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A RANDOMIZED, PROSPECTIVE TRIAL OF STAPLED LUNG REDUCTION VERSUS LASER BULLECTOMY FOR DIFFUSE EMPHYSEMA

Two procedures (laser bullectomy and lung reduction surgery with staples) are currently available for the surgical treatment of patients with diffuse emphysema. We compared the efficacy of these two surgical approaches in 72 patients, aged 67 ± 7 years (mean \pm standard deviation), who had diffuse emphysema scored as severe on computed tomography and severe fixed expiratory airflow obstruction. The patients were prospectively randomized to undergo either neodymium:yttrium aluminum garnet contact laser surgery ($n = 33$) or stapled lung reduction surgery ($n = 39$) by unilateral thoracoscopy. The operative mortalities were 0% and 2.5%, respectively. No significant differences were noted between the groups ($p < 0.05$) with respect to operating time, hospital days, or air leakage for more than 7 days. However, a delayed pneumothorax developed in six patients (18%) who had laser treatment ($p = 0.005$). The operations eliminated dependency on supplemental oxygen in 52% of the laser group and 87.5% of the stapled lung reduction group ($p = 0.02$). The mean postoperative improvement in the forced expiratory volume in 1 second at 6 months was significantly greater for the patients undergoing the staple technique (32.9% vs 13.4%, $p = 0.01$) than for the laser treatment group. (J THORAC CARDIOVASC SURG 1996;111:317-22)

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Resurgence of interest has been noted in the surgical treatment for patients with diffuse emphysema. Forty years ago, Brantigan and Mueller¹ performed multiple wedge resections for diffuse emphysema through a posterolateral thoracotomy

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incision. Although significant clinical improvement occurred in 75% of their patients, the mortality was 16%, and the procedure never became popular.¹

Recently, Wakabayashi and associates² performed laser bullectomy on such patients via unilateral thoracoscopy. Short-term follow-up showed a 3-month mortality of 14% (3/22 patients) and a 36% improvement in the forced expiratory volume in 1 second (FEV₁).^{2,3} The degree of improvement is artificially inflated by the inclusion of some patients with giant bullae.

In 1994, Cooper and coworkers^{4,5} rekindled interest in resectional treatment of diffuse emphysema via a median sternotomy with bovine pericardium to buttress the staples. They reported an 82% improvement in the FEV₁ (mean follow-up 6.4 month) and improvement in dyspnea index, exercise tolerance, and quality of life in 20 patients.

This randomized, prospective trial was designed to compare the efficacy of these two surgical ap-

Table I. Baseline comparison of patients in the laser and staple-treated surgical groups

	Laser	Staple	P Value
No. of patients	33	39	NS
Male (No.)	26	32	NS
Age (yr)	69 ± 6	66 ± 8	NS
FEV ₁ (L)	0.7 ± 0.2	0.7 ± 0.2	NS
FVC (L)	2.1 ± 0.7	2.1 ± 0.7	NS
RV (L)	5.1 ± 1.1	5.4 ± 0.2	NS
TLC (L)	7.6 ± 1.4	7.9 ± 1.3	NS
DLCO _{SB} (ml/min/mm Hg)	5.4 ± 3.0	8.6 ± 1.9	NS
PaO ₂ (mm Hg)	65 ± 12	66 ± 12	NS
Paco ₂ (mm Hg)	43 ± 7	44 ± 8	NS
SGaw (L/sec/cm H ₂ O/L)	0.03 ± 0.01	0.03 ± 0.01	NS
Smoking (pack-years)	62 ± 20	68 ± 24	NS
CT emphysema score ⁸	60 ± 21	56 ± 21	NS
Dyspnea grade ⁷	3.1 ± 0.6	3.1 ± 0.7	NS
Oxygen use (No. of patients)	25	27	NS

FEV₁, Forced expiratory volume in 1 second; FVC, forced expiratory volume; RV, residual volume, TLC, total lung capacity; DLCO_{SB}, single-breath diffusing capacity; PaO₂, arterial oxygen tension; Paco₂, arterial carbon dioxide tension; SGaw, specific airway conductance; CT, computed tomography; NS, not significant. Data are presented as mean ± standard deviation.

proaches. Because laser bullectomy is performed unilaterally by thoracoscopy, the stapled lung reduction technique was also performed unilaterally by thoracoscopy.

Patients and methods

Between June 1994 and November 1994, 72 patients aged 67 ± 7 years (mean ± standard deviation [SD]) were randomized. All patients had severe symptoms with a substantial decrease in the dyspnea index and poor quality of life despite maximal medical management. Preoperatively, 49 (68%) patients were receiving steroids and 52 (72%) were using supplemental oxygen. No patients had been accepted for lung transplantation or had α₁-antitrypsin deficiency. Chest roentgenograms showed hyperexpansion with flattening or inversion of the diaphragm. The heterogeneous pattern of emphysema on computed tomography (CT) was graded as severe and without isolated bullae larger than 5 cm.

Contraindications included current cigarette smoking, age older than 75 years, carbon dioxide retention greater than 55 mm Hg, severe cardiac disease, history of cancer within the past 5 years, ventilator dependency, presence of a lung mass, or prior thoracic surgery. All patients who underwent surgery for emphysema were randomized into this study unless (1) they had previously undergone an operation on the contralateral lung for emphysema at another institution, (2) a lung mass was identified, or (3) a large (>5 cm), discrete bulla was present.

This protocol was approved by the Institutional Review Board at Chapman Medical Center. After informed consent was obtained, patients were blindly randomized to either neodymium:yttrium-aluminum-garnet (Nd:YAG)

contact laser or resection of severe emphysematous areas of lung with staples and bovine pericardium. No patient refused randomization or crossed over to the other technique.

Baseline characteristics of the two surgical patient groups appear in Table I. All of the patients had severe fixed airflow limitation. The forced vital capacity (FVC) was 58% ± 9% of predicted values (mean ± SD) and the FEV₁ was 27% ± 6% of predicted values (mean ± SD). There were no statistically significant differences between the two groups with respect to age, sex, lung function, arterial oxygen tension, arterial carbon dioxide tension, CT emphysema score, smoking, and need for daily oxygen use for an arterial oxygen tension of less than 55 mm Hg at rest or during exercise. There was no significant difference between the laser and staple treatment groups (*p* = NS) with respect to right versus left lung or upper versus lower prevalence of emphysema.

Pulmonary rehabilitation was not routinely done before the operation, but all patients began rehabilitation in the hospital after the operation. This included education regarding proper breathing techniques, anxiety control, stretching and strengthening exercises, and walking on the stairs and treadmill. The program was continued on an outpatient basis at Chapman Medical Center for 2 to 3 weeks after discharge. The vast majority of patients lived a long distance from our hospital, and they were eager to return home. They were strongly encouraged to join a Better Breathers' Club and rehabilitation program at home.

Operative technique. All patients underwent unilateral video-assisted thoracic surgery (VATS). They were paralyzed with pipecuronium and given general anesthesia with isoflurane. The procedure was done through a left-sided double-lumen tube (Mallinckrodt Anesthesia, St. Louis, Mo.). The trocar and thoracoscope were placed through the tenth intercostal space in the posterior axillary line. Three additional 1 to 2 cm incisions were made for standard instruments, such as ring forceps.

The laser procedure was performed with a contact tip on the Nd:YAG laser at 10 W. The entire pleural surface of the lung, including the fissures, was treated with the laser until maximal shrinkage was obtained. The less involved areas showed minimal shrinkage. The average number of joules per case was 22,598 (range 14,156 to 29,115 joules).

For the staple procedure, the worst areas of destroyed lung identified by the preoperative CT were resected. Ring forceps manipulated the lung into a 60 mm endoscopic stapler (ELC 60, Ethicon, Inc., Somerville, N.J.) with bovine pericardium (Peristrips, Biovascular, St. Paul, Minn.) to buttress the staples. The average number of staples fired per case was 9 (range 4 to 14). Approximately 20% to 30% of the lung was resected. Specimen weight ranged from 30 to 90 gm. Pleural tents and pleurodesis were not performed.

For both procedures, the chest was drained with two apically placed chest tubes. The patients routinely were taken to the intensive care unit for an overnight stay.

Lung function studies. All patients underwent studies of arterial blood gases and lung function that included static lung volumes measured by plethysmographic tech-

niques,⁶ as well as timed spirometry and single-breath diffusing capacity in accordance with American Thoracic Society recommendations.^{7, 8} Values were then compared with those predicted.⁹⁻¹¹ All patients were considered to have fixed airflow limitation because the FEV₁ after three inhalations of aerosolized albuterol (670 µg) improved more than 12% or more than 200 ml.⁶ Maximum inspiratory and expiratory flow volume curves, thoracic gas volume,¹⁰ and airway resistance¹¹ were measured in a plethysmograph (models 2800 and 6200, SensorMedics, Inc., Yorba Buena, Calif.) and compared with predicted values.¹⁰ The reciprocal of airway resistance¹⁰ is conductance; it was divided by the thoracic gas volume at which it was measured and specific conductance was calculated. Normal values are greater than 0.7 L per second per centimeter of water per liter.¹² Residual volume was calculated by subtracting vital capacity from total lung capacity. Complete lung function studies were obtained before the operation and only timed spirometry and arterial blood gas studies were obtained 6 months after the operation.

Statistical methods. Group description statistics are expressed as mean ± standard error of the mean unless otherwise specified. Differences between groups are compared by means of two-tailed paired *t* tests with *p* < 0.05 being considered significant. Pearson's χ^2 statistics are used to determine differences in laser- versus staple-treated groups for categorical variables.

Clinical evaluation. Before the operation and 6 months after the operation, an MOS-36 quality-of-life questionnaire¹² and dyspnea index were scored to document lifestyle improvement and response to surgical intervention.

Results

The mean postoperative length of stay was 10.6 ± 2.0 days (range 4 to 20 days) for the laser group and 13.7 ± 1.9 days (range 3-66 days) for the staple treatment group (*p* = NS). All chest tubes were removed before discharge, and in most cases the patients were discharged on the day that the chest tubes were removed. The chest tubes were in place for 9.8 days for the laser group and 13.2 days for the staple-treatment group (*p* = not significant). Prolonged air leak was primarily responsible for the longer length of stay in the staple-treatment group.

Mortality. No deaths occurred in the laser group and one death (2.5%) in the staple-treatment group owing to a contralateral tension pneumothorax. No further deaths have occurred in the staple-treatment group, but three patients in the laser group have died since discharge from the hospital. One patient, whose clinical condition had improved, died of a self-inflicted gunshot wound 6 weeks after the operation. Another patient was clinically well but died 3 months later in his sleep. The condition of the third

Table II. Comparison of the complications for the two procedures

	Laser (n = 33)	Staple (n = 39)	<i>p</i> Value
Hospital days (mean ± SD)	11 ± 12	13 ± 11	NS
Air leak >7 days (No.)	11 (33%)	19 (48%)	NS
Death (No.)	0	1 (2.5%)	NS
Respiratory failure (No.)	0	1 (2.5%)	NS
Operating time (hr)	2.1 ± 0.7	1.9 ± 1.0	NS
Take back (No.)	1 (3%)	1 (2.5%)	NS
Ileus (No.)	1 (3%)	0	NS
Deep vein thrombosis (No.)	0	1 (2.5%)	NS
Delayed pneumothorax (No.)	6 (18%)	0	0.005

Respiratory failure is reintubation and use of mechanical ventilator, *take-back* is second thoracotomy for persistent air leaks, and *pneumothorax* is pneumothorax requiring chest tube and hospitalization. Data are presented as mean ± standard deviation or percent incidence.

patient steadily deteriorated after laser bullectomy and he died of respiratory failure 3 months later.

Morbidity. The morbidity for the two procedures is shown in Table II. In each group, one patient underwent reoperation for closure of a persistent air leak. One patient in the staple-treatment group had a 48-day postoperative course complicated by respiratory failure when massive hyperexpansion that physiologically behaved like a tension pneumothorax developed in the contralateral lung. This decreased the cardiac index to 0.8 L/m² and the patient required separate ventilators for the right and left lungs. He ultimately made a full recovery, and 6 months later he has a 75% improvement in the FEV₁ compared with the preoperative value. One patient in the laser group had massive intestinal air and an ileus that prolonged the hospital course to 12 days.

Delayed pneumothorax occurred 2 weeks to 4 months after discharge in six (18%) patients who underwent the laser procedure. This occurrence resulted in significant clinical deterioration that lasted months before recovery. This complication did not occur in patients who underwent the staple procedure (*p* = 0.005).

Clinical status. The MOS-36 quality-of-life questionnaire showed significant improvement and dyspnea index improved by more than one grade in eight of the 33 (24%) laser-treated patients compared with 26 of the 39 (66%) patients treated with the staple technique (*p* = 0.003).

Oxygen use. Of the 25 patients who were dependent on supplemental oxygen before laser bullectomy, 13 (52%) no longer require supplemental

Table III. Results of various techniques for lung reduction surgery for diffuse emphysema

First author	Procedure	Method	No. of patients	FEV ₁ (%)
McKenna	YAG contact	Unilateral	33	13.4
Little ¹³	YAG	Unilateral	55	18
Eugene ¹⁴	YAG/KTP + Staples	Unilateral	28	34
McKenna	Staples	Unilateral	39	33
Cooper ⁴	Staples	Bilateral	20	82

The laser procedure was performed in the free beam mode unless otherwise stipulated. *Method* indicates whether the procedure was performed unilaterally or bilaterally.

oxygen 6 months after the procedure. Of the 27 patients who were receiving supplemental oxygen before stapled lung reduction, 22 (87.5%) did not require supplemental oxygen 6 months after the procedure ($p = 0.02$).

Lung function (Table III). Pulmonary function test follow-up was obtained from 26 of 30 surviving laser patients (87%) and 36 of 38 surviving staple-treatment patients (95%). The six other patients refused to undergo follow-up pulmonary function tests. The mean improvement in FEV₁ at 6 months was 0.09 L (13.4% \pm 5.5%) for the laser group and 0.22 L (32.9% \pm 4.8%) for the staple-treatment group ($p = 0.01$).

Six months after the operation, the mean increase in the FVC was 0.13 L (6% \pm 3%) for the laser bullectomy group and 0.35 L (21% \pm 6%) for the staple-treatment group ($p = 0.07$). Only in the staple-treatment group was the improvement in the FEV₁ and the FVC from baseline significant ($p < 0.006$).

Discussion

Operations for emphysema are currently being performed unilaterally and bilaterally at various institutions, and the technique for the lung reduction operation may be either laser or stapling techniques, or a combination of the two. This study was specifically designed to compare the efficacy of the laser and stapling techniques. Because laser bullectomy is performed by unilateral thoracoscopy, the stapling technique was also performed by unilateral thoracoscopy.

This prospective, blindly randomized study demonstrates that patients in whom lung volume reduction surgery is done with staples and bovine pericardium have a lower morbidity (fewer delayed pneumothoraces), as well as greater improvement in

oxygen independence, lung function, and overall lifestyle and dyspnea scale, than patients treated with the Nd:YAG contact laser.

Little information has been published regarding the efficacy of the various procedures for the surgical treatment of diffuse emphysema. Little and associates¹³ reported a series of 55 patients with diffuse emphysema who underwent unilateral free-beam laser treatment with the Nd:YAG laser. The preoperative FEV₁ improved from 0.74 to 0.85 L (18%).

Eugene and coworkers¹⁴ reported the results of staples and either free-beam potassium-titanyl-phosphate or Nd:YAG laser therapy for 28 patients with diffuse emphysema. The FEV₁ increased from 0.68 to 0.91 L (34%). There were no hospital deaths, but three patients died within 3 months (11%). Subjective improvement occurred in 22 of 28 patients (78.6%), and the preoperative oxygen dependence was eliminated in five of 23 (21%) patients.

With a bilateral stapling technique, Cooper⁵ reported marked clinical improvement and a mean increase of 82% in the FEV₁ and 27% in the FVC compared with baseline at 6 months in patients with lung function similar to that of the patients in the current study. In his 20 patients, Cooper reported no mortality, a mean hospital stay of 15 days, air leak for more than 7 days in 11 patients, and reexploration in four patients.

The results of the current study are compared with the results of these studies in Table III. The Nd:YAG laser without staples shows similar results with either a free beam (Little and coworkers¹³) or contact tip (current study). The combination of the staples and laser procedure (Eugene and colleagues¹⁴) provided the same improvement in pulmonary function achieved with staples alone (current study). Little's group reported a 20% incidence of delayed pneumothorax, which is similar to our 18% incidence. Delayed pneumothorax is not mentioned by Eugene and associates. The risk of additional morbidity (delayed pneumothorax) and the lack of additional benefit from the use of the laser has led us to abandon its use until a definite role for it can be identified.

Mechanisms for improved pulmonary function after operations for emphysema have been studied. Rogers,¹⁵ Gelb,¹⁶ and their colleagues have found that resection of large bulla in isolated bullous disease and bullous emphysema resulted in improvement in expiratory airflow and airway conductance that could be accounted for by the improve-

ment in elastic recoil. Similar mechanisms may explain the improved lung function after lung reduction operations for generalized emphysema.

Most patients who are candidates for lung reduction surgery have a thin superficial layer of better lung tissue and clusters of 1 to 2 cm bullae (severe emphysematous change) located deeper within the lobe. The laser is excellent for shrinking superficial areas of emphysema but does not have much effect on lung tissue with minimal emphysematous change. The laser does not penetrate to the deeper emphysematous areas within the lobe. The staple procedure may be more effective because aggressive resection of emphysematous areas can provide greater lung reduction than the shrinkage that results from the use of the laser. This allows for the greatest potential improvement in lung elastic recoil.

On the basis of the results of this study and previous studies,¹⁻⁵ our current procedure of choice for diffuse emphysema is bilateral lung reduction surgery with staples. We have used the median sternotomy, but thoracoscopy continues to be the primary method of performing these lung reduction procedures at our institution. The lateral approach (with thoracoscopy) provides better access than the median sternotomy if the area of emphysema targeted for resection is located posteriorly and better access for lysis of posteriorly located adhesions (which have been found in approximately 30% of our patients). The majority of the operations can probably be performed equally well through either approach.

The surgical treatment of emphysema is palliative, and patients are expected to eventually return to their preoperative level of dyspnea if they survive long enough. Numerous patients in this study are no longer significantly limited by dyspnea. This fact raises the question of whether this procedure should be performed unilaterally or bilaterally. If preoperative testing could identify which patients can be adequately treated by a unilateral operation, perhaps the other side should be saved for the future in case of subsequent development of new-onset dyspnea. Long-term follow-up will answer this question.

In conclusion, our results demonstrate a lower morbidity (fewer delayed air leaks) and a greater overall improvement in clinical status for patients with generalized emphysema after surgery with staples and bovine pericardium than with the Nd:YAG contact laser.

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