Pulmonary resection for malignancy in the elderly: is age still a risk factor?  

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Abstract  

Objective: There is an increasing number of elderly patients presenting with potentially-resectable lung malignancy. The objective of this study is to evaluate the modern perioperative morbidity and mortality in patients undergoing oncologic lung resection and to analyse the trend over a 26-year period in our experience. Methods: Between 1971 and 1996, 1506 patients underwent lung resection for malignancy. We reviewed the 30-day perioperative risk in a group of 385 (25.6%) patients aged 70 years and older operated on for intended cure of lung malignancy. Operations included 293 (77%) lobectomies, 24 pneumonectomies (6%), 16 bilobectomies (4%) and 52 wedge or segmental resections (13%). The pathology was bronchogenic carcinoma in 89% and metastasis or other tumours in 11% of patients. We compared the 30-day perioperative risk between the elderly group (age 70 or greater) and a cohort of 180 patients (control) 69 years and younger. Results: The mortality for all resections in elderly group was 4.2% (16/385) and was 1.6% for the control group. Mortality in the octogenarian group was 2.8%. Female gender correlated with a decreased risk of death, with only two of 16 deaths in females (P, 0.005). Overall morbidity was higher in the study than in control patients (34% vs. 25%, n.s.), although major morbidity was similar in both groups (13.2% vs. 13%). Abnormal pulmonary-function testing and positive cardiac history did not correlate with increase overall or specific risk. Pneumonectomy carried a higher risk for death, with three of 24 deceased (12.5%; P, 0.05). Changes in outcome were analysed over two time periods: the mortality in the early period (1971–1982), 11.1% (8/72), was significantly elevated above the control group, while mortality in the modern period (1983–1994) was not, with a rate of 2.6% (8/313). Conclusions: In our series, mortality associated with operative treatment for lung malignancy in the elderly declined, so age alone no longer appears to be a risk factor. Age remains a risk factor for overall, but not major, morbidity. Pneumonectomy should undertaken cautiously in this age group. Based on this data, functional elderly patients should not be denied curative lung resection based on age alone. © 1998 Elsevier Science B.V. All rights reserved  

Keywords: Lung resection; Cancer; Elderly  

1. Introduction  

Pulmonary resection has often been found to have a substantial higher perioperative risk in the elderly (70 years and older), than in younger cohorts. Previous reports on thoracotomy for malignancy in the elderly have shown mixed results [1–3]. Although the mortality has decreased, the morbidity has remained high, mainly due the age-related premorbid factors. Concern about excessive operative risk has led some to use lesser operative approaches, however not with a defined survival benefit [4,5].  

In the past 15 years, notable advances have occurred in anaesthetic management and perioperative care, with a modern trend to a decreased perioperative risk. Nevertheless, surgery in the elderly still represents a clinical challenge frequently-faced by the thoracic surgeon.  

To examine this premise, we reviewed our experience...
with lung resection in 385 elderly patients with lung cancer, and analysed the perioperative risk over an interval of 26 years.

2. Materials and methods

The records of patients aged 70 years and older who underwent intended curative pulmonary resection for cancer between 1971–1996, were reviewed. To analyse the trend in outcome, the study was divided into an early period, between 1971 and 1982 (n = 72), and a modern period between 1983 and 1996 (n = 313). Demographic and clinical variables analysed included age, gender, pulmonary functional status and cardiovascular history. Perioperative data correlating to the 30-day perioperative risk consisted of extent of resection, length of hospital stay and venue of care after discharge.

Functional and laboratory assessment were derived entirely from the medical history, physical examination, routine blood tests, electrocardiogram and standard pulmonary function studies. Clinical and operative staging was based on history, physical exam and radiologic review including chest X-rays and CAT scans, including portions of the upper abdomen. CAT scans were more commonly performed in the modern period of the study. Mediastinoscopy was selectively used based on history, location of tumour and radiologic mediastinal assessment.

The inclusion of complications was complete and strict, and was divided in two groups. Major complications consisted of any event leading to a hospital stay greater than 11 days or ICU stay greater than 4 days, need for reoperation or additional procedures, mechanical ventilation longer than 48 h, prolonged air leaks (longer than 7 days) and serious cardiac problems. Minor complications encompassed the rest of the recorded events.

Exploratory thoracotomy, wedge biopsy or tumours with final benign histology were excluded from the study. The extended operation was defined as the resection of a pulmonary lobe associated with chest wall resection, additional parenchyma from an adjacent lobe, and or bronchoplastic operation.

Statistical analysis was performed using chi-square and two-tailed student tests for comparison of variables. Results were considered significant at P-values less than 0.05. Block randomisation was used to select 180 patients younger than 69 years old (mean = 63 years) for control comparison.

3. Results

Pulmonary resection was performed in 385 elderly patients, representing 25.6% of the 1506 operations for lung malignancy performed during the review period. Notably, 313 (81.3%) of patients underwent surgery in the second or modern period. There were 206 males and 179 females, ranging in age from 70 to 96 years (mean, 75.2 years). Seventy-one (18.5%) patients were octogenarians. Pathological diagnosis is summarised in Table 1. Of the patients with bronchogenic carcinoma, 21 underwent preoperative radiation and/or chemotherapy. Twelve patients were undergoing a second resection and were considered as separate patients.

One hundred and forty two patients (39%) had moderate chronic obstructive pulmonary disease, but only 73 were taking oral bronchodilators and 11 had been on steroid therapy. One hundred and seventy five patients (45%) had a history of coronary disease, cardiac arrhythmia’s or arterial hypertension. Forty-two patients (42) had prior unrelated malignancy that was treated for cure. Despite the significant degree of co-morbidity in this patient population, all patients met standard cardiopulmonary criteria for the elected resections. Specifically, a clinical history of angina, recent myocardial infarction or moderate dyspnea on exertion would frequently lead to further testing. Exercise stress test, persantine thallium test, echocardiography and ventilation perfusion scan might then be analysed prior to any intervention. The procedures performed are listed in Table 2. Most lung cancers were treated with lobar or greater resections, while most metastases were treated by non-anatomic resections.

The results of morbidity and mortality in the study group are detailed as follows. There were 16 perioperative deaths, yielding an overall mortality rate of 4.2%. Causes of death were myocardial infarction in three, pulmonary embolism in three, sepsis in four, respiratory failure in four and stroke

Table 1

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchogenic carcinoma</td>
<td>342</td>
<td>(88.8%)</td>
</tr>
<tr>
<td>Adeno carcinoma</td>
<td>204</td>
<td></td>
</tr>
<tr>
<td>Squamous-mixed carcinoma</td>
<td>117</td>
<td></td>
</tr>
<tr>
<td>Large-cell carcinoma</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Small-cell carcinoma</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Metastases</td>
<td>28</td>
<td>(7.3%)</td>
</tr>
<tr>
<td>Other\textsuperscript{2}</td>
<td>15</td>
<td>(3.9%)</td>
</tr>
</tbody>
</table>

\textsuperscript{2}Carcinoid, carcinosarcoma.
and bleeding, one of each. Two of these deaths (2.8%) occurred in the octogenarian subgroup.

One hundred and thirty one patients (34%) had non-fatal complications, and 51 of those had major events (13.2% major morbidity). The complete listing of all complications is summarised in Table 3. One hundred ten patients suffered one complication, 20 had two events and seven had three events. Cardiovascular complications were the most common, with 51 of the 69 complications being supra-ventricular arrhythmias and all but one controlled pharmacologically. Forty-three patients suffered respiratory complications. Prolonged air-leak occurred in 26 patients (range 7–30 days, mean 11.5) with three of them requiring reoperation. Major atelectasis occurred in seven patients, and only three require bronchoscopy. The low incidence of retained secretions is attributed to the use of a strict policy of perioperative pulmonary physiotherapy. Other morbidity included urinary retention, often requiring surgery or prolonged hospital stay and confusion.

Female gender correlated with a better outcome. The mortality and morbidity rates (1.2% and 28%) were significantly lower than in the male cohort (6.8% and 40%, \( P < 0.05 \)). There were no significant differences in the specific perioperative risk when patients were stratified by abnormal pulmonary function tests (FEV1, FVC or DLCO <60% of predicted value) or a positive cardiac history. The mean postoperative length of stay (LOS) was 8.5 days (range 2–34) for all patients. The LOS has been significantly decreased from an average of 12.5 days in the early period to 7.6 days in the modern period (\( P < 0.05 \)).

The mortality and morbidity in the elderly group was compared to a control group (mean = 63 years) of patients operated on during the same time period Table 4. For the elderly, the overall mortality in the early period, 11.1%, was significantly elevated above control (2.2%, \( P < 0.05 \)) while the 2.6% mortality in the recent era was not. The overall mortality rate after pneumonectomy (12.5%) was higher than in control patients (4.3%; \( P < 0.05 \)). Although the mortality decreased to 5.8% in the second period, the acute risk remains significantly elevated compared to the standard lobar resection.

4. Discussion

Surgical resection remains the primary modality for the treatment of lung cancer, and has an important role in the management of pulmonary metastatic disease [6–8]. As a result of an increasing life expectancy and a stable incidence of lung cancer, more elderly patients present with potentially-resectable lung malignancy. Age as an independent risk factor has been considered a limiting factor when performing curative resections. Mortality rates of close to 20% led to the consideration that advancing age was a contraindication for surgery [6–15]. Ginsberg et al. from lung cancer study group (LCSG) [16] reported in 1983 an accep-

Table 3

<table>
<thead>
<tr>
<th>Event</th>
<th>Major</th>
<th>Minor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular complications</td>
<td>69</td>
<td>17/15</td>
</tr>
<tr>
<td>Supraventricular arrhythmia</td>
<td>51</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Surgical bleeding</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Peripheral art. embolus</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Phlebitis</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary complications</td>
<td>52</td>
<td>27/25</td>
</tr>
<tr>
<td>Air leak</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Vocal cord palsy</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>41</td>
<td>12/11</td>
</tr>
<tr>
<td>Urinary retention/infection</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>Confusion</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Renal failure</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>162</td>
<td>56/51</td>
</tr>
<tr>
<td></td>
<td>131</td>
<td>106/80</td>
</tr>
</tbody>
</table>

No. events/ no. patients.

*Sixteen patients had two events and three had three or more events.

Table 4

<table>
<thead>
<tr>
<th>Study</th>
<th>All resections, ( n = 385 ) (n, %)</th>
<th>Pneumonectomy, ( n = 24 ) (n, %)</th>
<th>Control</th>
<th>All resections, ( n = 180 ) (n, %)</th>
<th>Pneumonectomy, ( n = 23 ) (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>16 (4.2%)</td>
<td>3 (12.5%)*</td>
<td>3 (1.6%)</td>
<td>1 (4.3%)</td>
<td></td>
</tr>
<tr>
<td>Major morbidity</td>
<td>131 (34%)</td>
<td>9 (37.5%)</td>
<td>45 (25%)</td>
<td>5 (21.7%)</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>51 (13.2%)</td>
<td>3 (12.5%)</td>
<td>23 (13%)</td>
<td>2 (8.6%)</td>
<td></td>
</tr>
</tbody>
</table>

\( *P < 0.05, \) Student’s t-test.
Major mortality is variable among various authors. Operative mortality reflects death occurring within 30 days or same hospitalisation.

Report Dates No. cases Morbidity Major\(^a\) Mortality\(^b\)
---|---|---|---|---|
Ginsberg [22] 1981–1983 416 NS NS 5.6
Thomas [26] 1980–1984 47 50 NS 12.6
Pagni (present) 1971–1996 385 34 13.2 NS

\(^a\)Definition of major mortality is variable among various authors.
\(^b\)Operative mortality reflects death occurring within 30 days or same hospitalisation.

Mortality must not be excessive or chronic in order to preserve quality of life. We documented standard criteria of morbidity but also listed excessive length of stay (LOS) or longer than normal ICU needs. These findings were always associated with greater morbidity. Tracking LOS and ICU needs also helps to determine if resource utilisation is excessive in elderly patients.

In this series, overall morbidity was 34% but major complications did not increase. Some reasons for increased morbidity are the inherently higher incidence of genitourinary complications in the elderly population as well as neuropsychiatric symptoms frequently associated with anaesthesia and narcotics when used in the elderly. Since 97% of our patients were discharge home (ten patients requiring transient nursing home care and two needing permanent stay) we take this as further evidence to support our conclusion that morbidity is tolerable after surgery. In addition, LOS continues to decline suggesting appropriate resource utilisation.

In this review, male gender and pneumonectomy continues to carry a higher perioperative risk. For men, the overall mortality was 6.8% compared to 1.2% for women. Morbidity outcome showed a similar difference (28% vs. 40%). One can assume that co-morbid conditions in the male gender (i.e. increased incidence of cardiopulmonary disease) might account for this discrepancy. Pneumonectomy has always carried a higher mortality, well documented in current reports [18–25]. For our series, a 12.5% mortality is reported, with a decline of the death rate to 5.8% in the modern period of the study. The decline is encouraging and likely related to improved selection as well as advances in perioperative care. However, it is still advisable that pneumonectomy should be undertaken with caution, but not avoided if a curative resection can be achieved.

Tumour stage was not looked at specifically in this study but we have recently reported [26] disappointing results for long-term survival in octogenarians with stage II and IIIa disease. The use of operative staging procedures (bronchoscopy, needle aspiration and mediastinoscopy) were used when so indicated by review of the patient’s CT scan and when one was to consider an extended resection (i.e. T3 lesion or pneumonectomy). The majority of patients in this series were clinical and pathological stage I disease (81% of 342 lung cancer patients). This may be another reason for the continued improvement in mortality in the modern period of the study.

Although there were no significant differences in perioperative mortality when stratifying patients with pulmonary disease, the use of pulmonary-function studies was liberal and lower values prompted us to further scrutinise the functional history. In such circumstances a quantitative ventilation–
perfusion scan and maximal O2 consumption evaluation may be indicated. The presence of cardiac disease alerted us to potential related problems, and functional cardiac evaluation (i.e. thallium stress test, echocardiography and coronary angiography) was performed if so indicated. More importantly, a close review of patients current functional status (i.e. lifestyle activity, ability to ambulate distances or stair-climbing) seemed to be a reliable predictor of outcome in this study.

Perioperative survival in the elderly population has improved in modern days, as shown reports in Table 5. This study correlates with this trend. The final decision for resection should be based on factors such as: type and extent of the pathology, curative potential, risk of the proposed procedure, age, gender and co-morbid disease. In addition, results at a given institution should be also considered in this equation to establish the potential survival benefit in these selected group of patients.

In summary, age per se is not a significant predictor of increased mortality in the modern period of this study, and properly-selected elderly patients should not be denied potentially-curative lung surgery. Male gender and pneumonectomy confer a higher mortality rate. Morbidity is higher but acceptable in the elderly.

Acknowledgements

We wish to thank Dr. Stanley Fell for his kind advice in the preparation of this manuscript.

References


Appendix A. Conference discussion

Dr K. Jeyasingham (Bristol, UK): I’m glad to notice that your co-author, John Federico, has continued the influence that he was subjected to at French's Hospital in Bristol. Now, there is obviously some impact of your practice in the modern period, as you call it, over the older practice. Could you pinpoint one or two factors which have altered in order to produce the improved mortality and morbidity figures in the later period? Dr Pagni: We can attribute the improvement in surgical risk to different factors. The major factor probably is patient selection and better oncoplastic staging prior to surgery. There have been notable improvements in perioperative management in terms of anaesthesia and pain control as well. In the modern period we have implemented a strict policy of perioperative management in terms of anaesthesia and pain control as well. This study correlates with this trend. The final decision for resection should be based on factors such as: type and extent of the pathology, curative potential, risk of the proposed procedure, age, gender and co-morbid disease. In addition, results at a given institution should be also considered in this equation to establish the potential survival benefit in these selected group of patients.

In summary, age per se is not a significant predictor of increased mortality in the modern period of this study, and properly-selected elderly patients should not be denied potentially-curative lung surgery. Male gender and pneumonectomy confer a higher mortality rate. Morbidity is higher but acceptable in the elderly.

Acknowledgements

We wish to thank Dr. Stanley Fell for his kind advice in the preparation of this manuscript.
Dr A. Lerut (Leuven, Belgium): You said in your initial statements that, of course, you want to match your survival with what the normal life expectancy would be. So how much has been the major morbidity playing a role or affecting the late survival? Because that’s then obviously coming up as an important issue.

Dr Pagni: Thank you for your comment. An answer to that is that morbidity is well tolerated by the elderly now. Proof of that is that 93% of our patients in the modern era have been able to be discharged home. Only ten patients have been transiently in a nursing home facility, and two of them stayed permanently. And that’s a very low number. I think that assessment of the functional status of the patient has been very important to achieve this.

Dr Lerut: Yes, okay, that’s an answer on the short-term follow-up. But in the late follow-up, how much has the 13% major morbidity that you had been influential on affecting the late survival? In other words, how many patients died later on, not from cancer recurrence, but as a consequence of a major event in the perioperative period?

Dr Pagni: We have not specifically looked at the long-term survival in this group of patients. We have recently published on the mortality and morbidity in an octogenarian group operated on for lung carcinoma, and we have seen that for stage I carcinoma of the lung, the overall 5-year survival was 57%, but in patients that had more advanced stages, they fared very poorly. So, in terms of that specific subgroup of patients, some of them part of this study, morbidity and mortality did not affect to a great degree the overall survival. Basically the higher stage was what really affected it.

Dr Lerut: And how much has been the performance status of the patient at the time of hospitalisation playing a part in excluding a patient from surgery?

Dr Pagni: That’s a good question. We don’t have the denominator of patients that were turned down from surgery. So we are highly selective of the patients going for resection. We have based this on a careful functional evaluation and the function status qualities over a Karnofski index of probably 80, but we have not based it on a specific number to select those patients.

Dr J. Svennervig (Oslo, Norway): I think this is a topic which is of interest to all of us, with the growing number of old patients. You reported the mortality rate of 4.2%, but in octogenarians you had a mortality rate of only 3.4%. I think we see the same phenomenon in cardiac surgery, that mortality rates may be even lower in the oldest patients, and I think that that must be because of our better patient selection. So my question to you would be, how many patients did you reject because of higher age?

Dr Pagni: Again, we don’t have that denominator of patients rejected. We don’t have that number. But we are very selective with patients. However, in a functional patient with a potentially curable lesion, we don’t deny an operation based on age alone if we think that we can achieve a beneficial survival, even in borderline operable patients.

Dr Lerut: May I ask you how much age, and very old age, the octogenarian group, is affecting factors such as radicality of resection during the operation?

Dr Pagni: Definitely we avoid major operations in the elderly. In this study, 90% of the patients had lung cancer, and 80% of them were stage I. That speaks for the fact that we are very selective. Also in oncologic terms we try to give them a resection with a potential of cure, usually stage I, cancer. For patients with a stage II or III, usually their pathological stage is found after surgery, but in those patients pre-operatively staged, we are very selective and we try to avoid surgery, more if they need a pneumonectomy or a bilobectomy that carries a significantly higher mortality as shown in these data.