery, Boston, Mass, May 4-7, 2003.

Received for publication April 26, 2003; revisions requested Aug 26, 2003; accepted for publication Sept 9, 2003.

Address for reprints: Bryan F. Meyers, MD, One Barnes-Jewish Plaza, 3108 Queeny Tower, St Louis, MO 63110 (E-mail: meyersb@msnotes.wustl.edu).

J Thorac Cardiovasc Surg 2004;127:829-35

0022-5223/$30.00

doi:10.1016/j.jtcvs.2003.09.004

Objectives: A report from the National Emphysema Treatment Trial indicated that lung volume reduction candidates with a forced expiratory volume in 1 second and a diffusing capacity of carbon monoxide of 20% or less of predicted value were at high risk for mortality and were unlikely to benefit from surgical intervention. This article examines the applicability of the National Emphysema Treatment Trial findings to our own patients.

Methods: We reviewed 280 patients who underwent bilateral lung volume reduction surgery at our institution between January 1993 and December 2001. All patients met our selection criteria, including heterogeneous distribution of emphysema. Of these 280 patients, 20 patients had both a preoperative forced expiratory volume in 1 second and a diffusing capacity of carbon monoxide of less than or equal to 20% of the predicted normal values, thus meeting one National Emphysema Treatment Trial criterion for high risk. Outcomes of the 20 patients were assessed through 5 years after the operation. The survival of the 20 patient cohort was compared with that of the 260 patients not meeting the National Emphysema Treatment Trial high-risk criterion.

Results: Ninety-day operative mortality included 1 (5%) patient. In all patients the forced expiratory volume in 1 second increased from 0.46 L (17%) to 0.78 L (32%), a 73% change; the diffusing capacity of carbon monoxide increased from 16% to 27%, a 70% improvement; residual volume decreased from 6.33 L (305%) to 4.26 L (205%), a 33% improvement; and room air arterial partial pressure of oxygen increased from 55 mm Hg to 64 mm Hg. Kaplan-Meier 5-year survivals did not differ between the high-risk and non–high-risk groups.

Conclusions: Patients with a forced expiratory volume in 1 second and a diffusing capacity of carbon monoxide of 20% or less of predicted value might experience improvements in lung function, exercise tolerance, and quality of life with acceptable morbidity and mortality after lung volume reduction surgery.

The concept of lung volume reduction as a therapy to reduce dyspnea in patients with emphysema is credited to Brantigan and Mueller.[1] Although the initial procedure failed to gather acceptance by surgeons, it was rediscovered and resuscitated by Cooper and colleagues[2] nearly 4 decades later. There are now long-term results available on a substantial number of patients, and the conclusion has been that tangible benefit with acceptable risk is available to well-selected patients.[3]

There has been no shortage of controversy associated with this operation since its reintroduction in 1995. Because of high risks and costs associated with the widespread application of the operation in 1995, Medicare funding for the operation was stopped as of 1996. The National Heart, Lung, and Blood Institute of the National Institutes of Health was tasked with devising a clinical trial to evaluate the benefit of the procedure. The result of this effort, the National Emphysema Treatment Trial (NETT), began enrolling patients in 1999.[4] The NETT investigators provided a preliminary report describing their identification of a high-risk subset of patients for whom a high risk of surgical intervention seemed to outweigh a low functional benefit.[5]

The NETT high-risk subgroup consisted of patients with a very low forced expiratory volume in 1 second (FEV_1) in combination with a very low diffusing capacity for carbon monoxide (DLCO), a diffuse pattern of emphysema on chest computed tomography, or both. The high mortality seen in such patients in the NETT prompted a modification of the protocol to exclude from randomization any patients meeting these criteria. As a direct result of the publicity surrounding the NETT report of the high-risk cohort, we reviewed our own results in patients meeting the NETT high-risk criteria. Because we had excluded patients with diffuse emphysema from lung volume reduction surgery (LVRS) from the beginning, the NETT high-risk classification criterion that applied to our patients was the combination of an FEV_1 of not more than 20% of predicted value and a DLCO of not more than 20% of predicted value. The specific objective was to assess the appropriateness of excluding patients with both FEV_1 and DLCO of not more than 20% of predicted value from receiving LVRS.

Methods

Patient Population

A prospective database has been maintained by the authors for all patients undergoing LVRS, including pulmonary function studies, exercise testing, and quality-of-life assessment. A review was conducted from records of the 280 consecutive patients who underwent bilateral LVRS at Barnes-Jewish Hospital between January 1993 and December 2001. This study is a retrospective analysis of prospectively acquired data. All research tests and protocols were approved by the human studies committee, and all patients provided informed consent for the studies and the operation. We attempted to assess patients at 6 months, 1 year, and subsequent yearly intervals after the operation. Many patients live a long distance from Missouri, and we could not require their return at fixed intervals. Follow-up data were collected during routine appointments and thus might have been collected months before or after the desired follow-up time point. Many of these patients have been included in previous clinical reviews of the outcomes of LVRS in our institution, but the detailed description of this small subset defined by NETT criteria has not been reported as a distinct cohort.[2,3,6-11]

Details of the selection process have been reported previously.[12] Critical selection criteria are marked hyperinflation of the chest and sufficient regional variation in the severity of the emphysema to provide target areas of useless lung accessible to surgical resection. The degree of regional parenchymal destruction is analyzed by using standardized computerized tomography of the chest, and the regional distribution of function is assessed by means of radionuclide ventilation-perfusion lung scanning. Thoracic distention is evaluated by means of chest radiography, and lung volumes are determined with plethysmography. No special screening was applied to the patients in this report because this cohort of 20 patients was identified retrospectively on the basis of NETT high-risk criteria.[5]

The initial evaluation includes physical examination, pulmonary function testing, arterial blood gas analysis (at rest with room air), 6-minute walk testing, and questionnaires assessing quality of life and dyspnea. Fifty percent of more than 800 on-site evaluations were excluded from surgical intervention. The most common reason for exclusion was lack of target areas for surgical resection (76%).[3] Patients judged suitable for surgical intervention were enrolled in a preoperative pulmonary rehabilitation program, usually for 3 months (median, 97 days). Medical therapy was optimized, and dietary regimens were prescribed.

Pulmonary function tests were performed with a Medgraphics System 1085 (Medical Graphics Corp, St Paul, Minn) before and after administration of aerosolized albuterol, and the best values for forced vital capacity and FEV_1 were chosen for the data analysis. Lung volumes were determined by means of plethysmography, and diffusion capacity for carbon monoxide (DLCO) was measured by using the single-breath technique. During the 6-minute walk test, supplemental oxygen was administered through a nasal cannula as needed to maintain the arterial oxygen saturation at 90% or better.

Quality of life was assessed by using the Medical Outcomes Study 36-Item Short-Form (SF-36) Health Survey. We specifically report the SF-36 Physical Component Summary Scale (PCS) and the SF-36 Mental Component Summary Scale (MCS), the Physical Functioning (PF) scale, and the response to a single question about health now compared with 1 year prior. The PCS, MCS, and PF scores can range from 0 (worst) to 100 (best). The PCS and MCS scores are standardized so that the general population has a mean $\pm$ SD score of 50 $\pm$ 10. A 10-point change in the PF score and a 3-point change in the PCS score are considered clinically important. Patients were asked to assess their own satisfaction with the operation on the basis of how they felt at present to measure preoperative patient satisfaction. There are 5 possible responses: poor, fair, good, very good, and excellent. All tests were performed during periods of clinical stability.

A complete battery of pulmonary function tests was performed at our institution during the postoperative follow-up periods; an abbreviated battery of tests (FEV_1 and RV) from other institutions was also used. Follow-up evaluation also included arterial blood gases on room air, a 6-minute walking test, and completion of dyspnea and quality-of-life questionnaires.

Surgical Technique

All procedures were performed through a median sternotomy. The operative technique has evolved very little since our initial expe-

TABLE 1. Preoperative characteristics of high-risk patients undergoing lung volume reduction surgery

Demographics	n = 20
Age (y)	62.7 ± 6.1 (range, 48.7-76.9)
Sex (female)	11 (55%)
Preoperative BMI (kg/m^2)	21.1 ± 2.8
Tobacco use	20 (100.0%)
Chronic oral steroid use	7 (35%)
Lower lobe predominant emphysema	1 (5%)

BMI, Body mass index.

rience. In 1 of 20 patients in this report, lobar destruction and complete fissures led to a complete lobectomy rather than wedge excision of lung tissue. Two chest tubes were placed on each side. The pleural space was closed bilaterally before closure of the sternotomy. The chest tubes were brought out through the upper abdomen in a subxiphoid position.

All patients were extubated in the operating room or shortly thereafter in the postanesthesia recovery area. One patient required immediate reintubation and spent the night attached to a ventilator, with successful extubation on the following morning. The surgical, anesthetic, and postoperative care techniques have been previously described.[2,9,13]

Statistical Analysis

Descriptive statistics were expressed as means ± SD unless otherwise specified. Categorical data were expressed as counts and proportions. Kaplan-Meier estimates were used to depict survival. The log-rank test was used to compare survival between groups. Patients who had lung transplantation after LVRS were censored for all observations at or beyond the time of transplantation. All data analysis was performed with Systat (Systat 10.0 for Windows; SPSS Inc, Chicago, Ill).

Results

Patient Characteristics

The 20 patients in this report included 11 women and 9 men with a mean age of 62.7 ± 6 years. All had previously smoked cigarettes, but all had quit more than 6 months before the operation in accordance with our usual criteria. One patient was known to have α_1-antitrypsin deficiency emphysema, and one patient had lower-lobe predominance with lower-lobe target areas. Seven of the 20 patients used chronic oral corticosteroids before the operation (Table 1).

Hospital Course

The hospital mortality in this series was 1 (5%) patient who died of adult respiratory distress syndrome on postoperative day 3 (Table 2). The most common complication was a prolonged air leak for longer than 7 days, and this was observed in 14 (70%) of the patients. Pneumonia was diagnosed in 3 (15%) patients, and respiratory failure requiring reintubation occurred in 1 (5%) patient. Two patients had

TABLE 2. Hospital course for high-risk patients undergoing lung volume reduction surgery

Event	Frequency (n = 20)
Morbidity	
Prolonged air leak (>7 d)	14 (70%)
Pneumonia	3 (15%)
Reintubation	1 (5%)
Small bowel obstruction/ileus	2 (10%)
Deep vein thrombosis	1 (5%)
Cecal perforation	1 (5%)
Subsequent reoperation	
Prolonged air leak	1 (5%)
Bleeding	1 (5%)
GI complication	1 (5%)
Hospital mortality	1 (5%)
Postoperative hospital LOS (survivors)	
Median	12 d
Range	5-76 d
IQR	10-22 d

GI, Gastrointestinal; *LOS*, length of stay; *IQR*, interquartile range.

important gastrointestinal complications, including one patient each with a small bowel obstruction and a cecal perforation. Reoperations were required in one patient for an air leak, one patient for bleeding from the chest, and one patient for the cecal perforation. The median length of hospital stay was 12 days, with a range of 5 to 76 days and an interquartile range of 10 to 22 days.

Follow-up Information

All 20 patients had complete vital status assessment through the entire study period. Postoperative follow-up ranged from 3 days for the single postoperative death to 9.3 years, with a median follow-up of 4.6 years. Three (15%) patients underwent lung transplantation with a mean time to transplantation of 3.1 ± 0.5 years after LVRS. There have been 11 late deaths: 7 were attributed to respiratory failure, 2 to bronchiolitis obliterans after transplantation (mentioned for completeness but censored in the Kaplan-Meier estimates), and 1 each to lung cancer and myocardial infarction. The Kaplan-Meier survival estimates are shown in Figure 1.

Functional Results

Pulmonary function test results are shown in Table 3 and demonstrate the typical degree of improvement in spirometry and exercise capability that we have reported in previous articles on our larger cohorts of patients undergoing LVRS. It is noteworthy that the D_{LCO} values in these patients improved from 16% of predicted value to 27% of predicted value between the preoperative and 6-month postoperative visits. Table 4 reports several subjective measures of health status and quality of life. Although such measures are prone to bias, especially when the described cohort

GTS

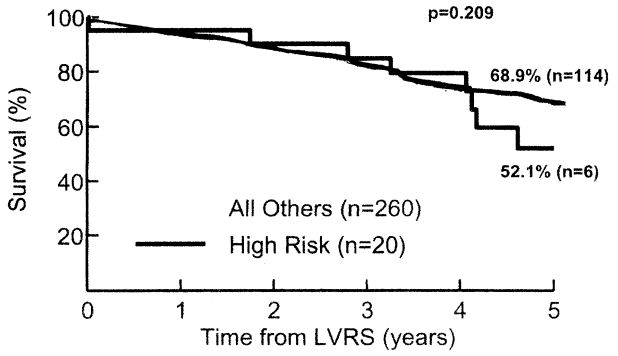


Figure 1. Kaplan-Meier survival graph after LVRS.

shrinks as the follow-up gets longer, the results do suggest a magnitude and duration of benefit that is comparable with that seen in our previously reported large experience with patients undergoing LVRS.[3]

Discussion

This retrospective analysis of 20 patients with heterogeneous emphysema demonstrated that some high-risk (FEV_1 and DLCO $\leq$20% of the predicted normal values) patients might experience improvements in lung function, exercise tolerance, and quality of life with acceptable morbidity and mortality after LVRS.

There have been many published reports describing the outcomes after lung volume reduction, with the majority describing a postoperative mortality of 3% to 8%. The health technology assessment report that led to the cessation of reimbursement by the Health Care Financing Administration reported a mortality of 6%.[14] It is typically accepted that properly selected patients will experience a perioperative mortality risk of less than 10%, with many high-volume centers reporting mortality clustered in the 4% to 6% range.[2,15-19]

Randomized controlled trials (RCTs) have advantages over individual case series by avoiding selection and reporting bias. An important contribution to knowledge about a procedure takes place when an RCT is interrupted or altered because of findings by a data and safety monitoring board. Two such trials have reported the need to restrict enrollment criteria during the trial because of an excessive observed mortality. The Geddes trial changed the enrollment criteria after 15 enrolled patients exhibited excessive risk of death. The trial subsequently excluded 2 groups: patients with DLCO values of less than 30% of predicted value and patients unable to achieve a specified minimum threshold in a pre-enrollment exercise evaluation.[20] The second RCT to adjust enrollment criteria occurred when the NETT trial acknowledged an excessive mortality in 2 subgroups of patients randomized to surgical intervention: patients with a very low FEV_1 and homogeneous emphysema and patients with a very low FEV_1 and a low DLCO.[5]

The findings in both of those trials corroborated observations from the early LVRS experience, and the statistically sound nature of a prospectively randomized trial has added additional weight of evidence to the belief that such patients were poor candidates. Because we have excluded patients with a homogeneous pattern of emphysematous destruction, our series cannot address the issue of whether homogeneous destruction is an absolute or relative contraindication. The NETT high-risk article identified 140 (13.6%) of 1033 patients as belonging to the high-risk group. Close analysis of the NETT data shows that 46 (66%) of 70 patients randomized to surgical intervention and 48 (69%) of 70 patients randomized to medical therapy were classified as having homogeneous emphysema and would therefore not be representative of patients in our series. Furthermore, the deaths reported in the NETT article for patients with LVRS with heterogeneous emphysema and both FEV_1 and DLCO values of not more than 20% of predicted value are 3 (12.5%) deaths in 24 patients. This death rate is not significantly different from that presented in the current article. The relative risk of early death in comparable patients in the NETT article versus our own results is 1.08 (95% confidence interval, 0.91-1.30). It seems that the apparent differences in outcome between the NETT high-risk patients and our own patients declared high risk by using the NETT criteria disappear when the patients with homogenous emphysema are excluded from the analysis.

The NETT high-risk patients fell into 2 subgroups, both of which had an FEV_1 of less than or equal to 20% of predicted value. The first group had a homogeneous pattern of emphysematous destruction (n = 94), and the second group had a DLCO of less than or equal to 20% of predicted value (n = 87). However, when the outcomes were reported as survival curves, the results of each subgroup were displayed without emphasizing the substantial overlap (n = 41) of patients who met all 3 criteria. Rather, 2 overlapping groups of patients were displayed: all patients with FEV_1 values of not more than 20% and homogeneous emphysema and all patients with DLCO and FEV_1 values both not more than 20%. In the overlap group patients with all 3 characteristics are reported twice because they appear in each of the previous groups. The true 2-factor groups were never described apart from the very high-risk patients in the overlap group.

We do agree that patients with severe functional impairment, as reflected by both an FEV_1 and a DLCO of 20% or less of predicted value might still represent relatively high-risk patients. The small number of patients presented here makes the mortality estimate of 5% susceptible to large fluctuations in the event of 1 or 2 deaths in future patients

TABLE 3. Pulmonary function testing in high-risk patients undergoing lung volume reduction surgery

	After rehab, preoperative	6 months postoperatively	1 y postoperatively	3 y postoperatively	5 y postoperatively
N	20	19	19	14	6
FEV_1, L (% predicted)	0.46 ± 0.1 (17%)	0.78 ± 0.3 (32%)	0.81 ± 0.3 (31%)	0.74 ± 0.3 (25%)	0.66 ± 0.2 (24%)
% Change*	NA	73 ± 63	82 ± 72	47 ± 91	36 ± 52
DLCO, mL · min^{-1} · mm Hg^{-1} (% predicted)	4.2 ± 0.9 (16%)	7.0 ± 3.1 (27%)	7.2 ± 3.2 (28%)	6.9 ± 3.4 (26%)	6.2 ± 2.3 (25%)
% Change*	NA	70 ± 82	78 ± 92	66 ± 88	50 ± 42
RV, L (% predicted)	6.33 ± 1.2 (305%)	4.26 ± 1.1 (205%)	4.26 ± 0.97 (202%)	5.29 ± 1.4 (242%)	6.38 ± 1.77 (267%)
% Change*	NA	−33 ± 17	−32 ± 13	−14 ± 26	−13 ± 16
$Paco_2$, mm Hg	46.6 ± 6.0	40.3 ± 6.4	40.3 ± 5.9	42.2 ± 6.7	46.4 ± 5.0
Pao_2, mm Hg	55.2 ± 7.5	64.1 ± 13.8	66.7 ± 11.4	70.3 ± 12.3	68.5 ± 4.1
O_2—Continuous/with exercise	60%/100%	32%/74%	22%/77%	50%/93%	57%/100%
Six-min walk, ft	913 ± 235	1158 ± 289	1179 ± 295	1124 ± 322	1100 ± 205
% Change*	NA	27 ± 41	28 ± 39	26 ± 42	25 ± 23
MRC dyspnea score	3.1 ± 0.9	1.5 ± 0.9	1.6 ± 0.9	2.1 ± 0.92	2.4 ± 0.8

FEV$_1$, Forced expiratory volume in 1 second; *DLCO*, diffusing capacity of carbon monoxide; *RV*, residual volume; *MRC*, medical research council.
*The mean percentage change of postoperative value from preoperative (postrehabilitation) value.

TABLE 4. Quality of life and satisfaction in high-risk patients undergoing lung volume reduction surgery

	After rehab	6 mo postoperatively	1 y postoperatively	3 y postoperatively	5 y postoperatively
N	20	19	19	14	6
SF-36 Physical Functioning	9.8 ± 11.0	44.5 ± 23.9	41.1 ± 26.6	29.3 ± 28.2	32.1 ± 21.4
SF-36 PCS	25.2 ± 7.1	31.9 ± 10.4	31.9 ± 11.6	27.0 ± 11.7	28.4 ± 9.5
SF-36 MCS	45.7 ± 9.9	53.6 ± 10.0	53.6 ± 11.1	52.2 ± 9.2	58.8 ± 9.7
"Compared to one year ago, how would you rate your health in general now?"					
Much better	NA	10 (52.6%)	10 (52.6%)	0 (0%)	0 (0%)
Somewhat better	NA	6 (31.6%)	6 (31.6%)	0 (0%)	0 (0%)
About the same	NA	2 (10.5%)	1 (5.3%)	5 (35.7%)	4 (66.6%)
Somewhat worse	NA	1 (5.3%)	1 (5.3%)	4 (50.0%)	2 (33.3%)
Much worse	NA	0 (0%)	1 (5.3%)	2 (14.3%)	0 (0%)
Patient satisfaction with surgery					
Excellent	NA	8 (42.1%)	7 (36.8%)	6 (42.9%)	2 (33.3%)
Very good	NA	7 (36.8%)	7 (36.8%)	0 (0%)	1 (16.7%)
Good	NA	3 (15.8%)	2 (10.5%)	4 (28.6%)	1 (16.7%)
Fair	NA	1 (5.3%)	2 (10.5%)	3 (21.4%)	1 (16.7%)
Poor	NA	0 (0%)	1 (5.3%)	1 (7.1%)	1 (16.7%)

PCS, SF-36 Physical Component Summary; *MCS*, SF-36 Mental Component Summary.

meeting this criterion. The median hospital stay was 3 days longer for the patients in this current report than for the recently reported larger cohort from which they were drawn.[3] It is also important to point out that the rates of prolonged air leak and pneumonia were higher in these patients than in the larger cohort, although these differences do not reach statistical significance. It is our habit to give thorough counseling to such patients about the possibility of lung transplantation as an alternative to lung volume reduction. Patients with severe destruction and homogeneous emphysema are steered preferentially toward transplantation because of our bias that LVRS requires heterogeneous target areas to be effective.

The DLCO determination does have limitations in its role as an exclusionary criteria for LVRS. One such limitation is the fact that many physiologic processes can lead to a low DLCO. For instance, it might result from combinations of extensive loss of diffusing surface caused by emphysematous destruction of alveolar walls and capillaries, thickening of the alveolar-capillary interface, reduction of red cells in capillaries, and marked hypoventilation of potentially functional pulmonary parenchyma. It has been the authors' belief that in heterogeneous emphysema compression of the spared lung by the diseased areas leads to focal hypoventilation and underestimation of the DLCO. Recruitment of capillaries after LVRS might account for an increase in

DLCO after resection of 20% to 30% of the lung parenchyma.

Another limitation of the DLCO is the problem of reproducibility. To evaluate the test-to-test variability of measuring the DLCO, we performed an exploratory analysis of our preoperative patients before and after pulmonary rehabilitation. In the initial evaluations of 280 patients undergoing LVRS, 63 (23%) had FEV_1 values of less than 20%, and 34 (12%) had DLCO values of less than 20%, with 13 (5%) patients meeting both criteria. However, after rehabilitation and immediately before the operation, 69 (25%) patients had FEV_1 values of less than 20%, and 40 (14%) had DLCO values of less than 20%, with 20 (7%) patients meeting both criteria. The fact that the cohort described in this article could vary from 13 to 20 patients on the basis of measurements taken a few weeks apart suggests that a fixed cut-off point of DLCO or FEV_1 applied to the selection criteria for LVRS would be inappropriate.

A limitation of this study is the retrospective nature of the analysis. We did not collect a full set of initial data on all patients referred for consideration for LVRS, and as a result, we have no ability to estimate what fraction of all patients with the criteria in question (FEV_1 and DLCO $\leq$20% of predicted value) were actually selected for surgical intervention. Presumably, as one or more relative contraindications are encountered, there must be other favorable criteria, such as youth or motivation, that tip the decision toward acceptance for LVRS. We performed an exploratory analysis to see whether the patients undergoing LVRS in our series had some evidence of selection bias in the form of favorable measurements on other known risk factors, such as sex, age, and exercise capability. These data (not shown) suggested an overrepresentation of female patients but did not otherwise support the hypothesis that the patients in this report had favorable observations on other covariables to explain their selection or their favorable outcome. Furthermore, there are no data about patients selected with such criteria who might have embarked on the preoperative rehabilitation and either failed to complete it or declined during that period to the extent that they were rendered unacceptable for the risk of surgical intervention.

Conclusion

These results of LVRS in patients with both DLCO and FEV_1 values of not more than 20% of the predicted normal values are in contrast to the results of the NETT high-risk report of 2001. Although it is difficult to generalize on the basis of the experience obtained with 20 carefully selected patients, these results show acceptable mortality, functional outcome, and long-term survival in this defined cohort. Individual patients referred for LVRS should be evaluated on the basis of all information available, and a hasty exclusion on the basis of the 2 variables, FEV_1 and DLCO, might exclude reasonable candidates from consideration.

GTS

References

1. Brantigan OC, Mueller E. Surgical treatment of pulmonary emphysema. *Am Surg*. 1957;23:789-804.
2. 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. *J Thorac Cardiovasc Surg*. 1996;112:1319-30.
3. Ciccone AM, Meyers BF, Guthrie TJ, Davis G, Yusen RD, Lefrak SS, et al. Long-term outcome of bilateral lung volume reduction in 250 consecutive patients with emphysema. *J Thorac Cardiovasc Surg*. 2003;125(3):513-25.
4. NETT Research Group. Rationale and design of the national emphysema treatment trial (NETT): a prospective randomized trial of lung volume reduction surgery. *J Thorac Cardiovasc Surg*. 1999;118:518-28.
5. NETT Research Group. Patients at high risk of death after lung-volume-reduction surgery. *N Engl J Med*. 2001;345:1075-83.
6. Meyers BF, Yusen RD, Lefrak SS, Cooper JD. Improved long-term survival seen after lung volume reduction surgery compared to continued medical therapy for emphysema. *Ann Thorac Surg.* 2001;71: 2081.
7. Meyers BF, Yusen RD, Guthrie TJ, Pohl MS, Davis G, Lefrak SS, et al. Outcome of lung volume reduction surgery in emphysema patients potentially eligible for lung transplant. *J Thorac Cardiovasc Surg*. 2001;122:10-7.
8. Meyers BF, Yusen RD, Lefrak SS, Patterson GA, Pohl MS, Richardson VJ, et al. Outcome of Medicare patients with emphysema selected for, but denied, a lung volume reduction operation. *Ann Thorac Surg*. 1998;66:331-6.
9. 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(1):106-16.
10. Yusen RD, Trulock EP, Pohl MS, Biggar DG, Patterson GA, Cooper JD. Results of lung volume reduction surgery in patients with emphysema. *Semin Thorac Cardiovasc Surg*. 1996;8(1):99-109.
11. Yusen RD, Lefrak SS, Gierada DS, Davis G, Meyers BF, Patterson GA, et al. A prospective evaluation of lung volume reduction surgery in 200 consecutive patients. *Chest*. 2003;123:1026-37.
12. Yusen RD, Lefrak SS, the Washington University Emphysema Surgery Group. Evaluation of patients with emphysema for lung volume reduction surgery. *Semin Thorac Cardiovasc Surg*. 1996;8:83-93.
13. Triantafillou AN. Anesthetic management for bilateral volume reduction surgery. *Semin Thorac Cardiovasc Surg*. 1996;8:94-8.
14. Holohan T, Handelsman H. Lung volume reduction surgery for end-stage chronic obstructive pulmonary disease. *Health Technol Assess*. 1996;10:1-30.
15. Argenziano M, Moazami N, Thomashaw B, Jellen PA, Gorenstein LA, Rose EA, et al. Extended indications for volume reduction pneumoplasty in advanced emphysema. *Ann Thorac Surg*. 1996;62:1588-97.
16. 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.
17. McKenna RJ, Brenner M, Fischel RJ, Gelb AF. Should lung volume reduction for emphysema be unilateral or bilateral? *J Thorac Cardiovasc Surg*. 1996;112:1331-9.
18. Naunheim KS, Hazelrigg SR, Kaiser LR, Keenan RJ, Bavaria JE, Landreneau RJ, et al. Risk analysis for thoracoscopic lung volume reduction: a multi-institutional experience. *Eur J Cardiothorac Surg*. 2000;17:673-9.
19. Serna DL, Brenner M, Osann KE, McKenna RJ, Chen JC, Fischel RJ, et al. Survival after unilateral versus bilateral lung volume reduction surgery for emphysema. *J Thorac Cardiovasc Surg*. 1999;118:1101-9.
20. Geddes D, Davies M, Koyama H, Hansell D, Pastorino U, Pepper J, et

al. Effect of lung-volume-reduction surgery in patients with severe emphysema. *N Engl J Med*. 2000;343:239-45.

Discussion

Dr Douglas E. Wood *(Seattle, Wash)*. Bryan, you have done your usual excellent job in the selection of an important study question, the analysis of your results, and a concise and clear presentation. I would like to emphasize to the audience that the manuscript is of equal quality and is a good read that is worth your time when it is published.

Although the much awaited primary outcomes of the NETT will be published in 2 weeks, to date, the NETT has published only the outcomes of this high-risk subgroup of patients that you have referenced, a group with modest functional benefit that was offset in the NETT by increased morbidity and mortality. You were right to question and challenge this conclusion with your own experience.

There is a subgroup of patients with heterogenous disease and low FEV_1 and D_{LCO} values with which comparisons can be made. Although your morbidity and mortality are somewhat similar to those of the NETT cohort, your patients were able to achieve a substantial clinical benefit compared with their baseline values. The beneficial functional outcomes potentially make the morbidity and mortality acceptable and call into question whether these criteria should be considered absolute contraindications, as suggested by the NETT. However, the NETT accepted all patients with these criteria, whereas you might have been able to select for other factors that overcome these risks.

Do you have an estimation of the number of patients with these clinical characteristics that were excluded from surgical intervention in your series, and do you have any ideas of factors that might have allowed better selection in your patients? Your group and others have postulated specific selection criteria to achieve optimal outcomes after LVRS. How would you propose that we challenge the extent or the limitations of these criteria and determine whether additional patients might benefit from lung reduction for emphysema?

Bryan, I appreciate the work of you and your group in this arena. I hope that others will examine their own experience with these high-risk patients to help define whether selected patients might be able to be offered LVRS in spite of NETT suggestions to the contrary. Thank you.

Dr Meyers. Thanks for your comments. The first question was an estimation of the fraction of patients who presented with these risk factors who were actually selected for surgical intervention, and unfortunately, we do not have that information. We did not collect a full set of data on patients who were evaluated and then not chosen for the operation. It turns out that this is 7% of the total population of patients who underwent LVRS.

As I pointed out earlier, in the NETT it was 13% of patients that constituted the high-risk group. But I think if you consider only the heterogeneous patients within the NETT, the overall fraction of patients represented in our group is comparable with the fraction of heterogenous patients in the NETT.

With regard to challenging the limitations that are placed on the operation, I think that the most important thing would just be ongoing discussion of subgroups of patients of interest and constantly being alert to any trends that develop in terms of poor or excellent outcomes, and I think forums such as this are useful. There is generally a bias toward the presentation of favorable results, and I think that we also have to be very tuned in to the potential of report bias in terms of extrapolating from presented or published work and using that as selection criteria for further operations.

Dr Thomas M. Egan *(Chapel Hill, NC)*. That was a nice presentation, Bryan. You mentioned that your actuarial survival analysis censored patients at the time of lung transplantation, and I was curious to learn whether your high-risk group had a higher incidence of lung transplantation than your low-risk group?

Dr Meyers. Of the subgroups that we have categorized, the patients who have had LVRS for lower-lobe emphysema or α_1-antitrypsin deficiency emphysema are the one subgroup that emerged as having a higher rate requiring lung transplantation than any other group. As far as the 20 high-risk patients presented here, their rate of transplantation is not statistically different from that of the rest of the cohort.

Dr Jean Deslauriers *(Ste Foy, Quebec, Canada)*. Do you think it is possible that both conclusions are quite right here? The NETT trial involves many surgeons that do probably very few procedures. In the general community you should really select patients, and these are some of the criteria that you can use for selection. On the other hand, in a large center like St Louis, where many cases are done every month, then you can extend the criteria and operate on higher-risk patients. What I understand here today is that there are 2 different points of view, and I think they are not exclusive. I think the conclusions are probably right as they apply to the center that you work in.

Dr Meyers. I agree with your comment. I think that, particularly if you compare the results of the NETT in heterogeneous patients and the results that I have just described, there is no statistical difference in terms of survival between those 2 very careful comparisons. Therefore I definitely agree with your comments.

GTS