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EXTENT OF MEDIASTINAL LYMPH NODE DISSECTION FOR CLINICAL T1 NON-SMALL CELL LUNG CANCER

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Abstract : The present study was designed to determine the extent of lymph node dissection for clinical T1 non-small cell lung cancer without negatively influencing curability. The study included 192 cases with clinical T1 non-small cell lung cancers who underwent lobectomy with mediastinal lymphadenectomy. Among 69 cases with right upper lobe tumors, metastasis was found in subcarinal lymph node in one case only. No metastasis was found in subcarinal node in cases free of metastasis in hilar and/or superior mediastinal nodes. Among 33 cases with right lower lobe tumors, metastasis was detected in the superior mediastinal node only in cases with metastasis in hilar and/or subcarinal nodes. Among 51 cases with left upper lobe tumors, no metastasis was found in the subcarinal node. Among 22 cases with left lower lobe tumors, metastasis was found in the superior mediastinal nodes only in cases with metastasis in hilar and/or subcarinal nodes. We propose the following scheme for the extent of mediastinal node dissection. Dissection of mediastinal node for clinical T1 non-small cell lung cancer cannot be omitted. But, 1) for upper lobe tumors, subcarinal lymphadenectomy could be omitted if no metastasis is found in hilar and superior mediastinal nodes based on gross and microscopic examination of frozen sections. 2) Similarly, for lower lobe tumors, superior mediastinal lymphadenectomy could be omitted if no metastasis is detected in the hilar and subcarinal nodes.

Key words : lung cancer, mediastinal lymph node dissection, frozen section

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INTRODUCTION

Lobectomy and hilar and mediastinal lymph node dissection are the standard surgical treatment for lung cancer. However, whether mediastinal node dissection provides survival benefits is controversial.¹⁾ Several groups advocate mediastinal node dissection because correct pathological staging can be determined only after mediastinal node dissection, and because such procedure is often safe and is not associated with specific postoperative complications. Others, however, argue that mediastinal node dissection is not always necessary, because most dissected mediastinal lymph nodes are found to be free of metastasis and that the dissection of the lymph nodes is an invasive procedure.

In these days, extent of lymph node dissection tends to be reduced. Because group examination using computed tomography increased diagnosis of small lung cancer. And thoroscopic surgery required the reconsideration of the extent of lymph node dissection. Several studies have examined this issue by investigating the impact of various parameters such as tumor size and pathological classification. The purpose of this study is to determine whether the extent of lymph node dissection for clinical T1 non-small cell lung cancer could be reduced than that of standard lymph node dissection (ND2a)²⁾ without jeopardizing curability.

SUBJECTS AND METHODS

The study included all 192 cases of clinical T1 non-small cell lung cancer who underwent lobectomy with mediastinal lymph node dissection at our Department during the period from January 1986 to June 2004. Cases needed pneumonectomy or cases needed bronchoplastic lobectomy were not included. The study conformed the general rule for clinical and pathological record of lung cancer (6th edition).²⁾ Lymph nodes were classified into superior mediastinal lymph nodes (right : # 1, 2, 3, 4 ; left : # 1, 2, 3, 4, 5, 6), subcarinal lymph node (# 7), inferior mediastinal lymph node (# 8, 9) and hilar lymph node (# 10, 11, 12). Histopathological diagnosis of lung cancer was adenocarcinoma in 139 (72.3%), squamous cell carcinoma in 36 (18.8%) and others in 17. The pathological extent of lymph node metastasis (pathological N) was N0 in 148 (77.2%), N1 in 16 (8.3%), and N2 or N3 in 28 (14.5%). The lung tumor was located in the right upper lobe in 69, right middle lobe in 17, right lower lobe in 33, left upper lobe in 51 and left lower lobe in 22 (Table I). We defined surgical N as the extent of lymph node metastasis diagnosed during surgery based on gross and histopathological findings of frozen sections of lymph nodes. We defined skip metastasis as metastasis of mediastinal node without hilar node.

Table I. Patient characteristics

	No	%
Sex		
Male	105	54.7
Female	87	45.3
Histologic type		
Adenocarcinoma	139	72.3
Squamous cell carcinoma	36	18.8
Others	17	8.9
Postoperative T status		
T1	165	86.0
T2	19	9.9
T3	2	1.0
T4	6	3.1
Postoperative N status		
N0	148	77.2
N1	16	8.3
N2	26	13.5
N3	2	1.0
Tumor location		
Right upper lobe	69	35.8
Right middle lobe	17	8.9
Right lower lobe	33	17.2
Left upper lobe	51	26.6
Left lower lobe	22	11.5

RESULTS

Lymph node metastasis in 119 cases with right lung tumors (Table II)

1. *Right upper lobe* : Among 69 cases in this lobe, metastasis in lymph node # 7 was found in only one tumor (1.4%). The stage was considered clinical N2 (preoperative CT finding showed swelling of mediastinal lymph node) and also showed metastasis of hilar and superior mediastinal nodes. Metastasis in node # 7 was never found in cases without metastasis in hilar and/or superior mediastinal nodes. In other words, metastasis in node # 7 was never found in clinical T1N0 tumors.

Among 69 cases, surgical N was misdiagnosed in 6 cases. Two of these 6 cases were misdiagnosed as surgical N1 though they were diagnosed as pathological N2 after operation. The other 4 cases were misdiagnosed as surgical N0 though they were diagnosed as pathological N2. However, none of these 4 cases showed metastasis in node # 7. The reason for the misdiagnosis of these 2 cases was that the frozen section of the mediastinal node examined during operation had no metastasis, while the other mediastinal node that was examined after surgery did show metastasis. The reason for the misdiagnosis of the other 2 cases was that no

Table II. Lymph node metastasis in 119 cases with right lung tumors.

LN station	Right upper lobe tumor (n=69)				
# 1-4	○	○	●	●	●
# 7	○	○	○	○	●
# 8, 9	○	○	○	○	○
# 10-12	○	●	○	●	●
total	57	1	3	7	1

LN station	Right middle lobe tumor (n=17)			
# 1-4	○	○	●	●
# 7	○	○	●	●
# 8, 9	○	○	○	●
# 10-12	○	●	○	○
total	14	1	1	1

LN station	Right lower lobe tumor (n=33)				
# 1-4	○	○	○	●	●
# 7	○	○	●	●	●
# 8, 9	○	○	○	○	○
# 10-12	○	●	●	○	●
total	26	3	1	1	2

● : lymph node with metastasis, ○ : lymph node without metastasis

frozen section of the mediastinal node was examined during operation though hilar node was examined.

2. *Right middle lobe* : Among 17 cases in this lobe, metastasis was detected in the superior mediastinal, # 7 and inferior mediastinal nodes in one case that did not have metastasis in the hilar node.

3. *Right lower lobe* : Among 33 cases in this lobe, metastasis was found in the superior mediastinal node in 3 cases (9.1%) that had also metastasis in the hilar and/or # 7 node. Metastasis was never detected in the superior mediastinal node in cases without metastasis in the hilar and/or # 7 nodes (Table II).

Among 33 cases, surgical N was misdiagnosed in 2 cases as surgical N1 though they were diagnosed as pathological N2 after operation. The reason for the misdiagnosis was that frozen section of # 7 was not examined during operation

though hilar node was examined. None of the cases of surgical N0 were diagnosed as pathological N2 after operation.

Lymph node metastasis in 73 cases with left lung tumors (Table III)

1. *Left upper lobe*: Among 51 cases in this lobe, no metastasis of #7 was found.

2. *Left lower lobe*: Among 22 cases in this lobe, metastasis was detected in the superior mediastinal node in 5 cases (22.7%). No metastasis was found in the superior mediastinal node in cases free of metastasis in the hilar and/or #7 nodes (Table III).

Among 22 cases, surgical N was misdiagnosed in 5 cases. Three of these 5 cases was misdiagnosed as surgical N0 as it was diagnosed pathological N1 postoperatively. The other 2 cases were misdiagnosed as surgical N0 and were diagnosed as pathological N2. These two patients subsequently underwent mediastinal lymph node dissection through median sternotomy. One patient remains alive more than 5 years even though metastasis was identified in lymph nodes #3, #7 and #11. The other patient is also alive more than 5 years in spite of detection of metastasis in nodes #5 and #12l.

Skip metastasis: Among 192 cases, pathological N2 or N3 were found in 28 cases. Skip metastases were found in 8 of 28 (28.6%). Tumor occupying lesions

Table III. Lymph node metastasis in 73 cases with left lung tumors.

LN station	Left upper lobe tumor (n=51)					
#1-4	○	○	○	○	●	
#5,6	○	○	●	●	●	
#7	○	○	○	○	○	
#8,9	○	○	○	○	○	
#10-12	○	●	○	●	●	
total	39	6	2	2	4	

LN station	Left lower lobe tumor (n=22)					
#1-4	○	○	○	○	●	●
#5,6	○	○	●	●	○	●
#7	○	○	○	○	●	○
#8,9	○	○	○	●	○	●
#10-12	○	●	●	●	●	●
total	12	5	1	1	1	2

●: lymph node with metastasis, ○: lymph node without metastasis

with skip metastasis were found in the right upper lobe in 3, right middle lobe in 2, right lower lobe in 1 and left upper lobe in 2.

Tumor size: Metastasis was detected in the mediastinal node in 1 of 21 (4.8%) with maximum tumor diameter of 1 cm, in 12 of 88 (13.6%) of >1 cm but ≤2 cm, and in 15 of 83 (18.1%) of >2 cm but ≤3 cm.

DISCUSSION

Standard extent of lymph node dissection for lung cancer is ND2a. But in these days, detection of small nodule was increased. So reconsideration of routine node dissection (ND2a) is needed. We studied the possibility of reduction of extent of lymph node dissection.

It is ideal to dissect only lymph nodes that enhance survival. It is also of no benefit to dissect lymph nodes that are free of metastasis. It could be argued also that there is no need to dissect lymph nodes that do not influence survival even if the node has metastasis. Dissection that contributes to survival benefit seems to be clinical N0, pathological T1, skip metastasis without hilar node metastasis, and metastasis of a single mediastinal station.^{3,4)}

Watanabe and colleagues⁵⁾ reported that mediastinal nodal dissection would be unnecessary in patients with peripheral small-size lung cancer fulfilling the following criteria: 1) squamous cell carcinoma ≤2 cm in diameter; 2) adenocarcinoma ≤1 cm; 3) localized bronchioloalveolar carcinoma ≤2 cm without foci of active fibroblastic proliferation when examined microscopically. In our study, mediastinal lymph node metastasis was noted in 13.6% of tumors with maximum diameter of >1 cm to ≤2 cm and in 4.8% of tumors with maximum diameter of ≤1 cm. Considered together, we believe measurement of tumor size alone is insufficient to allow decision making regarding mediastinal lymphadenectomy.

Several studies reported the feasibility of omission of dissection of #7 for upper lobe tumor.^{6,7-9)} Tsubota and colleagues⁷⁾ indicated that dissection of the subcarinal nodes in upper-lobe tumors can be omitted when gross and frozen section findings are negative in the superior mediastinum and upper lobe are intact. Furthermore, Asamura and colleagues⁹⁾ reported that subcarinal lymphadenectomy is not always necessary for tumors of the right upper lobe and left upper segment. Our study indicated that in tumors of both upper lobe, metastasis of #7 was never found in cases free of metastasis in hilar and/or superior mediastinal nodes. It is problematic to misdiagnose as surgical N0 and omit dissection of #7 with metastasis. In our study, 4 cases with right upper lobe tumors were misdiagnosed as surgical N0. However, these 4 cases did not have metastasis of #7 but superior mediastinal lymph node metastasis.

Several studies reported the omission of superior mediastinal lymphadenectomy in lower lobe tumors.^{6,7-9)} Anatomically, lymphatic pathways exist from the right

lower lobe to the superior mediastinal lymph nodes without passing through the subcarinal node. This fact indicates that we cannot omit the dissection of superior mediastinal lymph nodes even if there is no metastasis in the hilar and/or subcarinal nodes. Tsubota and colleagues⁷⁾ indicated that superior mediastinal dissection is not required for lower-lobe tumors with negative hilar and subcarinal nodes. Asamura and colleagues⁹⁾ advised superior mediastinal dissection, but indicated that superior mediastinal metastasis should be viewed as a marker of poor prognosis in tumors of both lower lobes. Our study indicated that metastasis of the superior mediastinal node was never identified in cases free of metastasis in the hilar and # 7 nodes.

It is problematic to misdiagnose as surgical N0 and omit superior mediastinal lymphadenectomy for lymph nodes with metastasis. In our study, there was no such case in patients with right lower lobe tumors. In contrast, in left lower lobe tumors, metastasis was found in the superior mediastinal node in 5 cases. Two cases among 5 was misdiagnosed as surgical N0 under operation. One of these 2 cases had micrometastasis in # 7 and the other had micrometastasis in # 5, so frozen sections of these lymph nodes were not useful.

Previous data generated from lymph node dissection showed that the extent of lymph node metastasis had similar tendency by tumor occupying lesion.⁶⁾ Lymph nodes most likely to be the first site of metastasis are # 12, # 11 and/or # 10 at N1 level. At the N2 level, # 3 and/or # 4 in right upper lobe tumors, # 3 and/or # 7 in right middle lobe tumors, # 7 in right lower lobe tumors, # 5 and/or # 6 in left upper lobe tumors, and, # 7 in left lower lobe tumors. These results should be taken into consideration when we examine the frozen sections of lymph nodes.

In adenocarcinoma, we were able to find metastases of # 7 in few cases of upper lobe tumors, and metastasis of superior mediastinal node in lower lobe tumors. However, in squamous cell carcinoma, we could not find metastasis of # 7 in both upper lobe tumors, or metastasis of superior mediastinal node in both lower lobe tumors. These results suggest it may be unnecessary to examine frozen sections of lymph nodes in squamous cell carcinoma.

We propose the following scheme for the extent of mediastinal node dissection. Dissection of mediastinal node for clinical T1 non-small cell lung cancer cannot be omitted. But, 1) for upper lobe tumors, dissection of # 7 can be omitted if no metastasis is found in hilar and superior mediastinal nodes based on gross examination and histopathological analysis of frozen sections. 2) Similarly, for lower lobe tumors, dissection of superior mediastinal node can be omitted if no metastasis is identified in hilar and # 7.

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