Pathologic Findings in Lung Volume Reduction Surgery*

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Purpose: Lung volume reduction surgery (LVRS) has re-emerged as an alternative in the management of patients with chronic, debilitating, emphysematous lung disease. This has permitted the formal evaluation of pathologic pulmonary changes present in these patients. This study seeks to describe systematically the pathologic findings present in patients undergoing LVRS.

Methods: Tissue sections stained with hematoxylin-eosin, as well as special stains, were retrospectively reviewed from the specimens of 65 nonconsecutive LVRS patients (male patients, 66%; female patients, 31%; mean age, 63.2 ± 6.76 yr). All operations were conducted via an open technique (bilateral, 83%; unilateral, 17%).

Results: Histologic emphysema grade was mild in 9%, moderate in 72%, and severe in 19% of patients. Microscopic bullae were noted in 75% of specimens. Three patients, each with radiographic evidence of a lesion preoperatively, had small (1.1 to 2.8 cm) adenocarcinomas. Granulomatous bronchiolitis and pneumonitis were noted in one patient who postoperatively developed progressive respiratory compromise. An old, inactive aspergilloma was found in the specimen of another patient. Additional findings of potential clinical significance included bronchiolitis (54), bronchiolectasis (6), and bronchoalveolar metaplasia (1). Incidental findings included interstitial fibrosis and scar (55), interstitial inflammation (20), calcification (20), and ossification (11), bone marrow emboli (4), chemodectoma (2), and carcinoid tumorlets (1).

Conclusion: This systematic analysis of the resected specimens from patients undergoing LVRS describes a wide range of pathologic findings, including those clinically relevant, as well as incidental. As the application of LVRS continues to expand, the likelihood of discovering clinically significant pathologic lesions (eg, carcinoma) will undoubtedly increase.

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Key words: emphysema; lung volume reduction surgery; pathology

Abbreviation: LVRS = lung volume reduction surgery

Lung volume reduction surgery (LVRS) was pioneered as a therapeutic modality for the treatment of end-stage emphysema by Brantigan and Mueller in 1957.1 Initial attempts were fraught with significant operative mortality and failure to objectively demonstrate improved pulmonary function.2 As a result, medical therapy persisted as the primary form of treatment for COPD.

The concept of surgical resection of diseased lung for the treatment of end-stage emphysema was reintroduced by Cooper and others3 in 1994. Refinement in surgical technique, improvement in preoperative evaluation and postoperative critical care, and enhancement of pulmonary function analysis have permitted LVRS to re-emerge as a truly viable alternative in the management of select patients with chronic, debilitating, emphysematous lung disease.4,6

Autopsy evaluations have served as the primary source of investigation of the pathologic changes in patients with COPD. The reinstitution of LVRS now permits formal evaluation of the diverse pathologic pulmonary findings present in this patient population at varying stages of disease development. Clinically significant lesions have been reported in patients who underwent LVRS. These primarily have consisted of preoperatively diagnosed mass lesions confirmed to be primary pulmonary carcinomas on subsequent postoperative histopathologic evaluation.7-9 A thorough, formal evaluation of symptom-
atic and asymptomatic, clinically significant, as well as potentially significant, pathologic lesions from the resected specimens of LVRS patients remains to be reported.

This study seeks to provide a retrospective, descriptive summary of anticipated and unusual pathologic findings present in patients undergoing LVRS for severe, emphysematous lung disease.

**Materials and Methods**

**Patient Population**

The clinical records of the initial 65 patients who underwent LVRS at Emory University Hospital (1994 to 1996) were reviewed for demographic and surgical data. Routine demographics including gender and age, as well as details of the operative technique, were registered. The tissue specimens from five additional patients who underwent LVRS at affiliated hospitals were not available for evaluation, and they were consequently not included in the study.

Criteria for LVRS were previously reported from this institution in a preliminary communication: clinically advanced generalized emphysema; no bullae greater than 5 cm in size; failure of maximum medical therapy; an age of less than 75 years; spirometry and arterial blood gas levels with an FEV1 of less than 30% of predicted, a carbon dioxide tension of 50 mm Hg or less, an oxygen tension of more than 40 mm Hg with the patient breathing room air; no significant coronary artery disease; no major psychiatric problems; no life-threatening illnesses; ability to perform pulmonary rehabilitation; abstinence from all tobacco use for a minimum of 6 months; prednisone dosages of less than 15 mg/d; and absence of generalized osteoporosis.10 All patients underwent a thorough preoperative evaluation prior to undergoing the open-lung volume reduction operation: inspiratory and expiratory chest radiographs, pulmonary function tests, arterial blood gas, value analysis, a 6-min walk test, high-resolution CT scan of the chest, split ventilation-perfusion nuclear scan, dobutamine stress echocardiography, catheterization of the right side of the heart, and catheterization of the left side of the heart when warranted. Furthermore, all candidates were enrolled in an aggressive pulmonary rehabilitation program for at least 6 weeks prior to the surgical operation.

**Histopathologic Evaluation**

Tissue specimens were received at the time of the initial surgical operation and were fixed in 10% neutral buffered aqueous formaldehyde solution (Formalin). At gross examination, sections of tissue from the mass lesions, indurated areas, cavity lesions, and uninvolved lung were sampled. The hematoxylin-eosin-stained sections from the specimens of these 65 patients were systematically reviewed with use of light microscopy. The average number of sections evaluated per case was 5±3 (range, 1 to 15). Special stains, including Gomori’s methenamine-silver for fungi, Ziehl-Neelsen stain for mycobacteria, Verhoeff-Van Gieson stain for elastic fibers, and Masson’s trichrome stain for collagen deposition, were similarly evaluated in select cases. Sections reviewed were evaluated without knowledge of clinical information.

The severity of emphysema was subjectively graded by one of the authors (A.A.G.); he determined the extent and distribution of changes in the tissue sections of nonbullous lung parenchyma from previously resected specimens (retrospective analysis). This evaluation was descriptive in nature and has not been previously reported. The pathologic evaluation of emphysema was based on nonbullous lung tissue to avoid overestimation of the extent and distribution of disease. Mild emphysema consisted of changes affecting less than 30% of alveolar spaces, moderate emphysema consisted of changes involving between 30 and 70%, and severe emphysema affected more than 70% of lung parenchyma. The severity of bronchiolitis was subjectively based on the degree of chronic inflammatory changes and mucous gland hyperplasia noted in bronchioles and was similarly graded as mild to severe. The type and location of fibrosis, interstitial vs subpleural, was also noted. Additional typical and unusual pulmonary pathologic findings also were documented.

**Results**

**Demographics**

The demographic and surgical data for the 65 patients are displayed in Table 1. Early mortality (≤30 postoperative days) was 4.6% (3 of 65). Late mortality was 6.1% (4 of 65).

**Histopathologic Findings**

**General Findings:** Though the type of emphysema could not always be clearly discerned from the tissue specimens evaluated, the majority of patients exhibited evidence of centrilobular emphysema. Histologic severity of emphysema was mild in 9% (6 of 65), moderate in 72% (47 of 65), and severe in 19% (12 of 65) of patients (Fig 1). The presence of bullous emphysema or of bullae was noted microscopically in 75% (49 of 65) of specimens. Bronchiolitis was present in 83% (54 of 65) of specimens; it was mild in 67% (44 of 65) and moderate in the remaining 16% (10 of 65).

**Clinically Significant Findings:** Three patients (4.6%) were found to have small (1.1 to 2.8 cm) primary, non-small cell carcinomas (Fig 2, top). Each of the three patients had radiographic evidence of a

**Table 1—Demographic and Surgical Data**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. (%)</th>
</tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>65</td>
</tr>
<tr>
<td>Age, yr (mean±SD)</td>
<td>63.2±6.76 (range: 50-75 yr)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>43 (66)</td>
</tr>
<tr>
<td>F</td>
<td>22 (34)</td>
</tr>
<tr>
<td>Cause of emphysema</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>63 (97)</td>
</tr>
<tr>
<td>α1-antitrypsin deficiency</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Surgical resection</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>54 (83)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>11 (17)</td>
</tr>
<tr>
<td>Right</td>
<td>6 (9)</td>
</tr>
<tr>
<td>Left</td>
<td>5 (8)</td>
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peripheral mass lesion (upper lobe of the right lung in each case) preoperatively, as demonstrated by high resolution CT scans (1 to 3 cm). In each case, the mass lesion was incorporated as part of the lung volume reduction excision. Final pathologic evaluation revealed the mass lesions to be primary, pulmonary adenocarcinomas, stage I, as per TNM classification (T1N0M0). All three patients were alive at the time of this report.

Potentially Significant Findings: Additional findings of potential clinical significance included granulomatous bronchiolitis and pneumonitis, noted in one patient who died postoperatively owing to progressive respiratory compromise (Fig 2, bottom). An old, inactive aspergilloma was found in the specimen of another patient with no known previous history of clinical Aspergillus infection (Fig 3). Further evidence of potential significance included bronchioloectasis (9% [6 of 65]) and bronchioloalveolar metaplasia (n=1).

Incidental Findings: Incidental findings included intraparenchymal fibrosis and scar formation in 85% (55 of 65) of patients and evidence of pleural changes in 77% (50 of 65) of all patients. These pleural changes include subpleural fibrosis in 52% (34 of 65) and subpleural elastosis in 25% (16 of 65) of patients. Interstitial inflammation was noted in 31% (20 of 65) of these surgical specimens. Interstitial granulomas were identified in 14 patients (22%), ranging from minute focal foreign body giant cell accumulations to granulomas with eosinophilic infiltrates and the aspergilloma previously described. Foci of calcification (31% [20 of 65]) and of ossification (17% [11 of 65]) were similarly documented. Additional findings included bone marrow emboli (n=4), chemodectoma-like lesions (n=2), and carcinoid tumorlets (n=1).
postoperative day 2, this patient developed a new pulmonary infiltrate visible on a chest radiograph, with fever and an elevated WBC count on postoperative day 5. His stay in the ICU was further prolonged by the presence of large, persistent air leaks, extensive subcutaneous emphysema, full ventilatory support, and the need for inotropic support. He eventually died after a cardiac arrest on postoperative day 60. The pattern of granulomatous bronchiolitis evident in the LVRS specimen may have been indicative of an underlying infectious pulmonary process, not detected preoperatively, that may have placed the patient at increased operative risk. No unique, identifiable pathologic characteristic was present in the specimens from the other patients who died.

Also of possible clinical relevance is the finding that a separate patient was found to have evidence of an old, inactive Aspergillus granuloma. The patient, however, had no previous history of Aspergillus infection, and his postoperative course was uncomplicated. This was most likely the result of a subclinical, innocuous fungal exposure.

Most significant, however, was the confirmation of the presence of a malignant tumor in the pulmonary tissues of three patients. McKenna et al9 recently reported 11 cases of patients undergoing video-assisted thoracoscopic LVRS and combined operation for lung cancer, with one additional patient having a primary pulmonary adenocarcinoma diagnosed only as an incidental pathologic finding.9 Pigula et al10 similarly described 1 of 128 patients undergoing a lung reduction operation having an unsuspected pulmonary carcinoma diagnosed from histopathologic evaluation, with an additional five patients preoperatively diagnosed with concomitant lung cancer while being evaluated for LVRS.7 The three patients in the initial series were found to have peripheral mass lesions consistent with lung cancer during their preoperative evaluation.13 These patients underwent wedge excision of the mass lesions as part of the LVRS, and this surgical intervention proved not only to be of symptomatic benefit, but also to be clearly of therapeutic importance.

CONCLUSION

In patients with severe, diffuse emphysema, tissue specimens from LVRS should expand our understanding of the diverse pathologic processes inherent in this category of COPD. Since the majority of LVRS patients are also at increased risk for smoking-induced lung carcinoma, the likelihood of discovering clinically significant lesions with LVRS will undoubtedly increase.
REFERENCES