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Lung Cancer in Octogenarians: Factors Affecting Morbidity and Mortality After Pulmonary Resection

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Background. **Predictors of morbidity and mortality after pulmonary resection for lung cancer in patients 80 years of age or older are unknown.**

Methods. **The medical records of all patients 80 years of age or older who had pulmonary resection for lung cancer from January 1985 through September 2004 were reviewed.**

Results. **There were 379 patients (248 men, 131 women). Median age was 82 years (range, 80 to 95 years). Pneumonectomy was performed in 25 patients (6.6%), bilobectomy in 7 (1.8%), lobectomy in 240 (63.3%), segmentectomy in 29 (7.7%), and wedge excision in 78 (20.6%). The cancer was squamous cell carcinoma in 143 patients (37.7%), adenocarcinoma in 166 (43.8%), bronchoalveolar cell carcinoma in 47 (12.4%), and other in 23 (6.1%). Complications occurred in 182 patients (48.0%). These included atrial fibrillation in 75 patients, pneumonia in 27, and retained secretions requiring bronchoscopy in 37. Morbidity predictors were male sex (odds ratio [OR], 1.6), hemoptysis (OR, 2.3), and previous stroke (OR, 3.8). Asymptomatic patients had a significantly decreased probability of complications (OR, 0.56). Operative mortality was 6.3% (24 of 379); significant predictors were congestive heart failure (OR, 6.0) and prior myocardial infarction (OR, 4.3). Factors not associated with mortality included previous myocardial revascularization, renal insufficiency (creatinine >1.5 mg/dL), and diabetes mellitus.**

Conclusions. **Pulmonary resection for lung cancer in octogenarians is feasible. Congestive heart failure and myocardial infarction, however, correlated with a significant increase in mortality. Prior myocardial revascularization, renal insufficiency, and diabetes were not associated with increased morbidity and mortality.**

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Individuals 80 years of age or older in the United States are the fastest growing segment of the population [1]. Accompanying this aging population will be an increase in the number of octogenarians with lung cancer, and pulmonary resection undoubtedly will become a more frequent clinical scenario. Appropriate patient selection is necessary to keep morbidity and mortality low, as advanced age is known to be associated with increased comorbidities.

Several recent surgical series have confirmed that long-term survival can be achieved in a significant proportion of octogenarians who undergo curative pulmonary resection for cancer [2–9]. However, considerable variation in outcome has been reported, with operative mortality ranging from zero to 16% [5, 8, 10]. This discrepancy highlights the importance of careful patient selection and the need for better understanding of the factors that increase the risk of pulmonary resection. The aim of this study is to define predictors of early morbidity and mortality after pulmonary resection for lung cancer in patients 80 years of age or older.

Material and Methods

From January 1985 through September 2004, 379 patients 80 years of age or older underwent pulmonary resection for non–small cell lung cancer (NSCLC) at Mayo Clinic in Rochester, MN. The medical records were analyzed for age, sex, comorbidities, presenting signs and symptoms, smoking history, preoperative pulmonary function tests, extent of resection, tumor histology, pathologic stage, complications, and outcomes. To analyze the association of forced expiratory volume in 1 second (FEV_1) with morbidity and mortality, patients were subdivided into three groups: FEV_1 less than 40% predicted, FEV_1 40% to

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70% predicted, and FEV_1 greater than 70% predicted. Operative mortality was defined as death within 30 days of the procedure or during the same hospital admission. This study was approved by the Mayo Clinic College of Medicine's Institutional Review Board on September 14, 2004, with waiver of informed consent and waiver of Health Insurance Portability and Accountability Act.

The association between risk factors and the end points of morbidity and operative mortality were evaluated with univariate analysis. Descriptive statistics for discrete variables are presented as frequencies and percentages. Medians and ranges are used for description of continuous measures. Logistic regression analyses were used to assess the associations between potential risk factors and the dichotomous outcomes of morbidity and operative mortality as defined above. Continuous potential risk factors were converted to categorical indicator variables for inclusion in the logistic regression analyses. Results are presented as odds ratio (OR) and 95% confidence intervals (CI). Probability values less than 0.05 are considered statistically significant.

There were 248 men (65%) and 131 women (35%). Median age at the time of pulmonary resection was 82 years (range, 80 to 95 years). One hundred twenty-five patients (32.5%) were symptomatic, and included cough in 43 (11.4%) patients, hemoptysis in 30 (7.9%), dyspnea in 23 (6.1%), chest pain in 18 (4.7%), weight loss in 8 (2.1%), and generalized muscle weakness in 1 (0.3%). Diagnosis in the remaining 254 patients (67.0%) was obtained through the identification of a pulmonary abnormality on chest roentgenogram obtained during routine examination or evaluation for other medical conditions.

A history of cigarette smoking was present in 71% of patients. Median pack-years were 30 and ranged from 1 to 180. The median FEV_1 was 1.79 L (range, 0.49 to 3.6 L), and the median FEV_1 percent predicted was 72% (range, 25% to 143%). The median diffusing capacity of carbon monoxide was 15.4 L (range, 7 to 29 L), and the median diffusing capacity of carbon monoxide percent predicted was 73% (range, 38% to 134%). Preoperative FEV_1 was less than 40% predicted in 19 patients, between 40% and 70% predicted in 129 (34.0%), and greater than 70% in 173 (45.6%). Preoperative FEV_1 was unavailable in 58 patients (15.3%). Comorbidities are shown in Table 1. One hundred twenty-seven patients (33.5%) had at least one cardiovascular comorbidity, and 73 (19.3%) had either an FEV_1 less than 50% predicted or a diffusion capacity of carbon monoxide less than 60% predicted.

Table 1. Comorbidities

Comorbidity	Number of Patients (%)
Previous malignancy	80 (21%)
Renal insufficiency (creatinine >1.5 mg/dL)	39 (11%)
Prior coronary artery bypass	34 (9%)
Prior myocardial infarction >6 months	32 (9%)
Congestive heart failure	29 (8%)
Diabetes mellitus	28 (8%)
Stroke	21 (6%)
Corticosteroid usage	14 (4%)
Percutaneous coronary intervention or stent	9 (2%)
Alcohol consumption >3 drinks/day	4 (1%)

Table 2. Complications

Complication	Number of Patients (%)
Atrial fibrillation	75 (21%)
Retained secretions requiring bronchoscopy	37 (10%)
Pneumonia	27 (7%)
New home oxygen requirement	26 (7%)
Air leak >5 days	26 (7%)
Postoperative mechanical ventilation	23 (6%)
Myocardial infarction	13 (4%)
Recurrent laryngeal nerve injury	7 (2%)
Pulmonary edema	6 (2%)
Stroke	4 (1%)
Chylothorax	4 (1%)
Reoperation for bleeding	3 (1%)
ARDS	2 (1%)
Empyema	1 (1%)
Other	45 (13%)

ARDS = adult respiratory distress syndrome.

Pneumonectomy was performed in 25 patients (6.6%), bilobectomy in 7 (1.8%), lobectomy in 240 (63.3%), segmentectomy in 29 (7.7%), and a wedge excision in 78 (20.6%). Complete mediastinal lymph node dissection was performed in 354 patients (93.4%). Video-assisted thoracoscopic resection was performed in 35 patients (9.2%). Seventy-seven patients (20.3%) underwent pulmonary resection from 1985 to 1989, 75 (19.8%) from 1990 to 1994, 104 (27.4%) from 1995 to 1999, and 123 (32.5%) from 2000 to 2004.

The cancer was a squamous cell carcinoma in 143 patients (37.7%), adenocarcinoma in 166 (43.8%), bronchoalveolar cell carcinoma in 47 (12.4%), and other in 23 (6.1%). Pathologic stage was IA in 135 patients (35.7%), IB in 119 (31.4%), IIA in 9 (2.4%), IIB in 43 (11.3%), IIIA in 48 (12.7%), IIIB in 18 (4.7%), and IV in 7 (1.8%).

Results

Complications (Table 2) occurred in 182 patients (48.0%), with atrial fibrillation and retained secretions requiring bronchoscopy being the most common. Twenty-four patients died (operative mortality, 6.3%). Cause of death was cardiac in 8 patients, respiratory failure in 4, sepsis in 2, and stroke in 1. The remaining 9 patients died elsewhere after hospital dismissal without an exact cause of death being documented.

Follow-up was complete in 363 patients (95.8%) and ranged from 2 to 13.7 years (median, 2.3 years). One hundred fourteen patients are currently alive and 249 have died. Cause of death was cancer related in 92

patients (36.9%), non–cancer related in 75 (30.1%), and unknown in 82 (32.9%).

Although mortality and morbidity did vary by age group and was 15.4% for patients older than 89 years, this variation was not statistically significant (Table 3). Male sex was associated with a higher incidence of complications ($p < 0.03$; OR, 1.64; 95% CI, 1.05 to 2.54); however, operative mortality did not differ significantly for men versus women (Tables 4, 5). Patients who smoked between 20 and 80 pack-years had a higher complication rate than nonsmokers ($p = 0.01$; OR, 1.99; 95% CI, 1.16 to 3.41). The extent of smoking, however, did not significantly affect operative mortality (Tables 4, 5).

Asymptomatic patients were less likely to develop a postoperative complication ($p = 0.02$; OR, 0.56; 95% CI, 0.35 to 0.89), but operative mortality was not statistically different. Hemoptysis was associated with a higher operative morbidity ($p = 0.049$; OR, 2.26; 95% CI, 1.00 to 5.13), but did not statistically affect mortality. The presence of cough, weight loss, chest pain, or dyspnea did not significantly affect operative morbidity or mortality.

Of the comorbidities listed in Table 1, only a history of a previous stroke was associated with a significantly higher morbidity ($p = 0.02$; OR, 3.80; 95% CI, 1.23 to 11.67). Both congestive heart failure ($p = 0.0003$; OR, 6.03; 95% CI, 2.26 to 16.07) and myocardial infarction older than 6 months ($p = 0.005$; OR, 4.25; 95% CI, 1.55 to 11.67) were associated with an increased risk of operative mortality (Table 5). Patients with an FEV_1 of 40% or less than predicted had a higher chance of postoperative morbidity than patients with FEV_1 greater than 70% ($p = 0.01$; OR, 5.67; 95% CI, 1.59 to 20.18); however, there was no difference in operative mortality among FEV_1 groupings (Tables 4, 5).

Operative morbidity was greater in patients who had a lobectomy or bilobectomy compared with a segmentectomy or wedge excision ($p = 0.02$; OR, 1.75; 95% CI, 1.10 to 2.81), but operative mortality was not statistically different on the basis of extent of resection (Table 6). Patients operated on between 1985 and 1994 were more likely to develop complications when compared with those treated between 2000 and 2004 (Tables 4, 5); however, no difference in operative mortality was noted.

Comment

According to the National Vital Statistics Reports published by the National Center for Health Statistics, a person 80 years of age in the United States in 2002 is expected to live to 88.8 years [11]. Moreover, people age 85 and 90 are expected to live to 91.5 and 94.8 years, respectively [11]. Despite these longevity predictions, elderly patients are less likely to have surgical resec-

Table 3. Morbidity and Mortality by Age Group

Age Group	Mortality ($p = 0.94$)	Morbidity ($p = 0.58$)
80–83 years	6.7%	52.0%
>83–86 years	4.5%	53.0%
>86–89 years	8.0%	35.9%
>89 years	15.4%	54.1%

Table 4. Risk Factors for Postoperative Morbidity

Univariate Risk Factor	Odds Ratio	95% Confidence Interval	p Value
Sex			
Male	1.64	(1.05, 2.54)	0.03
Categorized date of surgery as compared with years 2000 through 2004			
1985 through 1989	2.20	(1.21, 4.02)	0.01
1990 through 1994	2.31	(1.27, 4.19)	0.01
1995 through 1999	1.50	(0.87, 2.58)	0.14
Categorized pack-years as compared with 0 pack-years			
0 to ≤20	1.16	(0.59, 2.29)	0.68
20 to ≤80	1.99	(1.16, 3.41)	0.01
>80	1.21	(0.48, 3.02)	0.69
Extent of resection as compared with wedge/segmentectomy			
Lobe/bilobectomy	1.75	(1.10, 2.81)	0.02
Pneumonectomy	2.36	(0.90, 6.19)	0.08
FEV_1% as compared with >70%			
≤40%	5.67	(1.59,20.18)	0.01
>40% to ≤70%	1.19	(0.75, 1.89)	0.47
Presenting complaint			
Asymptomatic status	0.56	(0.35, 0.89)	0.02
Hemoptysis	2.26	(1.00, 5.13)	0.049
Cough	1.57	(0.81, 3.06)	0.18
Weight loss	1.61	(0.38, 6.84)	0.52
Chest pain	1.53	(0.58, 4.05)	0.39
Dyspnea	1.16	(0.49, 2.75)	0.74
Comorbidities			
Congestive heart failure	1.52	(0.69, 3.34)	0.30
Prior myocardial infarction ≥6 months	1.62	(0.74, 3.53)	0.23
Prior myocardial infarction <6 months[a]			
Prior coronary artery bypass graft	0.57	(0.27, 1.22)	0.15
Percutaneous coronary intervention	0.26	(0.05, 1.29)	0.10
IDDM	1.27	(0.28, 5.77)	0.75
NIDDM	1.05	(0.43, 2.54)	0.92
Creatinine >1.5 mg/dL	0.94	(0.48, 1.85)	0.87
Stroke	3.80	(1.23,11.67)	0.02
Corticosteroids	0.81	(0.27, 2.46)	0.71
>3 alcoholic drinks/day	N/A		
Prior malignancy	1.11	(0.67, 1.84)	0.70

[a] No patient who had surgery had a myocardial infarction within 6 months.

FEV_1 = forced expiratory volume in one second; IDDM = insulin-dependent diabetes mellitus; N/A = no patients in the category; NIDDM = non–insulin-dependent diabetes mellitus.

tion for early stage lung cancer, as shown by a 1998 study that revealed that 80% of patients younger than 65 underwent surgery whereas only 55% of patients older than 65 underwent surgery for resectable lung cancers [12]. In addition, recent publications have demonstrated good long-term survival after lung cancer surgery in octogenarians; therefore, age alone should not contraindicate pulmonary resection for lung cancer [2–10].

Table 5. Risk Factors for Operative Mortality

Univariate Risk Factor	Odds Ratio	95% Confidence Interval	*p* Value
Sex			
Male	2.78	(0.93, 8.31)	0.07
Categorized date of surgery as compared with years 2000 through 2004			
1985 through 1989	1.92	(0.67, 5.53)	0.23
1990 through 1994	0.95	(0.27, 3.35)	0.93
1995 through 1999	0.87	(0.27, 2.84)	0.82
Categorized pack-years as compared with 0 pack-years			
0 to ≤20	0.98	(0.16, 6.07)	0.98
20 to ≤80	2.18	(0.61, 7.86)	0.23
>80	4.00	(0.75,21.25)	0.10
Extent of resection as compared with wedge/segmentectomy			
Lobe/bilobectomy	0.69	(0.28, 1.72)	0.43
Pneumonectomy	1.67	(0.41, 6.81)	0.47
FEV_1% as compared with >70%			
≤40%	0.74	(0.09, 6.00)	0.78
>40% to ≤70%	1.00	(0.41, 2.46)	1.00
Presenting complaint			
Asymptomatic status	1.00	(0.41, 2.52)	0.98
Hemoptysis	1.60	(0.45, 5.72)	0.47
Cough	0.31	(0.04, 2.33)	0.25
Weight loss	2.01	(0.24,17.01)	0.52
Chest pain	0.80	(0.10, 6.29)	0.83
Dyspnea	2.22	(0.61, 8.06)	0.23
Comorbidities			
Congestive heart failure	6.03	(2.26,16.07)	0.0003
Prior myocardial infarction ≥6 months	4.25	(1.55,11.67)	0.005
Prior myocardial infarction <6 months[a]			
Coronary artery bypass graft	1.44	(0.41, 5.11)	0.57
Percutaneous coronary intervention	1.83	(0.22,15.23)	0.58
IDDM	N/A		
NIDDM	0.71	(0.09, 5.49)	0.74
Creatinine >1.5 mg/dL	1.77	(0.57, 5.46)	0.32
Stroke	2.59	(0.71, 9.49)	0.15
Corticosteroids	1.11	(0.14, 8.84)	0.92
>3 alcoholic drinks/day	N/A		
Previous malignancy	1.22	(0.47, 3.17)	0.69

[a] No patient who had surgery had a myocardial infarction within 6 months.

FEV_1 = forced expiratory volume in one second; IDDM = insulin-dependent diabetes mellitus; N/A = no patients in the category; NIDDM = non–insulin-dependent diabetes mellitus.

Table 6. Mortality by Type of Resection

Type of Resection	Number of Patients/ Mortality (%)	Number of Patients/ Morbidity (%)
Pneumonectomy	2/25 (8%)	13/25 (52.0%)
Bilobectomy	1/7 (14.3%)	5/7 (71.4%)
Lobectomy	12/240 (5.0%)	123/240 (51.2%)
Segmentectomy	1/29 (3.5%)	11/29 (37.9%)
Wedge resection	8/78 (10.3%)	28/78 (35.9%)

The current study evaluates short-term outcomes of pulmonary resection for non–small cell lung cancer in octogenarians during the past two decades. We found that overall mortality was 6% but significantly higher in patients with congestive heart failure or a prior myocardial infarction. These were the only factors that we identified that significantly affected operative mortality. Other comorbidities, such as prior myocardial revascularization, renal insufficiency, diabetes, and steroid use, did not increase the risk of operative death. In addition, the amount of smoking, extent of pulmonary resection, and presenting complaint did not affect operative mortality. Our results are similar to other smaller reports in the literature [3, 9]. In 2004, Brock and colleagues [9] published a series of 68 octogenarians who underwent pulmonary resection for early stage lung cancer with an 8.8% operative mortality, but they did not report statistical analysis of the predictors of operative mortality. Two series from Japan regarding pulmonary resection for lung cancer in octogenarians both report no operative death; however, comparison is difficult given their sample size (35 and 18 patients). Furthermore, one of these studies excluded patients with chronic obstructive pulmonary disease or coronary artery disease, whereas the other study had minimal information regarding pulmonary function. Naunheim and coauthors [10] reported that age was a predictive risk factor for operative death in their series of 37 octogenarians who underwent resection for lung cancer. They found that the median age in survivors was 82.2 years versus 84.3 in nonsurvivors. In contrast, although older age in our series was associated with increasing operative mortality, we did not find this to be a statistically significant predictor. The difference may be explained by the larger size of our cohort or the different statistical methodology.

As would be expected in this group of patients, morbidity was considerable in our experience, with at least one complication occurring in 48% of patients. We found that male sex, operation before 1995, extent of resection, prior smoking history, poor pulmonary function, and prior stroke all increased the risk of complications. Sur-

prisingly, no other comorbidity increased the risk of complication. Comparison with other studies is difficult because of the variable definitions of what constitutes a complication. However, similar to almost all other studies, atrial fibrillation, pulmonary difficulties, and prolonged air leak were among the predominant complications [2–10]. In the few reports that have looked for predictive factors of morbidity, the results are varied. Port and colleagues [4] did not find any predictive value in comorbidities or preoperative pulmonary function tests; however, there were only 61 patients in their series. Aoki and coinvestigators [5] found a higher incidence of complications in those patients with a low partial pressure of oxygen and a prolonged operative time. These variable conclusions are likely the result of differences in methodology of the various reports. The lack of knowledge about this group of patients is well recognized, as it has been reported that elderly patients are underrepresented in cancer clinical trials [13].

Our study does have limitations. Although our patients were selected from a prospective database, it remains a retrospective series. Undoubtedly this potentially results in an inherent selection bias, because patients included in this series are only those who underwent resection. Thus, patients who may have been excluded because they were deemed poor risks for resection because of perceived high risk are not included in the analysis. The nature of the selection bias would only be apparent after systemic review of all patients 80 years and older who were diagnosed with lung cancer during the study period. Another limitation is exclusion of other risk factor that may be relevant in octogenarians. Owing to its retrospective nature and its inherent limitations, our study does not address factors such as nutritional status, psychological condition, or family support [14].

Nevertheless, the results of this study do provide guidance when an octogenarian presents with a potentially resectable lung cancer. Patients with congestive heart failure or prior myocardial infarction should have a complete preoperative cardiovascular evaluation, because this group is at high risk for operative mortality. Additionally, male smokers with poor pulmonary function should be observed closely for postoperative complications, and preventative measures such as pulmonary rehabilitation, smoking cessation, or bronchodilator therapy should be considered. Importantly, these findings should not be used to deny potential surgical cure to patients. The decision as to whether to proceed with pulmonary resection is multifactorial, and the results of this series serve as another piece of information that is useful in making a careful decision regarding operability. As observed by Wang and colleagues [15], identifying preoperative risk factors may allow preoperative intervention to decrease operative risks.

As the number of patients 80 years of age and older continue to increase, thoracic surgeons will face the difficult task of selecting those octogenarians who will have the best chance of avoiding complications and, ultimately, benefit from prolonged survival after pulmonary resection. By careful selection outcomes can be improved while at the same time providing patients the chance for long-term cure of lung cancer.

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