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Lung Resection in Patients With Preoperative FEV<sub>1</sub> < 35% Predicted*

Philip A. Linden, MD; Raphael Bueno, MD, FCCP; Yolonda L. Colson, MD, PhD; Michael T. Jaklitsch, MD, FCCP; Jeanne Lukanich, MD, FCCP; Steven Mentzer, MD, FCCP; and David J. Sugarbaker, MD, FCCP

Objectives: To determine the morbidity, mortality, and feasibility of lung resection in patients with tumors and preoperative FEV<sub>1</sub> < 35% predicted.

Design: Retrospective review.

Setting: A 734-bed, tertiary care, academic hospital with a dedicated general thoracic surgery unit performing > 2,000 operations per year.

Patients: One hundred consecutive patients with discrete lung tumors and with preoperative FEV<sub>1</sub> < 35% predicted undergoing lung resection between September 1997 and May 2003. Only operations with curative intent were included. Average preoperative predicted FEV<sub>1</sub> was 26%. Sixteen percent of the patients were oxygen dependent prior to the operation.

Results: Open and thoracoscopic wedge resections, segmentectomies, lobectomies, and combined lung resections with lung volume reduction were performed. Sixty-six of the lesions were malignant, and 57 were primary lung cancers. Only one patient left the operating room with positive margins. There was one in-hospital or 30-day mortality. Thirty-six percent of the patients had one or more complications. Twenty-two percent of the patients had prolonged air leaks requiring a chest tube for > 7 days. One patient left the hospital ventilator dependent, 3 additional patients required intubation > 48 h, and 11 patients were discharged with a new oxygen requirement. There were four pneumonias, one myocardial infarction, and two reoperations for bleeding. Male gender (p = 0.003), preoperative oxygen dependence (p = 0.03), and pack-year history (p = 0.006) were associated with a higher overall incidence of complications, while age, incision, diabetes, coronary artery disease, duration of smoking cessation, amount of lung resected, size of lesion, and preoperative percentage of predicted FEV<sub>1</sub> did not correlate with the overall incidence of complications.

Conclusions: In a large academic center, minimally invasive surgical techniques, intensive pulmonary care, and advanced anesthetic techniques allow for curative lung tumor resections in patients with very low preoperative FEV<sub>1</sub> with a very low mortality and very low incidence of ventilator dependence. Other serious complications such as pneumonia, myocardial infarction, and bleeding are uncommon. An extended hospital stay and a high incidence of prolonged air leak should be expected, especially in patients with preoperative FEV<sub>1</sub> ≤ 20% predicted.


Key words: complications of surgery; emphysema; less invasive surgery; lung cancer diagnosis and staging; lung cancer surgery

Abbreviations: DLCO = diffusion capacity of the lung for carbon monoxide; VATS = video-assisted thoracoscopic surgery

Cigarette smokers are at increased risk for lung cancer as well as emphysema. Low FEV<sub>1</sub> has been established as a major limiting factor in lung tumor resection. Several studies<sup>1,2</sup> have shown an increase in mortality and morbidity if the predicted postoperative FEV<sub>1</sub> is < 35 to 40% (the predicted postoperative FEV<sub>1</sub> is calculated by taking the total FEV<sub>1</sub> and subtracting the amount of lung function to be removed [estimated as a percentage of functioning segments]). Not uncommonly, patients with predicted FEV<sub>1</sub> < 35% predicted are deemed inoperable and may be denied referral to a thoracic surgeon.

While lobectomy is the preferred resection for lung cancer,<sup>3</sup> lung-sparing resections such as segmentectomy<sup>4,5</sup> and wedge resection<sup>6</sup> are alternatives in patients with poor lung function. In addition, lung resection in association with lung volume reduction surgery may allow for removal of minimally functioning lung parenchyma containing tumor with improvement in lung function as measured by FEV<sub>1</sub>.

While previous studies<sup>7–9</sup> have examined lung...
resection in patients with poor lung function, prior studies have either been small or have examined patients with only moderately reduced (ie, FEV1 40 to 45% predicted) lung function. In an attempt to quantitate the current morbidity and mortality associated with resections in a larger number of patients, we examined our previous 100 consecutive lung tumor resections in patients with markedly impaired lung function (preoperative FEV1 < 35% predicted). Our review differs from prior studies7–9 in that it includes all patients with discrete, suspicious lung masses and severely compromised lung function undergoing potentially curative lung tumor resection. Following resection, some patients were found not to have malignancy; however, all were suspected of harboring malignancy prior to resection, all were potentially curable, and all had lung function below that which some would deem safe to allow for resection.

### Materials and Methods

One hundred consecutive patients with suspicious lung masses and preoperative FEV1 < 35% predicted underwent lung tumor resection between September 1997 and May 2003. The average age of patients undergoing operation was 64 ± 10 years (± SD) [range, 48 to 87 years]; 52% were male. Fifteen of the patients were oxygen dependent prior to operation. All patients had discrete lung masses; patients undergoing thoracoscopic biopsy for interstitial lung disease were excluded. All patients underwent surgery with curative intent. If more than one mass was present, the intention was complete resection. Some patients had a preoperative diagnosis established by needle biopsy; others were brought to the operating room for simultaneous definitive diagnosis and resection. All patients underwent preoperative pulmonary function testing and chest CT scanning including imaging of the upper abdomen. In addition, all patients in whom an anatomic dissection (lobectomy or segmentectomy) was contemplated underwent preoperative staging including head CT or MRI, bone scan or positron emission tomography, and preoperative mediastinoscopy.

In this group of patients with very low FEV1 (35%), the general algorithm for resection involved thoracoscopic wedge resection whenever feasible. These patients had intraoperative margins assessed by frozen section. If the tumor was deemed to be too central or large (usually > 3 cm) to allow for adequate margins, then consideration was given to either a thoracoscopic or muscle-sparing anatomic resection (segmentectomy or lobectomy). In these patients, the bronchial margin was checked using intraoperative frozen section. Frozen section examination of the parenchyma was used in cases where the tumor was near the fissure or staple line. Patients with heterogeneous emphysema (as determined by ventilation/perfusion scanning) with a tumor in a poorly functioning area of the lung were considered for tumor resection with concomitant lung volume reduction.

All patients underwent routine preoperative epidural catheter placement as well as invasive arterial line monitoring. Following the operation, all were monitored in a dedicated thoracic surgery intermediate care unit with 1:2 nursing, and continuous arterial line and pulse oximetry monitoring. Patients were ambulated beginning postoperative day 1.

Preoperative characteristics measured included age, gender, presence or absence of coronary artery disease, presence or absence of diabetes, oxygen dependence, size of lesion as measured by CT scan, and pulmonary function testing including FEV1. Measures of diffusion capacity of the lung for carbon monoxide (DLCO) were available in a minority of patients. In addition, smoking history, including number of pack-years smoked and length of cessation prior to resection, was noted. Perioperative measurements included type of incision, and amount of lung resected, final margins, and lung tumor histology. Postoperative complications monitored included myocardial infarction, bleeding, and infection. Respiratory complications measured included pneumonia, prolonged ventilator dependence, new oxygen dependence, or air leak > 7 days. Pneumonia was defined by the presence of two or more of the following three findings: increased fever/WBC count, infiltrate, and positive sputum Gram stain finding. Operative mortality was defined as either death within 30 days or in-hospital death.

The treating institution is a 734-bed, tertiary care, teaching facility with a dedicated general thoracic surgical ICU (10 beds) and 12 general thoracic surgical intermediate care unit beds. Eight staff general thoracic surgeons perform > 2,000 operations per year at the treating institution. This study was reviewed and approved by the institutional review board at Brigham and Women’s Hospital (protocol approval date, July 31, 2003).

### Statistical Methods

The outcome variables for the purposes of statistical analysis included death, length of stay, new oxygen dependence, respiratory failure, pneumonia, and air leak > 7 days. The explanatory variables included gender, age, presence or absence of coronary artery disease, presence or absence of diabetes, pack-year smoking history (number of packs per day smoked multiplied by number of years), duration of smoking cessation (if any), tumor size, preoperative oxygen dependence, FEV1, percentage of predicted FEV1, type of incision (thoracoscopic, video-assisted thoracoscopic surgery [VATS]), thoracotomy), amount of lung resected (wedge, segment, lobe), and DLCO (in a limited number of patients).

Both univariate and multivariate analyses were conducted. Univariate statistical methods included summary statistics, two-sample Wilcoxon rank-sum test, and Fisher exact test. Multivariate methods were multiple regression and logistic regression analyses.

### Results

The operations performed are detailed in Table 1. The average hospital stay was 8.3 ± 7 days. Univariate analysis revealed that male gender (p = 0.02, Wilcoxon rank-sum test) and preoperative oxygen...
dependence \( (p = 0.01, \text{ Wilcoxon rank-sum test}) \) were significant predictors of increased length of stay. The amount of lung resected did not predict the length of stay in this patient subgroup, as the average length of stay for patients undergoing wedge resection, segmentectomy, lobectomy, or wedge resection plus lung volume reduction were from 8.0 to 8.8 days. Preoperative \( \text{FEV}_1 \), percentage of predicted \( \text{FEV}_1 \), and type of incision did not predict length of stay.

There was one in-hospital or 30-day mortality. This occurred in a 69-year-old man with severe emphysema who underwent apical nodule resection via lung volume reduction. He had a diverticular abscess requiring colectomy complicated by sepsisemia and prolonged intubation resulting in death on postoperative day 21. Thirty-six percent of patients had one or more complication (Table 2). Nonpulmonary complications included myocardial infarction in one patient and reoperation for bleeding in two patients. Pneumonia developed in four patients. Four patients required intubation for \( > 48 \) h; one of these patients left the hospital ventilator dependent. Eleven patients were discharged with a new oxygen requirement. Twenty-two percent of the patients had prolonged air leaks for \( > 7 \) days; the average length of stay in these patients was 13.3 days. The length of stay in the remainder of the patients averaged 5.2 days.

Male gender \( (p = 0.01, \text{ Fisher exact test}) \), preoperative oxygen dependence \( (p = 0.01, \text{ Fisher exact test}) \), and preoperative percentage of predicted \( \text{FEV}_1 \) \( (p = 0.03, \text{ Wilcoxon rank-sum test}) \) were significantly correlated with prolonged air leak. Age, size of lesion, incision used, and amount of lung resected were not predictive. Male gender \( (p = 0.003, \text{ Fisher exact test}) \), preoperative oxygen dependence \( (p = 0.03, \text{ Fisher exact test}) \), and number of pack-years smoked \( (p = 0.006, \text{ Wilcoxon rank-sum test}) \) were associated with a higher overall incidence of complications, while age, coronary artery disease, diabetes, duration of smoking cessation, incision, amount of lung resected, size of lesion, and percentage of predicted \( \text{FEV}_1 \) did not correlate with the overall incidence of complications (Fig 1).

Multivariate analysis showed that only age was an independent predictor of length of stay \( (p = 0.02, \text{ multiple regression}) \). Male gender was the only independent predictor of one or more complications \( (p = 0.01, \text{ logistic regression}) \).

The average diameter of the resected tumors was 2.73 cm. Sixty-six percent of the lesions were malignant. Complete resection was achieved in all of these patients except one. Fifty-eight patients \( (88\% \text{ of all malignant lesions}) \) had primary lung cancer. Of the benign lesions, 9 were mycobacterial infections, there was 1 hemangioma, and 24 other benign lesions including granuloma, fibrosis, pneumonitis, and other inflammatory lesions (Table 3).

### Comments

This article represents a modern assessment of lung resection in a large group of patients presenting with lung masses and severely compromised lung function. Prior studies have examined lung resection in lung cancer patients with moderately and severely compromised lung function. Cerfolio et al examined 85 lung cancer patients with mean \( \text{FEV}_1 \) of 44% predicted undergoing resection and quoted a mortality rate of 2.4% and complication rate near 50%. Teneick et al looked at 73 lung cancer patients with a mean \( \text{FEV}_1 \) of 42% predicted and noted a mortality rate of 1.4% and a morbidity rate of only 4%. A smaller study of lung resection in 32 lung cancer patients with \( \text{FEV}_1 < 1.0 \text{ L} \) without peroperative mortality was described by Miller and Hatcher. This study represents an assessment of a larger number of patients whose lung function is more severely impaired than those previously examined. Moreover, unlike prior studies, we did not limit our review to patients with lung cancer; rather, we evaluated resections in patients with suspicious lung masses and severely compromised pulmonary function. In patients with clinically suspicious lung masses, it is often not possible to obtain a diagnosis prior to operation. Inclusion of all patients with a clinically suspicious lung mass provides a more clinically useful assessment of operative risk than does retrospective selection of only those found to have lung cancer.

The incidence of pulmonary complications in our study, other than prolonged air leak, was very low, and compares favorably to that described in prior series (Table 4). Four percent had pneumonia, 4% required prolonged mechanical ventilation, and 11% were discharged with a new oxygen requirement. Several factors may explain the low incidence of pulmonary complications in this high-risk group. First, a limited (both in terms of incision used and

### Table 2—Incidence of Complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>1</td>
</tr>
<tr>
<td>Prolonged air leak</td>
<td>22</td>
</tr>
<tr>
<td>New oxygen requirement</td>
<td>11</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>4</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4</td>
</tr>
<tr>
<td>Reoperation for bleeding</td>
<td>2</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
</tbody>
</table>
amount of lung resected) operation was performed whenever possible. Patients with lesions ≤ 3 cm in the peripheral third of the lung could be resected via thoracoscopic wedge resection. The majority of patients in this series (65%) were treated in this manner. Lesions > 3 cm or those more centrally located generally required segmentectomy or lobectomy for removal. In patients with an occluded bronchus, lobectomy was performed without concern of diminishing lung capacity. In those patients with heterogeneous, upper lobe-predominant emphysema, wedge resection or upper lobectomy as a mode of lung volume reduction was employed. Second, placement of a thoracic epidural was routine in all of these patients, even if the operation was to be limited to a thoracoscopic resection. The amount of postoperative pain following thoracoscopy can be difficult to predict. Any significant amount of chest wall pain in this group of patients with severely compromised function can have a significant negative impact on pulmonary toilet and clearance. Third, all patients were cared for in a dedicated thoracic surgical intermediate care unit with nurses trained in pulmonary care, and all patients ambulated with the aid of a walker beginning the first postoperative day. Preoperative dependence on oxygen was not a prohibitive risk factor in this group of patients. In those patients who were dependent on oxygen preoperatively, the only pulmonary complication seen was prolonged air leak (8 of 15 patients).

The three predictors of prolonged air leak were

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**Table 3—Histology Results**

<table>
<thead>
<tr>
<th>Variables</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant lesions</td>
<td>66</td>
</tr>
<tr>
<td>Primary lung cancer</td>
<td>58</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>26</td>
</tr>
<tr>
<td>Squamous</td>
<td>23</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>7</td>
</tr>
<tr>
<td>Bronchoalveolar</td>
<td>1</td>
</tr>
<tr>
<td>Small cell</td>
<td>1</td>
</tr>
<tr>
<td>Metastatic cancer</td>
<td>8</td>
</tr>
<tr>
<td>Benign lesions</td>
<td>34</td>
</tr>
<tr>
<td>Mycobacterium</td>
<td>9</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>24</td>
</tr>
</tbody>
</table>
male gender, preoperative oxygen dependence, and preoperative percentage of predicted FEV₁. In our series, the overall incidence of prolonged air leak was 22%. This is very similar to an incidence of 21% as described by the Video Assisted Thoracic Surgery Study Group¹ in a group of patients with mean FEV₁ of 0.85; in this study, the incidence of prolonged air leak in patients with FEV₁ < 1.2 L/min was only 2.3%. Low preoperative FEV₁, as well as other spirometric indicators of COPD are the most reliable predictors of prolonged air leak, while other factors such as preoperative steroid use, neoadjuvant chemoradiation, and prior surgery have also been shown in some studies¹¹,¹² to be predictors of air leak. Prolonged air leak is also more common with lobectomy or segmentectomy than with wedge resections.¹¹ In our study, the majority of patients with prolonged air leak had wedge resection rather than an anatomic resection (only four patients with prolonged air leak), although this factor was not independent of preoperative FEV₁. In our study, no patients with FEV₁ < 20% predicted underwent curative resection with preoperative FEV₁ < 35% predicted.

![Figure 2](https://www.chestjournal.org)  
**Figure 2.** Incidence of prolonged air leak in relation to preoperative percentage of predicted FEV₁.

### Table 4—Comparison With Prior Studies of Lung Resection in Patients With Low FEV₁

<table>
<thead>
<tr>
<th>Source</th>
<th>Description†</th>
<th>Percentage of Predicted FEV₁, %</th>
<th>Mortality, %</th>
<th>Morbidity, %</th>
<th>New Oxygen Requirement, %</th>
<th>Air Leak, %</th>
<th>Pneumonia, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerfolio et al⁷</td>
<td>Text A</td>
<td>44</td>
<td>2.4</td>
<td>49</td>
<td>8</td>
<td>21</td>
<td>3.5</td>
</tr>
<tr>
<td>Temeck et al⁸</td>
<td>Text B</td>
<td>42</td>
<td>1.4</td>
<td>4.1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Miller and Hatcher⁹</td>
<td>Text C</td>
<td>1.2 L/min</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>16</td>
<td>NA</td>
</tr>
<tr>
<td>Current study</td>
<td>Text D</td>
<td>26</td>
<td>1</td>
<td>36</td>
<td>11</td>
<td>22</td>
<td>4</td>
</tr>
</tbody>
</table>

*NA = not available.
†Text A = 85 consecutive lung cancer patients with FEV₁ < 1.2 L/min; text B = 73 lung cancer patients undergoing wedge resection; text C = 32 lung cancer patients undergoing resection smaller than lobectomy; text D = 100 consecutive lung mass patients undergoing curative resection with preoperative FEV₁ < 35% predicted.
buttresses has not conclusively been shown to reduce the incidence of prolonged air leak.\textsuperscript{12,13}

In patients with adequate cardiopulmonary reserve, lobectomy is the preferred operation for lung cancer. This is based on the Lung Cancer Study Group trial,\textsuperscript{3} which randomized 276 stage I nonsmall cell lung cancer patients to lobectomy or lesser resection. There was no statistically significant difference in survival, but there was a threefold increase in local recurrence with limited resection (segmentectomy or wedge resection).\textsuperscript{3} In patients with severely compromised lung function, however, the risk of resection must be balanced against the risk of recurrence. We were able to limit perioperative morbidity through minimally invasive approaches, limited resection (no patient underwent lobectomy with FEV\textsubscript{1} < 26\%), and concomitant lung volume reduction. Although we only examined perioperative morbidity and mortality, there is increasing evidence that lobectomy in patients with COPD carries an increased risk of delayed death from respiratory causes. A recent retrospective study\textsuperscript{14} of 402 stage I non-small cell lung cancer patients undergoing lobectomy showed that aside from tumor size and gender, preoperative percentage of predicted FEV\textsubscript{1} was the most significant independent predictor of long-term survival. Preoperative FEV\textsubscript{1} percentage of predicted < 70\% was independently associated with a higher noncancer-related death rate in the ensuing 5 years. The vast majority of these deaths were from respiratory causes. A separate study of 244 patients showed that although overall survival was no different following lung resection in COPD and non-COPD patients, the intercurrent 5-year survival (noncancer related) was only 60\% in COPD patients vs 86\% in those without COPD.\textsuperscript{15} In patients with severe COPD and smaller tumors (\textless{} 3 cm), an argument can be made favoring limited resection over lobectomy.\textsuperscript{16}

All of our patients had severely compromised lung function, but complete resection was still possible in 65 of 66 patients with malignant disease. These patients, after a thorough evaluation by a thoracic surgeon, could appropriately be selected with a high likelihood of complete resection. Many of these patients with very poor lung function were not candidates for anatomic resection. The ability to determine preoperatively if a tumor is resectable via wedge is important, as the long-term survival in patients left with a positive margin is no better than those not undergoing resection.

The 33\% incidence of resection for benign disease in this series is significant, but is generally less than other thoracoscopic resection series. Prior series by Allen et al,\textsuperscript{17} Decamp et al,\textsuperscript{18} Liu et al,\textsuperscript{19} and Mack et al\textsuperscript{20} had incidences of 47\%, 40\%, 38\%, and 52\% of resection for benign nodules, respectively. Our incidence of benign disease may be lower two reasons. First, our patients were believed to be at higher risk for operation because of their very poor lung function, and every effort was made to establish a diagnosis prior to subjecting them to lung resection. Second, at least in the last several years, positron emission tomography has become a more commonly utilized tool to distinguish scar from neoplastic and infectious masses.

Approximately one fourth of benign lesions (9 of 34 lesions) and nearly 10\% of all lesions in our patient subgroup were caused by mycobacterial infections. This incidence is similar to the incidence of tuberculous infections as a cause of solitary pulmonary nodules in the older literature (14\%).\textsuperscript{21} Even with needle biopsy, the differentiation between a tuberculosis and lung cancer may be difficult. Growth pattern, response to treatment, and certain CT characteristics may help distinguish between the two processes. The current incidence of tuberculosis as a cause of a solitary pulmonary nodule may be lower.\textsuperscript{20}

There are limitations in this study. First, this is a study of perioperative risk only; no recurrence or survival data are noted. Second, it represents the perioperative complication rate that can be expected at a large (> 2000 operations/year), academic, tertiary referral center for thoracic surgery, and results may not be applicable to smaller centers. Third, other tests such as DLCO and exercise testing were not uniformly performed or recorded in all patients and were not included in the analysis.

\section*{Conclusion}

This study provides a useful estimation of the risks of potentially curative lung resection in patients with suspicious lung masses and preoperative predicted FEV\textsubscript{1} < 35\%. A variety of procedures, including thoracoscopic wedge, segmentectomy, thoracoscopic lobectomy, and combined lung volume reduction and tumor resection, as well as conventional open resections, were employed with a low rate of morbidity and mortality. Of 100 consecutive patients, there was one perioperative death and one patient discharged receiving mechanical ventilation. Nearly all (> 98\%) patients were able to undergo complete resection of their cancers despite their severely compromised lung function. Prolonged air leak was the only frequent complication, and was seen most commonly in those with preoperative predicted FEV\textsubscript{1} < 20\%.

\section*{Acknowledgment}

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