

Outcomes in lung transplantation after previous lung volume reduction surgery in a contemporary cohort

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Objectives: Lung volume reduction surgery (LVRS) provides palliation and improved quality of life in select patients with end-stage chronic obstructive pulmonary disease (COPD). The effect of previous LVRS on lung transplant outcomes has been inadequately studied. We report our experience in the largest single institution series of these combined procedures.

Methods: The records of 472 patients with COPD undergoing lung transplantation or LVRS between 1995 and 2010 were reviewed. Outcomes of patients undergoing transplant after LVRS were compared with outcomes of patients undergoing transplant or LVRS alone. Survival was compared using log-rank tests and the Kaplan-Meier method.

Results: Demographics, comorbidities, and spirometry were similar at the time of transplantation. Patients who had undergone lung transplant after LVRS had longer transplant operative times (mean 4.4 vs 5.6 hours; $P = .020$) and greater hospital length of stay (mean 17.6 vs 29.1 days; $P = .005$). Thirty-day mortality and major morbidity were similar. Posttransplant survival was reduced for transplant after LVRS (median, 49 months; 95% confidence interval [CI], 16, 85 months) compared with transplant alone (median, 96 months; 95% CI, 82, 106 months; $P = .008$). The composite benefit of combined procedures, defined as bridge from LVRS to transplant of 55 months and posttransplant survival of 49 months (total 104 months), was comparable with survival of patients undergoing either procedure alone.

Conclusions: Lung transplant after LVRS leads to minimal additional perioperative risk. The reduced posttransplant survival in patients undergoing combined procedures is in contradistinction to reports from other smaller series. When determining the best surgical treatment for patients with more severe disease, the benefit of LVRS before transplant should be weighed against the consequence of reduced posttransplant survival. (J Thorac Cardiovasc Surg 2014;147:1678-83)

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Chronic obstructive pulmonary disease (COPD) is the third leading cause of death in the United States accounting for more than 130,000 deaths each year.¹ Medical therapy and supportive care may improve symptoms and quality of life but are unable to reverse the course of the disease.

For many patients, surgical intervention offers the best long-term outcomes. Surgical treatment of end-stage COPD consists of either lung volume reduction surgery (LVRS) or lung transplantation. Early results from LVRS in the 1990s, demonstrated significant improvements in pulmonary function tests (PFTs), dyspnea, and quality of life.^{2,3} The results were further substantiated by the publication of the National Emphysema Treatment Trial (NETT), which refined patient selection and identified those who derive optimal benefit from this surgical therapy.⁴ Lung transplantation has also benefitted patients with limited life expectancy from end-stage COPD. It is associated with improved physical and social functioning, mental health, health perceptions, and patient-reported quality of life.⁵⁻⁸ However, not all patients with end-stage COPD meet the requirements for lung transplantation, and for those who do, the shortage of organ donors limits the number of lung transplants that can be performed. Thus, many have advocated for use of LVRS as a palliative surgical procedure in lieu of or as a bridge to lung transplantation. The posttransplant outcomes of these surgical procedures used in combination have been incompletely described. For this study, we reviewed our institutional

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Abbreviations and Acronyms

COPD	= chronic obstructive pulmonary disease
CI	= confidence interval
FEV ₁	= forced expiratory volume in 1 second
ICU	= intensive care unit
LAS	= lung allocation score
LVRS	= lung volume reduction surgery
NETT	= National Emphysema Treatment Trial
PFT	= pulmonary function tests
PVR	= pulmonary vascular resistance
RV	= residual volume
SD	= standard deviation

experience with patients with end-stage COPD who underwent LVRS, lung transplant, or both procedures to characterize posttransplant outcomes.

METHODS**Patient Cohort and Variables**

The University of Washington Investigational Review Board for human subjects approved the study protocol. We reviewed the records of 473 adults with end-stage COPD undergoing lung transplantation or LVRS at our institution between 1995 and 2010. Patients presented to our multidisciplinary clinic for evaluation for either or both surgical procedures. A nurse coordinator screened patients who were further reviewed by 2 physicians before surgical consultation. The University of Washington was a participating site for the NETT and thus patients evaluated in the clinic during this time were also considered for enrollment in this trial. Patients undergoing LVRS after publication of the NETT results were selected based on NETT criteria. A total of 138 patients underwent lung transplantation and 335 patients underwent LVRS as their initial surgical therapy. Of the latter, 37 patients subsequently received a lung transplant. The record of 1 patient undergoing transplant after LVRS had insufficient follow-up data and was excluded from our analyses.

Clinical variables included patient demographics, PFTs, and preoperative comorbidities. The primary outcome of interest was overall survival after LVRS or transplantation. Secondary outcomes included perioperative and long-term complications after either procedure.

LVRS and Lung Transplantation Surgical Techniques

LVRS was performed via median sternotomy or video-assisted technique with sequential stapling and buttress. Areas of most severe hyperinflation, identified using preoperative imaging and intraoperative assessment, were selected for resection. Bilateral lung transplant was performed using a bilateral sequential technique via anterior thoracotomies with or without transverse sternotomy. Single lung transplant was performed via unilateral anterior thoracotomy. Cardiopulmonary bypass was used only in select cases.

Statistical Analysis

Descriptive statistics were expressed by median (95% confidence interval [CI]) or mean (standard deviation [SD]). Comparisons of categorical variables were made using the χ^2 test or the Fisher exact test when applicable. Continuous variables were compared using the Student *t* test or analysis of variance. Survival analysis was conducted using the Kaplan-Meier method

and compared using the log-rank test. All statistical analyses were performed using STATA version 12.1 (Stata Corporation, College Station, Tex).

RESULTS

Patients undergoing LVRS alone were older (mean 63.3 years, SD 7.6 years) than patients who had lung transplantation after LVRS (mean 54.7 years, SD 6.9 years) or those undergoing lung transplantation alone (mean 57.8 years, SD 6.0 years) ($P = .024$). Mean follow-up after LVRS was 19 months (SD 26 months) for LVRS alone. Mean follow-up after transplant was 50 months (SD 44 months) for combined LVRS and lung transplant, and 59 months (SD 38 months) for transplant alone (Table 1).

Transplantation Outcomes

When we compared posttransplant outcomes for those patients undergoing transplant after LVRS or transplant alone, we found similar pretransplant comorbidities and PFTs. Pretransplant pulmonary vascular resistance (PVR) was higher in those patients presenting for transplant after LVRS than patients undergoing transplant alone (2.2 vs 4.0 Woods units; $P = .002$) (Table 2). Transplant operative times were also longer for patients with transplant after LVRS (5.57 hours, SD 1.24 hours vs 4.40 hours, SD 1.20 hours; $P = .020$). All other intraoperative variables, including the need for cardiopulmonary bypass, estimated blood loss, and fluid and blood transfusion requirements, were similar between groups. Perioperative mortality was not significantly different between groups (30-day mortality 5.6% for transplant after LVRS vs 3.6% for transplant alone; $P = .599$). Mean hospital length of stay was longer in patients undergoing transplant after LVRS (29.06 days, SD 32.82 days) compared with transplant only patients (17.57 days, SD 16.97 days; $P = .005$).

LVRS Outcomes

We further compared the surgical outcomes for patients undergoing LVRS alone with those undergoing LVRS and subsequent transplant (Table 3). Nearly all patients undergoing LVRS had bilateral procedures. In pre-LVRS PFTs, forced expiratory volume in 1 second (FEV₁) percentage predicted was significantly lower in the group undergoing subsequent transplant compared with patients undergoing LVRS alone (22.39%, SD 6.06% vs 27.02%, SD 7.80%, $P = .003$). Residual volume (RV) percentage predicted was also higher in the group undergoing subsequent transplant (262.4%, SD 54.8% vs 229.9%, SD 57.7%, $P = .009$) compared with LVRS alone. All other PFTs showed no difference between groups. The data were also examined by date of LVRS using 2003 as a cut-off coincident with the publication of the results of the NETT. Of patients undergoing LVRS during the pre-NETT era (1995-2002), 16% had subsequent lung transplant compared with 4% of patients undergoing LVRS post-NETT (2003-2010)

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