Prediction of pulmonary complications after a lobectomy in patients with non-small cell lung cancer

H Uramoto, R Nakanishi, Y Fujino, H Imoto, M Takenoyama, T Yoshimatsu, T Oyama, T Osaki, K Yasumoto

Abstract

Background—Although the preoperative prediction of pulmonary complications after lung major surgery has been reported in various papers, it still remains unclear.

Methods—Eighty nine patients with stage I–IIIA non-small cell lung cancer (NSCLC) who underwent a complete resection at our institute from 1994–8 were evaluated for the feasibility of making a preoperative prediction of pulmonary complications. All had either a predicted postoperative forced vital capacity (FVC) of >800 ml/m2 or forced expiratory volume in one second (FEV1) of >600 ml/m2.

Results—Postoperative complications occurred in 37 patients (41.2%) but no patients died during the 30 day period after the operation. Pulmonary complications occurred in 20 patients (22.5%). Univariate analysis indicated that the factors significantly related to pulmonary complications were FVC < 80%, serum lactate dehydrogenase (LDH) level > 230 U/l, and arterial oxygen tension (PaO2) < 10.6 kPa (80 mm Hg). In a multivariate analysis the three independent predictors of pulmonary complications were serum LDH levels of >230 U/l (odds ratio (OR) 10.5, 95% CI 1.4 to 77.3), residual volume (RV)/total lung capacity (TLC) > 30% (OR 6.0, 95% CI 1.1 to 33.7), and PaO2 < 10.6 kPa (OR 5.6, 95% CI 1.4 to 22.2).

Conclusions—The above findings indicate that three factors (serum LDH levels of >230 U/l, RV/TLC > 30%, and PaO2 < 10.6 kPa) may be associated with pulmonary complications in patients undergoing a lobectomy for NSCLC, even though the patient group was relatively small for statistical analysis of such a diverse subject as pulmonary complications.

(Thorax 2001;56:59–61)

Keywords: non-small cell lung cancer; pulmonary complications; morbidity

Lung cancer is the leading cause of death among cancer patients.1 The necessity for surgical treatment is increasing because complete surgical removal of a tumour offers the best chance for a cure in patients with non-small cell lung cancer (NSCLC).2,3 A lobectomy remains the standard therapeutic option in most patients with early stage NSCLC. Although the operative mortality and morbidity following a lobectomy has decreased over the past decade, both factors still contribute significantly to the cost of treating such patients. Careful selection of the operative modalities is therefore required to reduce the overall mortality and morbidity.

Clinicians are often faced with the problem of morbidity, especially pulmonary complications, which tend to be impossible to predict. Pulmonary complications after lung resection can have serious consequences because the remaining lung tissue is severely compromised during the immediate postoperative period. In the present study we have reviewed a series of patients with NSCLC to evaluate the feasibility of preoperatively predicting pulmonary complications.

Methods

PATIENTS

From April 1994 to December 1998, 299 patients with primary lung cancer underwent lung resection at the Department of Surgery II, University of Occupational and Environmental Health, Kitakyushu, Japan. Of these, 89 patients with stage I–IIIA NSCLC in whom lobectomy was performed were assessed. All patients underwent the following diagnostic procedures preoperatively: brain computed tomographic (CT) scan, body CT scan, a pulmonary perfusion scintigraphic scan, and a bone scintigraphic scan. Spirometric tests were performed according to established guidelines.1 We calculated the predicted residual pulmonary function combined with xenon ventilation/perfusion scans from the ratio of right versus left fractional perfusion. The formula for the predicted residual pulmonary function is as follows:

Predicted residual pulmonary function = pulmonary function × (1 — ratio of lung perfusion on the resected side × number of resected pulmonary segments/number of pulmonary segments on the resected side)

In our institution surgery is indicated in patients with a predicted postoperative forced vital capacity (FVC) of >800 ml/m2 or a forced expiratory volume in one second (FEV1) of >600 ml/m2. Routine systematic lymphadenectomy of hilar and mediastinal lymph nodes was performed in all cases. The charts were then retrospectively reviewed. The ineligibility factors are shown in table 1. The 19 variables listed in table 2 were evaluated.

POSTOPERATIVE COMPLICATIONS

The pulmonary complications included atelectasis and sputum retention requiring bron-
Table 1  Ineligible factors

<table>
<thead>
<tr>
<th>Personal characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Karnofsky performance status: 70% or less</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, cardiac disease or others requiring medication</td>
<td></td>
</tr>
<tr>
<td>Preoperative chemotherapy and/or radiotherapy</td>
<td></td>
</tr>
<tr>
<td>Interstitial change detected by CT scan</td>
<td></td>
</tr>
<tr>
<td>Pulmonary function test</td>
<td></td>
</tr>
<tr>
<td>Both predicted postoperative FVC of 800 ml/m(^2) or less and predicted postoperative FEV(_1) of 600 ml/m(^2) or less</td>
<td></td>
</tr>
</tbody>
</table>

Tumour characteristics

Small cell carcinoma or low grade malignant tumour

Confirmed histological diagnosis of stage IIB or IV

Surgical characteristics

Residual tumour at the surgical margin

Incomplete systematic lymphadenectomy such as sampling

Less than lobectomy such as wedge resection or partial resection

Extent resection such as bilobectomy or pneumonectomy

Mechanical stapling devices for bronchial stump closure

Combined resection

Previous thoracic surgery such as thoracoplasty

Blood transfusion at operation

CT = computed tomography; FEV\(_1\) = forced expiratory volume in one second; FVC = forced vital capacity.

LDH = lactate dehydrogenase; FVC = forced vital capacity; PaO\(_2\) = arterial oxygen tension.

PaO\(_2\) (kPa) <10.6 15 8 (53.3%) 0.002

Table 4 Univariate analysis of the perioperative variables contributing to the occurrence of pulmonary complications following a lobectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>No of patients</th>
<th>No (%) of patients with pulmonary complications</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum LDH (U/l)</td>
<td>&lt;230</td>
<td>83</td>
<td>16 (19.3%)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>≥230</td>
<td>6</td>
<td>4 (66.7%)</td>
<td></td>
</tr>
<tr>
<td>FVC (%) (&lt;80)</td>
<td>&lt;80</td>
<td>5</td>
<td>3 (60.0%)</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>≥80</td>
<td>84</td>
<td>17 (20.2%)</td>
<td></td>
</tr>
<tr>
<td>PaO(_2) (kPa)</td>
<td>&lt;10.6</td>
<td>15</td>
<td>8 (53.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>≥10.6</td>
<td>74</td>
<td>12 (16.2%)</td>
<td></td>
</tr>
</tbody>
</table>

LDH = lactate dehydrogenase; FVC = forced vital capacity; PaO\(_2\) = arterial oxygen tension.
Table 5 Multivariate analysis of the perioperative variables contributing to the occurrence of pulmonary complications following a lobectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum LDH (U/l)</td>
<td>≥230</td>
<td>10.530</td>
<td>1.434 to 77.331</td>
<td>0.0207</td>
</tr>
<tr>
<td></td>
<td>&lt;230</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥30</td>
<td>6.015</td>
<td>1.074 to 33.688</td>
<td>0.0412</td>
</tr>
<tr>
<td></td>
<td>&lt;30</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO2 (kPa)</td>
<td>&lt;10.6</td>
<td>5.584</td>
<td>1.407 to 22.168</td>
<td>0.0145</td>
</tr>
<tr>
<td></td>
<td>&gt;10.6</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LDH = lactate dehydrogenase; RV = residual volume; TLC = total lung capacity; PaO2 = arterial oxygen tension.

Discussion

Advances in operative techniques and postoperative care have led to a further decline in the postoperative complication rates following a lobectomy with a mortality rate of 1–9% reported in recent studies.9–10 and morbidity occurring at an alarming rate of 11–47%.3–10 These mortality and morbidity data are generally obtained from eligible patients who are selected on the basis of their pulmonary function and other organ functions. We also selected surgical candidates on the basis of either a predicted postoperative FVC of >800 ml/m2 or an FEV1 of >600 ml/m2. The resulting 0% mortality suggests that our criteria appear to be generally acceptable. However, some morbidity still remains even in these selected patients. We therefore evaluated whether it is possible to predict pulmonary complications after a lobectomy because even patients eligible for surgery develop pulmonary complications.

Many investigators have tried to identify the factors that predict the occurrence of postoperative complications following a lobectomy. Previous studies have shown a relationship between perioperative pulmonary complications and preoperative variables including age,8–10 sex,8 obesity,11 chronic obstructive pulmonary disease,12–15 cigarette smoking,16 the measurement of maximum oxygen consumption during exercise,14 FEV1,9,15 predicted FEV1,15 and transfer factor (TLCO).16–17 However, these factors are not yet applicable at all institutions because the eligibility for surgery at each institution is different.

Our results suggest that the serum LDH level is strongly associated with postoperative morbidity. To our knowledge, only one report to date has previously evaluated the LDH level for predicting postoperative morbidity.9 A high LDH level indicates interstitial fibrosis of the lung following alveolar damage. No interstitial changes were detected on the CT scan and no liver dysfunction was seen in patients with a high LDH level in our series, although we did not investigate the isozyme of LDH. A high LDH level may indicate minimal interstitial damage of the lung which is not seen radiographically. We suggest that measurement of the LDH level, which is widely available, inexpensive, and quick and easy to perform, may have the potential to predict the occurrence of pulmonary complications.

In general, respiratory muscle weakness and semi-starvation is observed in patients following surgery. The contributing factors in these patients are postulated to be malnutrition related to biochemical, physiological, and anatomical changes, reduced blood flow to the respiratory muscles, and increased RV. An increase in RV means that the lung is still hyperinflated even after maximal expiratory effort, thereby increasing the lower secretion of sputum resulting from impaired movement of the diaphragm. An increased RV/TLC may thus also have an impact on the gas component in the alveolar space.

A low PaO2, which reflects diffusion impairment, unevenness of perfusion/ventilation, or existence of shunt, was independently associated with the occurrence of major postoperative pulmonary complications. Careful management may therefore be required for patients who simultaneously have a high level of LDH, a raised RV/TLC, and a low PaO2 because these three factors seem to be correlated. In these patients preoperative pulmonary rehabilitation should be performed to prevent pulmonary complications, including the immediate cessation of smoking, use of bronchodilators and/or antibiotics, hydration, and chest physiotherapy.

In conclusion, LDH levels of ≥230 U/l, RV/TLC of ≥30%, and PaO2 of <10.6 kPa (80 mm Hg) are the most predictive criteria for postoperative morbidity in surgical candidates who had both a predicted postoperative FVC of >800 ml/m2 and FEV1 of >600 ml/m2. An accurate prediction of postoperative morbidity would improve patient selection for operative procedures and also help to reduce the overall medical costs related to the treatment of such patients. Further studies in a prospective setting with a larger series of patients are required.

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