Institutional report - Pulmonary

Worsened long-term outcomes and postoperative complications in octogenarians with lung cancer following mediastinal lymph-node dissection

Masayuki Chida a,⁎, Muneo Minowa b, Yoko Karube b, Syunsuke Eba c, Yoshinori Okada c, Shinichiro Miyoshi a, Takashi Kondo a

⁎Corresponding author. Tel.: +81-282-87-2160; fax: +81-282-86-6390.
E-mail address: chida-ths@umin.ac.jp (M. Chida).

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1. Introduction

The incidence of primary lung cancer is increasing as life expectancy increases, and with the general aging of society the numbers of patients suffering from lung cancer and candidates for lung resections are increasing [1]. We previously reported functional evaluations for pulmonary resection for lung cancer patients over 80 years old [2], which indicate that selected octogenarians could be candidates for a lung resection.

The standard surgical procedure for lung cancer is a lobectomy with mediastinal lymph-node dissection. The procedure has been shown superior to a sublobar resection such as a wedge resection or a segmentectomy, because of its good local control [3], while mediastinal lymph-node dissection seems to be superior to lymph-node sampling [4]. However, it is still unclear whether octogenarians should undergo a standard or limited operation.

A limited operation is composed of two factors, a limited lung volume resection procedure, such as a wedge resection or a segmentectomy, and a limited lymph-node dissection, such as regional dissection or sampling. In this report, we focused on the efficacy of lymph-node dissection as treatment for octogenarians with lung cancer.

2. Subjects and methods

A total of 48 patients of at least 80 years old with primary lung cancer who underwent an anatomical resection procedure from 1981–2006 at the authors’ institutions were investigated retrospectively. All patients were performance status 0–1. All patients who met functional criteria underwent surgery. The functional criteria [2] were 1) predicted-contralateral value of forced expiratory volume 1 > 800 ml/m², or 2) total pulmonary vascular resistance index calculated by unilateral pulmonary artery occlusion test <700 dyne-s-cm⁻²-m⁻². There were no difference of PS or pulmonary functions in each group.

We defined an anatomical lung resection as a lobectomy, pneumonectomy, or segmentectomy, with the latter (left upper divisionectomy and lingulectomy) chosen only when it showed a good indication for the patient. Cases with a wedge resection were excluded from the present analysis, even if the margin was wide. Patients with a performance status grade of 0 or 1 and who met the indications of cardiopulmonary functional tests were selected. In addition, each provided consent to undergo a lung resection.
The patients were divided into two groups; those who received an anatomical lung resection and mediastinal lymph-node dissection (ND2 group), and those who received an anatomical lung resection and regional (hilar) lymph-node dissection and/or sampling (ND0-1 group). In this retrospective study, the selection of candidates for each group depended upon each operator. The pathological stage of the disease was determined using the Union Internationale Contre Cancer (UICC) TNM classification.

During the early postoperative period, patients who showed arrhythmia on electrocardiograms for more than two consecutive days were considered to have cardiac complications. Those who underwent a bronchoscopic procedure more than twice or a tracheotomy because of difficulties with expectorating sputum, as well as cases with atelectasis shadows on chest X-ray images for more than three consecutive days were considered to have pulmonary complications.

Statistical analysis between the two groups was performed using a χ²-test to compare variables. The Kaplan–Meier method was used for calculation of survival from death by any cause. Comparisons within each group were performed using a log-rank test. Differences were considered significant at $P < 0.05$, with borderline significance considered at $P < 0.10$.

3. Results

Twenty-three patients underwent a mediastinal lymph-node dissection (ND2 group) and 25 a limited lymph-node dissection (ND0-1 group). Histologically, there were 25 patients with adenocarcinomas, 17 with squamous cell carcinomas, three with large cell carcinomas, and three with other carcinomas (Table 1). The most commonly performed surgical procedure in both groups was a lobectomy and each group had a similar percentage of pathological stage I patients.

The five-year survival rate for all of the present patients was 35.0% and the median survival time was 40.2 months (Fig. 1). Those in pathological stage I comprised 43.3%.

Table 1  Characteristics of patients with a mediastinal (ND2) and limited lymph-node dissection (ND0-1)

<table>
<thead>
<tr>
<th>ND2 ($n=23$)</th>
<th>ND0-1 ($n=25$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>81.5 (80–85)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>AD</td>
<td>10</td>
</tr>
<tr>
<td>SCC</td>
<td>10</td>
</tr>
<tr>
<td>LCC</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
</tr>
<tr>
<td>Incomplete resection</td>
<td>1</td>
</tr>
<tr>
<td>cStage I</td>
<td>16</td>
</tr>
<tr>
<td>II</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
</tr>
<tr>
<td>pStage I</td>
<td>14</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>21</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>2</td>
</tr>
<tr>
<td>Segmentectomy</td>
<td>3</td>
</tr>
</tbody>
</table>

ND0-1 symptoms: AD, adenocarcinoma; SCC, squamous cell carcinoma; LCC, large cell carcinoma; LUD, left upper divisionectomy; Ling, lingulectomy.

while 21.2% were pathological stage II or III ($P=0.082$). The five-year survival rate for the ND2 group was 21.7% and it was 54.3% for ND0-1 (Fig. 2), which was a statistically significant difference ($P=0.022$). For pathological stage I patients in each group (Fig. 3), the five-year survival rate was 28.6% in ND2 and 61.9% in ND0-1 ($P=0.041$). In cases that underwent a lobectomy (Fig. 4), the five-year survival rate was 23.8% in ND2 and 48.3% in ND0-1 ($P=0.075$). Thus, mediastinal lymph-node dissection worsened the outcomes of the present octogenarians with lung cancer.

Twenty-one patients in the ND2 group died (11 from cancer) as did 13 patients in the ND0-1 group (7 from cancer) (Table 2). There was not a significant difference in the rate of death from cancer extension during the observation period between the groups (ND2: 52.3%, ND0-1: 53.8%). On the other hand, 9 of 21 patients (42.8%) died from other diseases in the ND2 group, while only 2 of 13 (15.3%) did in the ND0-1 group ($P=0.092$). Thus, patients...
4. Discussion

Although an increasing number of octogenarian patients with lung cancer are expected to undergo lung resections because of the rapid aging of society, there is scant accumulation of knowledge in regard to such cases. Herein, we report that a mediastinal lymph-node dissection is associated with worsened outcomes in patients with lung cancer who are 80 years old and older.

It has been reported that age does not influence early and late tumor-related outcome in lung cancer cases [5, 6], and we routinely perform lobectomy and mediastinal lymph-node dissection procedures for elderly patients, including octogenarians. Shimizu et al. [7] found that a radical operation was associated with long-term survival in elderly subjects, whereas Kobayashi et al. [8] recommended limited operations for octogenarians from the viewpoint of increasing postoperative complications. A so-called limited operation is composed of two factors; reduction of lung volume via resection, such as a wedge resection or a segmentectomy, and omitting the lymphadenectomy, such as sampling or regional lymphadenectomy. However, it is unclear which factors have an influence on outcome, especially the long-term results of octogenarians with lung cancer. Since most of the present patients underwent a lobectomy, our results were clearly dependent upon whether a lymphadenectomy was performed.

Izbicki et al. [9] reported that there was no difference in outcomes between mediastinal lymph-node dissection and sampling, while Keller et al. [4] pointed out the advantages of mediastinal lymph-node dissection for patients with stage II or IIIa lung cancer. It remains controversial whether a mediastinal lymph-node dissection has a firm advantage in regard to survival of patients with lung cancer. Although we believe that it has some advantage for long-term survival, the merits do not seem to outweigh the demerits for poor-risk patients such as octogenarians. Recently, Allen et al. [10] performed an intermediate analysis of the prospective randomized trial ASCOSOG Z0030. In their report, there was no difference for morbidity or mortality between mediastinal lymph-node dissection and sampling. In contrast, the present results indicated an increase in cardiac complications in patients who underwent a mediastinal lymph-node dissection. Since our subjects were octogenarians, it is possible that elderly patients, especially those at least 80 years old, may be more susceptible to surgical stress caused by such procedures as major pulmonary resection and radical lymph-node dissection.

In our analysis of cause of death, we found no significant differences in regard to cancer death between the groups, though those who underwent a mediastinal lymph-node dissection showed a greater tendency to die from a disease other than cancer extension.

Postoperative complications were fully recorded in the records of 33 patients and those were used for analysis (Table 3). There was no difference in pulmonary complications between the groups, though there was one hospital death due to interstitial pneumonia in ND2. Arrhythmia occurred in a total of 12 patients after surgery, 10 with supra-ventricular arrhythmia, one with ventricular arrhythmia, and one with combined arrhythmia. Those with supra-ventricular arrhythmia included four patients with atrial fibrillation, two with paroxysmal tachycardia, two with those in combination, and three with premature atrial contraction. Thus, a mediastinal lymph-node dissection procedure was associated with a significantly greater incidence of cardiac complications as compared to a regional lymphadenectomy ($P=0.004$).
In conclusion, octogenarians with lung cancer who underwent a mediastinal lymph-node dissection had increased postoperative cardiac complications and worsened long-term survival.

References


eComment: Long-term outcomes in octogenarians with lung cancer following mediastinal lymph node dissection

Authors: Nikolaos Barbetakis, Thoracic Surgery Department, Theagenio Cancer Hospital, A. Simeonidi 2, 54007 Thessaloniki, Greece; Georgios Samanidis, Dimitrios Paliouras, Christodoulos Tsilikas

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We would like to congratulate Dr Chida et al. for their excellent analysis regarding the impact of mediastinal lymph node dissection on the outcome and postoperative complications in octogenarians [1].

Age is a recognized risk factor for death after thoracotomy in elderly patients with lung cancer. Among other factors, the genesis of this risk is the physiologic debilitation that occurs after division of respiratory muscles during thoracotomy, as well as the loss of lung tissue after lung resection.

The main question, which is also addressed by the authors is: is radical lymph node dissection responsible for the worsened outcomes or major surgery itself? Did the authors notice any differences between patients who underwent VATS lobectomy compared to those who underwent open procedure? Were the two groups similar in terms of coexistent diseases preoperatively?

According to Allen et al. there is no difference for mortality and morbidity between patients with early stage lung cancer who underwent mediastinal lymph node dissection or sampling only [2]. Probably smaller lung resections (video-assisted limited wedge resection vs. lobectomy with thoracotomy) could be adequate oncologic procedures in octogenarians with limited life expectancy but resectable disease.

References
