BEST PRACTICES IN: Lung Volume Reduction Surgery for Emphysema

Emphysema is associated with the loss of lung elastic recoil, collapse of small airways, hyperinflation of the lungs, increased work of breathing, and progressive disability. Lung Volume Reduction Surgery (LVRS) is designed to remove the most diseased portions of the lung, reducing hyperinflation and improving respiratory mechanics, dyspnea, and quality of life.

In 1994 we presented our initial results with bilateral LVRS for emphysema,[1] and subsequently published results of the initial 250 consecutive patients undergoing this procedure.[2] The 90-day mortality was 4%, the median follow-up was 4.4 years, and the 5-year survival was 68%. The mean pre-op forced expiratory volume in 1 second (FEV_1) was 26% of predicted and increased by 54% at 6 months and by 31% at 3 years, with significant benefit out to 5 years. The mean pre-op residual volume (RV) was 280% of predicted and was decreased by 31% at 6 months and 28% at 3 years with significant benefit out to 5 years. Other documented benefits included a reduction in dyspnea and supplemental oxygen requirements with improved exercise tolerance and quality of life.

Reports from other centers confirmed the benefits of LVRS, but rapid proliferation of LVRS with less stringent patient selection, variability in surgical procedures, and in reported outcomes generated uncertainty regarding the true benefits of LVRS. In January 1996 Medicare suspended payment for LVRS and co-sponsored a long-term randomized trial with the National Institutes of Health comparing LVRS with ongoing medical management.

During the development of the National Emphysema Treatment Trial (NETT) protocol, an analysis of available LVRS data was undertaken to help guide the study protocols. A hypothesis was generated which stated that patients who have "heterogeneously distributed emphysema involving the upper lung zones predominantly" would be those most likely to benefit from LVRS.[3] The actual selection criteria for patients enrolled in the NETT, however, were much broader and "were crafted to include all patients who might benefit from LVRS."[4]

The trial was a multicenter randomized clinical trial of medical therapy versus medical therapy plus bilateral lung volume reduction surgery. The primary outcome to be assessed was survival,[5] and an additional primary outcome was exercise tolerance as measured by cycle ergometry. A number of secondary outcomes were defined including pulmonary function, dyspnea, and quality of life.

Patients with a homogeneous pattern of emphysema were initially excluded from the NETT if either the FEV_1, or the diffusing capacity was less than 25% of the predicted value or if the residual volume was less than 220% of predicted. Because of overall disappointing recruitment to the trial, the above exclusion criteria for patients with a homogeneous pattern of emphysema were eliminated, permitting such patients to be enrolled in the trial at the discretion of the individual centers.[6]

In August 2001, following randomization of 1,033 patients, the NETT data safety monitoring board identified a subgroup of patients who were at high risk of death following lung volume reduction surgery and who appeared to achieve little benefit from the procedure.[7] Nearly two thirds of these patients had homogeneous disease and were ineligible according to the initial criteria, but were enrolled after the orginal exclusions were dropped.

This early report of patients at high risk for LVRS was the subject of widespread publicity and dealt a major blow both to NETT recruitment and to the general perception as to the value of LVRS. In May 2003, the NETT reported on the 2-year follow up results of the medical and surgical arms of the NETT.[6] Among the conclusions were that for the overall group, LVRS does not confer survival advantage over medical therapy but does increase the chance for improved exercise capacity. Retrospective analysis suggested a survival advantage for a subgroup of patients with predominantly upper lobe emphysema and low baseline exercise capacity. Following the report, Medicare restored coverage for patients with predominantly upper lobe emphysema.

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Under The Freedom of Information Act, we obtained the NETT data set, which contained follow-up data as of May 2006 and identified which medical and surgical patients pre-operatively met the NETT criteria for a heterogeneous pattern of emphysema with upper lobe predominance, a group we refer to as the "target group". Of the 1,218 patients enrolled in the NETT, 511 patients met these criteria and included 261 patients who received bilateral LVRS and 250 patients who received medical management. For these patients, LVRS compared with medical management produced significant benefit in terms of 5-year survival, exercise capacity, quality of life, and measured lung function. 5-year survival was 70% for the surgical group and 60% for the medical group (P=0.02). Following LVRS, improvement in the FEV_1 over baseline values were 42%, 35%, and 26% at 6 months, 1 year, and 3 years, respectively. The residual volume declined by 30%, 28%, and 25% at the same time periods. All of these results were highly statistically significant compared with the corresponding medical group, as shown in **Figures** 1 and 2.

Figure 1. FEV_1% Predicted

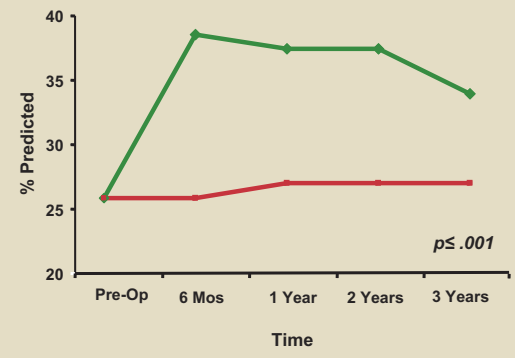
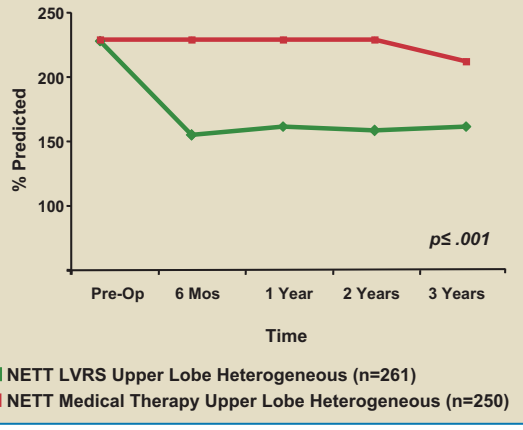


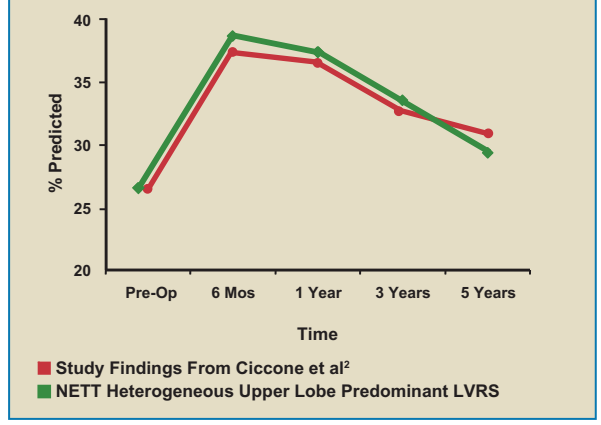
Figure 2. RV% Predicted



We analyzed the results of LVRS in the "target group" of NETT patients stratified for high or low baseline exercise capacity using the NETT criteria. Contrary to the initial report of the NETT, we found that the benefits of LVRS applied equally to both groups of patients.

We compared the results of LVRS in the NETT "target group" of patients with those we previously reported in the series of 250 consecutive bilateral LVRS patients. The results were remarkably similar between the two series in terms of survival, improvement in FEV_1, and reduction in residual volume. The change in FEV_1 over time for the two series is depicted in **Figure** 3.

Figure 3. FEV_1% Predicted



In retrospect, much of the confusion and conflicting results generated by the NETT were due to the fact that only 42% of patients enrolled in the trial met the eligibility criteria consistent with the NETT hypothesis as to who would likely benefit from LVRS, but there was no stratification or separate analysis of these patients. Furthermore, the eligibility criteria were changed twice after the trial began.

Because reduction of hyperinflation by LVRS has been shown to significantly benefit appropriately selected emphysema patients, a number of endoscopic procedures have been proposed in an attempt to achieve a "volume reduction" effect. At the present time, none of these experimental procedures (valves, adhesive, airway bypass) has demonstrated sufficient efficacy to warrant FDA approval. This, coupled with the reduction in priority status for COPD patients seeking a lung transplant, greatly increases the current role of LVRS in the management of patients with severe COPD.

Conclusion

Overall, the NETT has proven to be extremely informative, having confirmed in a randomized trial the value of LVRS for appropriately selected candidates.

The patients most likely to benefit from LVRS have heterogeneously distributed emphysema involving the upper lung zones predominantly, and the significant benefit in terms of survival, functional improvement, and quality of life apply equally to patients with either high or low baseline exercise capacity.

References

1. Cooper JD, Trulock EP, Triantafillou AN, et al. Bilateral pneumonectomy (volume reduction) for chronic obstructive pulmonary disease. *J Thorac Cardiovasc Surg.* 1995;109:106-119.
2. Ciccone AM, Meyers BF, Guthrie TJ, et al. Long-term outcome of bilateral lung volume reduction in 250 consecutive patients with emphysema. *J Thorac Cardiovasc Surg.* 2003;125:513-525.
3. Minutes of NETT Steering Committee. March 24-25, 1997.
4. Fishman A, Martinez F, Naunheim K, et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. *N Engl J Med.* 2003;348:2059-2073.
5. The National Emphysema Treatment Trial Research Group. Rationale and design of The National Emphysema Treatment Trial: A prospective randomized trial of lung volume reduction surgery. *Chest.* 1999;116:1750-1761.
6. Minutes of NETT Steering Committee. Approved October 30, 1998.
7. The National Emphysema Treatment Trial Research Group. Patients at high risk of death after lung-volume-reduction surgery. *N Engl J Med.* 2001;345:1075-1083.

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