

Institutional report - Thoracic general

The new strategy of selective nodal dissection for lung cancer based on segment-specific patterns of nodal spread[☆]

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Abstract

A new strategy for selective nodal dissection in non-small cell lung cancer (NSCLC) patients according to the segment of primary tumor was explored. Data on 504 patients with NSCLC of less than 5 cm, histologically revealed to be N2 disease after thoracotomy, were analyzed. In right upper lobe (RUL) tumor, when the pretracheal node was negative, the incidence of subcarinal involvement was 3.8%. In lower lobe tumor, superior segment (RLL-Superior and LLL-Superior) tumor showed a significantly higher incidence of superior mediastinal involvement than basal segment (RLL-Basal and LLL-Basal) tumor (right, $P=0.0036$; left, $P=0.0499$). When the subcarinal node was negative, the incidence of superior mediastinal metastasis in RLL-basal and LLL-Basal tumor was 11% and 8%, respectively. In left upper lobe tumor, superior segment (LUL-Superior) tumor showed a significantly lower incidence of subcarinal involvement than lingular segment (LUL-Lingular) tumor ($P=0.0381$). When aortic nodes were negative in LUL-Superior tumor, the incidence of subcarinal metastasis was 6%. Collectively, in RUL and LUL-Superior tumors, subcarinal dissection may be unnecessary if superior mediastinal node is negative. In RLL-Superior and LLL-Superior tumors, extensive dissection is required. In RLL-Basal and LLL-Basal tumors, superior mediastinal dissection may be unnecessary if subcarinal node is negative.

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1. Introduction

Since Cahan (1960) [1] reported the first 48 cases that successfully underwent lobectomy with regional lymph node dissection, which was called radical lobectomy, this procedure has been a standard surgery for lung cancer. In 1978, Naruke [2] suggested an anatomical map in which the lymph node stations were numbered, and since then this map has been used for nodal dissection. With this map, extensive nodal dissection including the superior and inferior mediastinum has been universally performed in lung cancer surgery. This technique, termed systematic nodal dissection (SND) remains an important component of the investigative and therapeutic process in all patients undergoing thoracotomy for lung cancer.

However, as the number of early-detected lung cancers is increasing with the recent development of the CT scanner, the extent of nodal dissection for lung cancer should be tailored to each case. That is, more selective dissection should be undertaken especially for early cancer by considering the tumor location-specific lymphatic pathway, simply

because nodal involvement is not so extensive in many cases. In this study, a new strategy for selective nodal dissection in non-small cell lung cancer (NSCLC) patients based on segment-specific patterns of nodal spread was explored.

2. Materials and methods

2.1. Patients

Data on 504 patients with NSCLC less than 5 cm, histologically revealed to be N2 disease between January 1977 and October 2003, were analyzed. Tumors invading the other lobe were excluded. All patients underwent at least lobectomy with hilar and mediastinal lymphadenectomy. The correlation between the segment of the tumor location and the involved hilar/mediastinal nodes were investigated in each case.

2.2. Surgical procedure

Pulmonary resection and SND were performed through posterolateral thoracotomy. At thoracotomy the diagnosis was confirmed by frozen-section analysis, if histological confirmation was not available preoperatively. Systematic nodal dissection, including the superior to inferior mediastinum, was then performed after pulmonary resection. In left thoracotomy, upper mediastinal dissection indicated aortic (#5, 6) and tracheobronchial (#4) node dissection.

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Table 1

Patient characteristics in pathological N2 non-small cell lung cancer patients less than 5 cm in size

Number of patients	504
Histological type	
Adenocarcinoma	367 (72.8%)
Squamous cell carcinoma	99 (19.6%)
Large cell carcinoma	27 (5.4%)
Adenosquamous carcinoma	9 (1.8%)
Others	2 (0.4%)
Tumor location	
Right	303
upper lobe	183
middle lobe	25
lower lobe	95
Left	201
upper lobe	140
lower lobe	61

2.3. Patient characteristics

Patient characteristics are shown in Table 1. The tumor cell types were adenocarcinoma in 367 (72.8%), squamous cell carcinoma in 99 (19.6%), large cell carcinoma in 27 (5.4%) and adenosquamous cell carcinoma in 9 (1.8%). Right thoracotomy was performed in 303 patients and left in 201. The lobe of origin was the right upper lobe (RUL) in 183 patients, right middle lobe (RML) in 25, right lower lobe (RLL) in 95 in 41 of whom it was the superior segment, left upper lobe (LUL) in 140 in 122 of whom it was the superior segment, and left lower lobe (LLL) in 61 in 23 of whom it was the superior segment.

2.4. Statistical analysis

The statistical significance of differences was determined using the chi-square test for independence. Relative risk and 95% confidence intervals were calculated. Values of *P* less than 0.05 were considered to be statistically significant.

3. Results

3.1. RUL tumor

The incidence of subcarinal involvement in RUL tumor was 18% (33/183). However, when the pretracheal lymph node

(#3) was negative, the incidence was only 3.8% (7/183). There were no significant differences in patterns of lymphatic pathway between the apical, posterior and anterior segments within the RUL.

3.2. RML tumor

The incidence of superior mediastinal (#1–4) and subcarinal (#7) involvement was 52% (13/25) and 72% (16/25), respectively. The incidence of lower mediastinal involvement was 8% (2/25). There were no significant differences in patterns of lymphatic pathway between lateral and medial segment within the RML.

3.3. RLL and LLL tumor

Among all of the segments in the lower lobe, 5 segments in the right lung and 4 in the left, there were significant differences in patterns of lymphatic pathway between the superior and basal segments on both sides, as shown in Table 2. The incidence of superior mediastinal involvement in superior segment tumor (right 65%, 26/41; left 65%, 15/23) was higher than that in basal segment tumor (right 33%, 18/54; left 39%, 15/38), with significant differences (right, *P*=0.0036; left, *P*=0.0499). When the subcarinal lymph node (#7) was negative, the incidence of superior mediastinal metastasis in RLL-basal and LLL-Basal segment tumor was 9% (5/54) and 8% (3/38), respectively.

3.4. LUL tumor

There were significant differences in patterns of lymphatic pathway between the superior and lingular segments within the LUL, as shown in Table 3. Superior segment tumor showed a significantly lower incidence of subcarinal involvement (14%, 17/122) than lingular segment tumor (33%, 6/18) (*P*=0.0381). When aortic lymph nodes (#5, 6) were negative in superior segment tumor, the incidence of subcarinal metastasis was 6% (7/122).

Collectively, the following eight segments, four in each side lung, with specific lymphatic pathways were identified: RUL (*n*=183), RML (*n*=25), superior segment of the RLL (RLL-Superior, *n*=41), basal segment of the RLL (RLL-Basal, *n*=54), superior segment of the LUL (LUL-Superior, *n*=122), lingular segment of the LUL (LUL-Lingular, *n*=18), superior segment of the LLL (LLL-Superior, *n*=23) and basal segment of the LLL (LLL-Basal, *n*=38). Based on the above-mentioned patterns of nodal spread, the proper strategy for the selective lymph node dissection of each segment is shown in Table 4.

4. Discussion

The pathological nodal status in lung cancer patients is not always the same as that predicted by pre-operative investigations. For TNM classification, CT scan has been used in the clinical diagnosis of nodal status, however, the sensitivity of CT scan for the N factor is reported about 64 to 77% [3]. Since a high incidence of false-negative nodes on CT scan has been reported [4], systematic nodal dissection (SND), which means extensive mediastinal dissection including superior to inferior mediastinum, has been per-

Table 2

The incidence of upper mediastinal metastasis in superior and basal segment tumor of the lower lobe

Side	Location of the primary tumor	No. of patients	Metastasis to the superior mediastinal nodes		
			No.	%	<i>P</i> value
Right	Superior segment	41	26	63	0.0036
	Basal segment	54	18	33*	
Left	Superior segment	23	15	65	0.0499
	Basal segment	38	15	39**	

* When subcarinal lymph node (#7) was negative, the incidence of superior mediastinal (#1–4) metastasis was 9% (5/54).

** When subcarinal lymph node (#7) was negative, the incidence of superior mediastinal (#4, 5, 6) metastasis was 8% (3/38).

Table 3

The incidence of superior mediastinal and subcarinal metastasis in superior and lingular segment tumor of the left upper lobe

Location of the primary tumor in the left upper lobe	No. of patients	Metastasis to the superior mediastinal nodes (#4,5,6)			Metastasis to the subcarinal node (#7)		
		No.	%	P value	No.	%	P value
Superior segment	122	118	97	NS	17	14*	0.0381
Lingular segment	18	13	72		6	33	

* When aortic nodes (#5, 6) were negative, the incidence of subcarinal metastasis was 6% (7/122).

formed for lung cancer patients undergoing thoracotomy. Pathological evaluation of nodal involvement at the mediastinal and hilar levels is essential for detailed assessment of the disease extent.

Graham and associates [5] suggested that SND could disclose unexpected N2 disease, irrespective of cell type, the size, location and lobe of origin of the primary tumor, and whether prior mediastinoscopy had been performed. Keller and associates [6] suggested that cure rates could be improved by SND. Therefore, SND has been accepted as an important component of the investigative and therapeutic process in NSCLC patients.

With the development of the CT scanner and the increased incidence of lung cancer, the number of early-stage lung cancer is rising. The incidence of small-sized lung cancer among resected primary lung cancers in recent years has exceeded 20% in Japan [4,7]. As the number of early-detected lung cancers is increasing, a new therapeutic strategy for nodal dissection is required. Proposals of limited surgery for lung cancer have been undertaken in some previous reports [8–10].

There are two methods of limited surgery, one is lung parenchyma-preserving surgery and the other is limited nodal dissection. Regarding the lung parenchyma-preserving surgery, Lung Cancer Study Group (LCSG) [11] reported the results of a randomized trial of lobectomy versus limited resection for T1N0 NSCLC. They observed a 75% increase in recurrence and a 50% increase in cancer death in the patients undergoing segmentectomy or wedge resection, compared to those in the patients who underwent lobectomy. It is difficult to select candidate patients for limited resection, because cT1N0 lung cancer patients show nodal disease with a 15 to 25% incidence [4,7].

As for limited lymph node dissection, Riquet and associates [12] reported that lung cancer metastasizes so easily to the mediastinum that selection of the patients for limited surgery should be discussed carefully. Some previous

reports have described the appropriateness of selective nodal dissection based on the lobe-specific extent of nodal spread [13–15]. In this study, we evaluated more meticulous data of the lymphatic pathway in not only T1 but also T2 tumors, to collect as much data as possible, and proposed a method of limited dissection from these results as shown in Table 4. The strategy of lymph node dissection should be changed from extensive dissection to selective dissection especially in early stage cancer or poor risk patients, because selective dissection will be able to reduce post-operative morbidity, such as bronchopleural fistula, chylothorax or recurrent nerve palsy. The establishment of a universally accepted method of selective nodal dissection for lung cancer would be indispensable.

5. Conclusions

Based on the patterns of nodal spread, a proper strategy for selective lymph node dissection of each segment was proposed as shown in Table 4. In RUL and LUL-Superior tumors, subcarinal dissection may be unnecessary if the superior mediastinal node is negative on frozen section. In RML and LUL-Lingular tumors, superior mediastinal and subcarinal dissection is necessary. In RLL-Superior and LLL-Superior tumors, extensive systematic dissection is routinely required. In RLL-Basal and LLL-Basal tumors, superior mediastinal dissection may be unnecessary if the subcarinal node is negative on frozen section.

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Table 4

The strategy of selective nodal dissection based on segment-specific patterns of nodal spread

	Location of the main tumor			
	RUL LUL-Superior	RML LUL-Lingular	RLL-Superior LLL-Superior	RLL-Basal LLL-Basal
Superior mediastinal nodes *3	⊙	⊙	⊙	⊙*2
Inferior mediastinal nodes				
Subcarinal node (#7)	⊙*1	⊙	⊙	⊙
Paraesophageal (#8) and pulmonary ligament (#9) nodes	×	×	⊙	⊙

⊙ dissection is advisable, ○ dissection is not always necessary, × dissection will be unnecessary.

*1: dissection may be unnecessary if pretracheal node (#3) is negative on frozen section.

*2: dissection may be unnecessary if subcarinal node (#7) is negative on frozen section.

*3: #1–4 for the right side, and #4–6 for the left.

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Appendix. Conference discussion

Dr. P. van Schil (Edegem, Belgium): I think this is especially important as within the ESTS we are working on guidelines for peroperative mediastinal staging.

I have two questions for you. Did you observe any difference with the previous studies performed by Japanese surgeons; for example, the classical studies by Naruke? Secondly, you state that you do segment-specific nodal dissection. On the other hand, you consider the upper lobe and the middle lobe just as 1 segment, but, in fact, anatomically there are 3 segments in the upper lobe and 2 in the middle lobe, or doesn't it matter for those 2 lobes?

Dr. Watanabe: Let me answer the second question first. I checked all of the segments in the right upper lobe and middle lobe, that is, the apical, posterior and anterior segment in the upper lobe, and the lateral and medial segment in the middle lobe. But there are no specific pathways among those segments, so I divided just the right upper lobe and the right middle lobe.

I'm sorry, what was the first question?

Dr. van Schil: Did you observe any differences with previous studies performed by the Japanese surgeons; for example, the studies by Naruke?

Dr. Watanabe: Unfortunately, no.

Dr. D. Branscheid (Grosshansdorf, Germany): Do you think that there are sometimes reasons why the lymph nodes are flowing more in a certain direction and all of a sudden there are 2 or 3 and the flow is to another side? Did you check if they have had tuberculosis or other infections? Have those lymph nodes been enlarged or have they been normal on the CR scan? Can you give us something about that?

Dr. Watanabe: I didn't check all of your suggestions. We basically do surgery only for clinical N0 and N1 patients.

Dr. Branscheid: Let me just ask another question. When the situation is like that, isn't it just an argument to do a complete dissection and not say, okay, this node is not involved, therefore I probably do not need to take the next one? This is the consequence that I take out of your presentation. Is that wrong, or do you see it like that also a little bit?

Dr. Watanabe: Your question is why we are exploring the selective nodal dissection, why we don't do systematic nodal dissection?

Dr. Branscheid: No. Is the consequence to do a complete dissection? Is this your consequence out of that?

Dr. Watanabe: No. Recently, with the development of the CT scanner in Japan, we are getting a large number of early lung cancers. Basically we need to do systematic nodal dissection for lung cancer patients, but for early stage lung cancer we don't think systematic dissection is required for all of the tumors. This is the reason why we started this study. But the candidate in this study was the patients who underwent systematic dissection. So basically we think that systematic dissection is very important for lung cancer.

Dr. S. Elia (Rome, Italy): You said that in 8 of 12 cases, actually in 66%, you would advice lymph node dissection. So you leave only 33% of lymph nodes that are actually doubtful. Would you feel safe in not performing complete lymphadenectomy in these patients? What is your conclusion?

Dr. Watanabe: I just took only pathological N2 patients. But among all patients, I mean N0, N1 and N2, if we included those patients, the incidence is going down, and I think the incidence will be one-third of this figure. So I think if the incidence is less than 10%, the incidence among all the lung cancer patients will be a few percent.

Dr. A. Turna (Istanbul, Turkey): Could you tell us how many of your patients had mediastinoscopy before resection? Did you perform mediastinoscopy in these patients?

Dr. Watanabe: Very few. Basically we do mediastinoscopy for clinical N2 patients, and they are actually N2 on the mediastinoscopy. So we excluded those patients. In this study, the number of patients who underwent mediastinoscopy is very few.

Dr. B. Passlick (Freiburg, Germany): What is your strategy for the future? Will you leave the upper mediastinal nodes in place if you have a right lower lobe tumor and a negative frozen section on the No. 7 lymph nodes?

Dr. Watanabe: We are now studying that kind of selective dissection. If the hilar lymph node and the No. 7 lymph node are negative in basal segment tumor, we can omit the upper mediastinal dissection. But now we are conducting only for poor-risk patients or very early lung cancer patients.