The spread of metastatic lymph nodes to the mediastinum from left upper lobe cancer: results of superior mediastinal nodal dissection through a median sternotomy

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Abstract

Background: This study endeavored to clarify the location, frequency, and prognostic value of metastatic lymph nodes in the mediastinum among patients with left upper lung cancer who underwent complete dissection of the superior mediastinal lymph node through a median sternotomy.

Methods: Forty-four patients with left upper lobe cancer underwent extended radical mediastinal nodal dissection (ERD), all of whom were analyzed in this retrospective study. The group comprised 12 females and 32 males, with ages ranging from 28 to 70 years (median age, 60 years). Mediastinal nodal status was assessed according to the systems of Mountain/Dresler 7 and Naruke 8. The clinicopathological records of each patient were examined for prognostic factors, including age, sex, histology, tumor size, c-N number, preoperative serum CEA level, metastatic stations and distribution of metastatic nodes according to Naruke’s system 8. The superior mediastinal lymph nodes which cannot be dissected through a left thoracotomy (bilateral #1 and #2, #3, right #3a, and right #4 according to Naruke’s map 8 were defined as extra-superior mediastinal nodes for left lung cancer (ESMD).

Results: Fourteen patients had one or more metastases to mediastinal lymph nodes, among whom the most common metastatic station was the aortic nodes: 71.4% had metastasis to #5 or #6 (57.1% to #5 and 50% to #6). The next most common metastatic station was the left tracheobronchial nodes (42.8%). Metastasis to the ESMD occurred in 7 of the 44 study subjects (16%), representing a 50% rate of occurrence (7/14) among those with mediastinal nodal involvement. Univariate analysis found that CN factor and aortic nodal involvement (#5, #6) were significant predictive factors for ESMD metastasis. Multivariate analysis determined that only aortic nodal involvement was significant (p = 0.008). Furthermore, ESMD metastasis was rare (5.8%) in the absence of aortic node metastasis. The overall survival rate at 5 years was 50% among the patients without ESMD metastasis. However, the survival rate was 32% at 3 years and 0% at 5 years among the seven patients with ESMD metastasis.

Conclusions: The aortic lymph node is the most common site of metastasis from left upper lobe cancer. Multivariate analysis demonstrated that aortic nodal involvement was an independent predictive factor for ESMD metastasis. Based upon the rates of metastasis and the post-operative prognosis in our study patients, dissection of aortic nodes and left tracheobronchial nodes may be important for patients with left upper lobe cancer. Whether ESMD dissection has a beneficial effect on prognosis remains controversial.

Keywords: Aortic lymph node; Median sternotomy; Extended radical lymph node dissection

1. Introduction

The lymphatic pathways paralleling the trachea represent one of the main routes of lymphatic drainage from both sides of the lung [1—3]. However, removing or sampling lymph nodes from these pathways paralleling the trachea (i.e. the superior mediastinal nodes) through a left thoracotomy (the standard surgical approach to left lung cancer) is difficult due to anatomical limitations imposed by the aortic arch and its branches. Therefore, few studies have examined metastases to superior mediastinal lymph nodes (paratracheal and highest mediastinal nodes) from left lung cancers [4].

Following publication by Hata et al. [4] of their favorable post-operative outcomes following dissection of superior mediastinal nodes (bilateral paratracheal and highest mediastinal nodes) through a median sternotomy in N2/N3 left lung cancers, we began performing median sternotomies in patients with left lung cancer in order to completely dissect the superior mediastinal nodes.

In this retrospective study, we have tried to clarify the pathways of lymphatic spread of metastatic cancer into mediastinal lymph nodes, including bilateral paratracheal and highest mediastinal nodes, from left upper lobe lung cancer and to clarify the prognostic significance of metastatic node location in patients with left upper lobe lung cancer.

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cancer who underwent complete-dissection of their superior mediastinal lymph nodes through median sternotomy.

2. Materials and methods

Between 1996 and April 2005, 560 patients underwent surgical resection of primary lung cancer within our department. For eligible patients with lung cancers in the left upper lobe, we performed surgery through a median sternotomy in order to completely dissect the superior mediastinal nodes [4,5] as part of an extended radical lymph node dissection. Patients 70 years of age or younger without major impairment in cardiac or respiratory function were eligible for the extended radical lymph node dissection. Patients whose radiological findings included pure ground glass opacity were categorically excluded from the extended radical lymph node dissection. A total of 44 patients with left upper lobe cancer underwent the extended radical lymph node dissection. An initial thoracoscopic exploration of the left thorax is conducted to confirm the absence of findings indicating incomplete resection of the tumor, such as pleural dissemination or malignant effusion. If the resection appears to be complete, a median sternotomy is made and the anterior mediastinal fatty tissue (including prevascular nodes) removed. The lymph nodes on the caudal side of the thyroid gland, which surround the right and left recurrent laryngeal nerves, constitute the upper limit of mediastinal dissection. The series of lymph nodes running bilaterally adjacent to the trachea (along the vagal nerve on the right side of the trachea, along the recurrent laryngeal nerve on the left side of the trachea) are next dissected [4,9]. The left tracheobronchial angle nodes are dissected through the left thorax successively with the mediastinal nodes. Finally, bilateral superior and tracheobronchial nodes, aortic nodes and subcarinal nodes were dissected as mediastinal nodes. The superior mediastinal lymph nodes which cannot be dissected through a left thoracotomy (bilateral #1 and #2, #3, right #3a, and right #4 according to Naruke’s map [8] or the bilateral highest mediastinal nodes, bilateral superior paratracheal nodes, and right tracheobronchial nodes according to the system of Mountain/Dresler [7] were defined as extra-superior mediastinal nodes for left lung cancer (ESMD) for this study.

The duration of follow-up ranged from 6 to 108 months (median: 58 months). The clinicopathological records of each patient were examined for prognostic factors, including age, sex, histology, tumor size, c-N number, preoperative serum CEA level, metastatic stations, and distribution of metastatic nodes according to Naruke’s system [8]. Patient characteristics are summarized in Table 1.

3. Statistical analysis

The duration of survival was defined as the interval between the date of surgery and the date of death by any cause or the interval between the date of surgery and the last follow-up date. Survival rates were calculated using the Kaplan–Meier method, and univariate analyses were performed using the log-rank test or the logistic regression procedure test. Multivariate analyses were performed by means of the Cox proportional hazards model, using Stat View J 5.0 (SAS Institute Inc., Cary, NC), for variables with p values less than 0.05 under univariate analyses. A p-value less than 0.05 was treated as significant.

4. Results

4.1. Distribution of mediastinal lymph node involvement

Of the 44 study subjects, 14 (31.8%) had one or more metastases to the mediastinal lymph nodes. The distribution of metastatic mediastinal nodes is summarized in Fig. 1. Skip N2 had a frequency of 21.4% (3/14). The most common metastatic station was the aortic nodes: 71.4% (10/14) had metastasis to #5 or #6 (57.1% (8/14) to #5, and 50% (7/14) to #6). The next most common metastatic station was the left tracheobronchial nodes: 42.8% (6/14). ESMD metastasis

Table 1

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28—69 (median, 60)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>32/12</td>
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<tr>
<td>C—N factor</td>
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<tr>
<td>CN0</td>
<td>33</td>
</tr>
<tr>
<td>CN1</td>
<td>6</td>
</tr>
<tr>
<td>CN2</td>
<td>5</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>28</td>
</tr>
<tr>
<td>Other</td>
<td>16</td>
</tr>
<tr>
<td>p—N factor</td>
<td></td>
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<tr>
<td>pN0</td>
<td>21</td>
</tr>
<tr>
<td>pN1</td>
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<td>7</td>
</tr>
<tr>
<td>p-IIIA 1</td>
<td>6</td>
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</table>
occurred in 7 of the 44 subjects (16%). That is, 50% (7/14) of patients with mediastinal nodal involvement also had ESMD metastasis. Skip ESMD metastasis occurred in two patients.

4.2. Association between extra-superior mediastinal nodal (ESMD) involvement and aortic or tracheobronchial nodes involvement

Five of the 10 cases (50%) with aortic nodal (#5, #6) involvement also had ESMD metastasis. Two of the six cases (33%) with left tracheobronchial nodal (left #4) involvement also had ESMD metastasis. Two of the four cases (50%) with aortic (#5, #6) and left tracheobronchial (left #4) nodal involvement had ESMD metastasis.

On the other hand, 2 of the 34 cases (5.8%) without aortic nodal involvement had ESMD metastasis. Five of the 38 cases (13.2%) without left tracheobronchial nodal involvement had ESMD metastasis. Two of the 32 cases (6.3%) with neither aortic nor left tracheobronchial nodal involvement had ESMD metastasis.

4.3. Predictive factors for ESMD metastasis

The variables listed in Table 2 were analyzed as predictive factors for ESMD metastasis. Univariate analysis found that CN factor and aortic nodal involvement (#5, #6) were significant predictive factors for ESMD metastasis, while tumor size, histologic type, hilar nodal involvement, and left tracheobronchial (left #4) involvement were not significant predictive factors for ESMD metastasis.

CN factor and aortic nodal involvement were further examined under multivariate analysis using a logistic regression procedure (Table 3). The multivariate analysis determined that aortic nodal involvement was significant for ESMD metastasis ($p = 0.008$, HR: 10.4, 95% CI: 2.7–41.6) but that CN factor was not significant ($p = 0.31$, HR: 2.0, 95% CI: 0.54–7.16).

Even among CN0 patients, aortic node metastasis was a significant predictive factor for ESMD metastasis ($p < 0.001$). Furthermore, no CN0 patient had ESMD metastasis in the absence of aortic node metastasis (0/27).

4.4. Survival rate as a function of ESMD metastasis

Post-operative prognosis as a function of ESMD involvement is shown in Fig. 2. The overall survival rate of N2 patients at 5 years was 50% among the patients without ESMD metastasis. Among the seven patients with ESMD involvement, two

![Fig. 1. Location and frequency of metastatic lymph nodes in patients with mediastinal nodal involvement. ESMD: extra-superior mediastinal lymph nodes. Station numbers are according to Naruke’s system 8.](https://academic.oup.com/ejcts/article-abstract/30/3/543/460742/11)

![Fig. 2. Five-year survival rates for patients with mediastinal nodal involvement, excluding the seven patients with extra-superior mediastinal lymph node involvement. ESMD: extra-superior mediastinal lymph nodes for left lung cancer.](https://academic.oup.com/ejcts/article-abstract/30/3/543/460742/11)
patients (one N2 and one N3) were 3-year survivors, and none were 5-year survivors (Table 4).

5. Comments

Aortic lymph nodes (#5 or #6, according to Naruke’s map) constituted the most common site of metastasis from left upper lobe cancer, occurring in 71.4% of patients with mediastinal nodal involvement, a frequency consistent with previous reports [10,11]. Surprisingly, we found that the rate of ESMD metastasis was 50% (5/10) when aortic nodes were involved. Multivariate analysis demonstrated that aortic nodal involvement was a significant predictive factor for ESMD metastasis, even among the CN0 patients.

In the present study, the frequency of skip aortic nodal involvement was only 10% (1/10). Marc et al. [12] reported that 34 out of their 77 patients with aortic nodal involvement (44.2%) were skip N2 patients and that outcomes were more favorable for skip N2 patients than for non skip N2 patients [12]. Our study suggested that patients with aortic nodal involvement and no skip involvement had a high rate of ESMD metastasis. Conversely, ESMD metastasis was rare (5.8%) in the absence of aortic node involvement. Furthermore, since no CN0 patient had ESMD metastasis in the absence of aortic node metastasis (0/27), our study results suggest that CN0 patients without aortic nodal involvement might not benefit from ESMD dissection.

The frequency of left tracheobronchial nodal metastasis was second only to that of aortic nodal metastasis, i.e. 42.8% of patients with mediastinal nodal involvement. However, left tracheobronchial nodal metastasis was not a significant predictive factor for ESMD metastasis under both univariate and multivariate analyses. Even when the left tracheobronchial node was involved, no patient had ESMD metastasis in the absence of concomitant aortic node involvement.

Post-operative prognosis was poor for the seven patients with ESMD metastasis (including four N3-cases). However, two of these patients were 3-year survivors despite their having multi-level mediastinal involvement. Although none of the patients received adjuvant therapy in our series, our findings suggest that consideration should be given to multimodal therapy, especially when managing patients with ESMD involvement. Whether dissection of ESMD in patients with lung upper lobe cancer has a beneficial effect on prognosis remains controversial. On the other hand, 5-year survival was 50% in N2 patients who did not have ESMD metastasis. Based upon the rates of metastasis and the post-operative prognosis, dissection of aortic nodes and left tracheobronchial nodes may be important for patients with left upper lobe cancer. Median sternotomy would appear to better facilitate complete dissection of tracheobronchial nodes compared with lateral thoracotomy.

In the present study, most cases (40 out of 44) were lung cancers located in the left upper segment. A scintigraphy study by Hata et al. demonstrated that the degree of contralateral mediastinal drainage from the left lung differed among the various lobes or segments. In particular, lymphatic drainage into the contralateral mediastinum was more common from the lingular segment and left lower lobe than from the upper segment (1). The frequency of ESMD metastasis and the outcome after surgery for patients with ESMD metastasis might be different in patients with lingular or left lower lobe lung cancers compared with patients with upper segment cancers.

Limitations of the present study include the retrospective nature of the analysis and the small sample size.

In conclusion, among our group of study patients with left upper lobe cancers, the aortic lymph node was the most common site of metastasis. Multivariate analysis demonstrated that aortic nodal involvement was a significant predictive factor for ESMD metastasis. Based upon the rates of metastasis and the post-operative prognosis in our study patients, dissection of aortic nodes and left tracheobronchial nodes may be important for patients with left upper lobe cancer. Whether ESMD dissection has a beneficial effect on prognosis remains controversial.

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References


