GENERAL THORACIC SURGERY

LYMPH NODE INVOLVEMENT, RECURRENCE, AND PROGNOSIS IN RESECTED SMALL, PERIPHERAL, NON-SMALL-CELL LUNG CARCINOMAS: ARE THESE CARCINOMAS CANDIDATES FOR VIDEO-ASSISTED LOBECTOMY?

Hisao Asamura, MD[a]
Haruhiko Nakayama, MD[a]
Haruhiko Kondo, MD[a]
Ryosuke Tsuchiya, MD[a]
Yukio Shimosato, MD[b]
Tsuguo Naruke, MD[a]

To determine the clinicopathologic characteristics of peripheral non-small-cell carcinomas, the cases of 337 patients undergoing major pulmonary resection with complete lymphadenectomy were retrospectively reviewed with regard to lymph node involvement, recurrence, and prognosis. All of the tumors were 3.0 cm or less in diameter and were categorized as T1 (318 patients) or T2 (19). Eighty-eight patients (26.1%) had lymph node involvement: 32 (9.5%) at N1 nodes, 55 (16.3%) at N2 nodes, and 1 (0.3%) at N3 nodes. Although the prevalence of lymph node involvement did not differ significantly with tumor histologic type, it was quite low in squamous cell carcinomas 2.0 cm or less in diameter. Of the 56 N2/3 metastases, 14 (25%) occurred in a "skipping" manner, and all but one had a nonsquamous histologic makeup. Of the 213 patients with a follow-up period of 5 years or more, 59 patients (27.7%) showed cancer recurrence. This occurred at a distant site in 67.8% of the cases. Five-year survival rates based on nodal status were 91.9% (N0), 61.8% (N1), 44.5% (N2), and 0% (N3). Because of the relatively high prevalence of lymph node involvement, complete hilar/mediastinal lymphadenectomy should be routinely done regardless of tumor histologic type and size, as long as patients are at good risk. However, in squamous cell histologic types, mediastinal lymphadenectomy might be dispensable if the tumor is less than 2.0 cm in diameter, or if the hilar node is proved to be tumor-free on pathologic examination of the frozen section during operation. Although video-assisted major pulmonary resection currently has limited application, this new technique may represent a surgical option in resection without complete lymphadenectomy. (J Thorac Cardiovasc Surg 1996;111:1125-34)

Among thoracic surgeons, the operative strategy for small, peripheral lung carcinomas can be addressed through the following questions: What should the extent of resection be?[1-3] Should a lymphadenectomy be done[4] and, if so, to what extent?

Since the advent of video-assisted thoracic surgery (VATS), this new technique has been applied to a wide variety of thoracic operations.[5, 6] In parenchymal lung resection, surgeons face a variety of challenges ranging from simple wedge resection to more complicated major resections such as lobectomy and pneumonectomy.[7] For lung carcinomas, however, there remains considerable controversy concerning the therapeutic role of VATS. Recently, the strategy for small, peripheral lung carcinomas has become more enthusiastically discussed in relation to VATS, because these tumors without nodal involvement were regarded as possible candidates for this new procedure. In several recent reports dealing with VATS major pulmonary resections, the

From the Division of Thoracic Surgery[a] and the Clinical Laboratory Division,[b] National Cancer Center Hospital Japan, Tokyo, Japan.

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Address for reprints: Hisao Asamura, MD, Division of Thoracic Surgery, National Cancer Center Hospital Japan, 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan.

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Table I. *Patient characteristics*

	No.
Gender	
Male	222
Female	115
Histologic type	
Adenocarcinoma	280
Squamous cell carcinoma	44
Large-cell carcinoma	10
Adenosquamous carcinoma	3
Tumor size	
≤1.0 cm	8
>1.0 cm and ≤2.0 cm	166
>2.0 cm and ≤3.0 cm	163
Tumor status	
T1	318
T2	19
Node status	
N0	249
N1	32
N2	55
N3	1
Postoperative stage	
I	246
II	31
IIIA	50
IIIB	1
IV	9
Tumor location by lobe	
Right upper lobe	122
Right middle lobe	31
Right lower lobe	64
Left upper lobe	83
Left lower lobe	37
Operation mode	
Pneumonectomy	6
Lobectomy	326
Sleeve lobectomy	5

Table II. *Lymph node location*

N2 node	*N1 node*
Superior mediastinal	Hilar
No. 1. Highest mediastinal	No. 10. Hilar
No. 2. Paratracheal	No. 11. Interlobar
No. 3. Pretracheal	No. 12. Lobar
No. 4. Tracheobronchial angle	Intrapulmonary
Aortic	No. 13. Segmental
No. 5. Botallo's	No. 14. Subsegmental
No. 6. Para-aortic (ascending aorta)	
Inferior mediastinal	
No. 7. Subcarinal	
No. 8. Paraesophageal	
No. 9. Pulmonary ligament	

definite indication for lung carcinomas was not clearly demonstrated.[8-10] To establish the surgical strategy for these tumors, it is important to know their clinicopathologic features.

In this retrospective study, we intended to clarify the characteristics of these tumors with special emphasis on the lymph node involvement, the mode of recurrence, and survival, the former being closely related to the operative procedures.

Material and methods

We surgically treated 337 patients with primary lung carcinoma (maximum tumor diameter of 3.0 cm or less) between 1980 and 1993 at the National Cancer Center Hospital, Tokyo. The median follow-up period was 1465 days. These tumors were all located at the periphery of the lung and were resected by either lobectomy or pneumonectomy combined with complete hilar and mediastinal lymphadenectomy. Five sleeve lobectomies and six pneumonectomies were done mainly for the purpose of eradicating the swollen hilar nodes (around the main bronchus or between different lobes) adherent to the bronchial wall. During the same period, 1914 primary lung carcinomas were treated by resection to various extents and lymphadenectomy. Therefore 337 patients comprised 17.6% of the total. The patients ranged in age from 26 to 85 years (mean age, 59.8 years). Two hundred twenty-two patients were male and 115 were female. Most of the patients underwent a physical examination, chest roentgenography, chest computed tomographic scan, bone scintigraphy, and abdominal ultrasonography for staging and evaluation of resectability before the operation. The clinical characteristics of the 337 patients are presented in Table I.

Resected specimens were examined histologically, and their histologic type was determined according to the World Health Organization classification[11] as adenocarcinoma, squamous cell carcinoma, large cell carcinoma, or adenosquamous carcinoma. The extent of lymph node spread was also recorded. The median number of lymph nodes resected and examined was 19 per patient (range, 6 to 71). The locations of intrapulmonary (Nos. 13 and 14, N1), hilar (Nos. 10 through 12, N1), mediastinal (Nos. 1 through 9, N2), and contralateral hilar (contralateral No. 10, N3) lymph nodes were expressed according to the lymph node map for lung cancer proposed by one of us (T. N., Table II).[12] Mediastinal metastasis was considered "skipping" if any one of the mediastinal lymph nodes was involved by the tumor, without hilar or intrapulmonary node metastasis. The stage of the disease was based on the TNM classification of the Union Internationale Contre Cancer.[13]

Cancer recurrence was carefully divided according to the site of the initial relapse into two categories: locoregional and distant recurrence. Locoregional recurrence was defined as any recurrent disease within the ipsilateral hemithorax, mediastinum, or supraclavicular lymph nodes. All other sites of recurrence were considered distant metastases. Second primary carcinoma of the lung was also documented, if the criteria proposed by Martini and Melamed[14] were met; in brief, if the carcinoma was a different histologic type, the same histologic type with a disease-free interval more than 2 years, or without either common lymphatic involvement or extrapulmonary metastases. The cause of death was recorded as either cancer-related, other disease, or unknown. Survival rate

Table III. *Preoperative and postoperative diagnosis of lymph node metastasis*

	Postop. node diagnosis				
Preop. node diagnosis	*N0*	*N1*	*N2*	*N3*	*Total*
N0	237	24	43	1	305
N1	5	5	8		18
N2	7	3	4		14
Total	249	32	55	1	337

Table IV. *Lymph node involvement according to tumor diameter*

Tumor diameter (cm)	*Nodal status*				
	N0	*N1*	*N2*	*N3*	*Total*
≤2.0	140 (80.5)	14 (8.0)	20 (11.5)	0 (0.0)	174 (100)
>2.0 and ≤3.0	10 (66.9)	18 (11.0)	35 (21.5)	1 (0.6)	163 (100)
Total	249 (73.9)	32 (9.5)	55 (16.3)	1 (0.3)	337 (100)

Numbers in parentheses indicate percentage. Statistically significant (χ^2 test, $p = 0.028$).

was calculated by the Kaplan-Meier life-table method[15] and compared by a log rank test[16] in which the initial day of treatment was the day of operation. Cases with death that was not caused by cancer were considered censored. A χ^2 test was used to compare the various rates, and $p < 0.05$ was considered statistically significant.

Patients with the following tumors or conditions were excluded from this study: (1) tumors with small-cell or low-grade malignant histologic makeup; (2) hilar tumors; (3) T3 or T4 tumors including those with malignant effusion and pleural dissemination; (4) tumors with distant metastasis; (5) operation with less than lobectomy for primary tumor; and (6) operation without hilar and mediastinal lymphadenectomy.

Carcinomas with minute, satellite nodules that were found incidentally within the same lobe of the resected specimen were not excluded from the study, because it was not certain whether these lesions should be considered local tumor spread or hematogenous spread (distant metastasis). However, these lesions were categorized as M1. Tumors with minute lesions within another lobe were excluded.

Results

Lymph node involvement. Lymph node involvement was recognized in 88 (26.1%) of the 337 patients: in 1 patient (0.3%) at the contralateral hilum, in 55 (16.3%) at the mediastinum, and in 32 (9.5%) at the hilum or within the lung. The distribution of preoperative and postoperative nodal status is shown in Table III. Lymph node involvement was compared in terms of tumor diameter and histologic type. Lymph node metastasis at the mediastinum and pulmonary hilum was significantly more common in tumors more than 2.0 cm in diameter (32.5%) than in those 2.0 cm or less in diameter (19.5%) ($p = 0.028$, χ^2 test, Table IV). However, there was no significant difference on the basis of tumor histologic type, even though patients with N2/3 disease more frequently had adenocarcinoma than squamous cell carcinoma (17.5% versus 11.4%, respectively, Table V). Lymph node involvement was also analyzed by histologic type in 174 patients with tumors 2.0 cm or less in diameter (Table VI). In this subgroup of patients, there was also no difference in the incidence of N2/3 metastasis according to histologic type.

Table V. *Lymph node involvement according to tumor histologic type*

	Nodal status				
Histologic type	*N0*	*N1*	*N2*	*N3*	*Total*
Adenocarcinoma	203 (72.5)	28 (10.0)	48 (17.1)	1 (0.4)	280 (100)
Squamous cell carcinoma	38 (86.3)	1 (2.3)	5 (11.4)	0	44 (100)
Large cell carcinoma	7 (70.0)	1 (10.0)	2 (20.0)	0	10 (100)
Adenosquamous carcinoma	1 (33.3)	2 (66.7)	0	0	3 (100)
Total	249 (73.9)	32 (9.5)	55 (16.3)	1 (0.3)	337 (100)

Numbers in parentheses indicate percentage.

Table VI. *Lymph node involvement of 174 patients with tumors 2.0 cm or less in diameter according to tumor histologic type*

	Nodal status			
Histologic type	*N0*	*N1*	*N2*	*Total*
Adenocarcinoma	120 (78.9)	13 (8.6)	19 (12.5)	152 (100)
Squamous cell carcinoma	15 (93.7)	0 (0.0)	1 (6.3)	16 (100)
Large cell carcinoma	5 (83.3)	1 (16.7)	0 (0.0)	6 (100)
Adenosquamous carcinoma	0	0	0	0
Total	140 (80.5)	14 (8.0)	20 (11.5)	174 (100)

Numbers in parentheses indicate percentage.

Involvement of the mediastinal (Table VII) and hilar/intrapulmonary (Table VIII) nodes was analyzed in terms of the location of the primary tumors. The most frequent site of metastasis in the mediastinum differed according to the location of the primary tumor: on the right side, the pretracheal (No. 3) nodes were the most common site of spread in tumors of upper and middle lobes, whereas the subcarinal (No. 7) nodes were the most common site of spread in tumors of middle and lower lobes. On the left side, the tracheobronchial (No. 4), Botallo's (No. 5), and paraaortic (No. 6) nodes were mainly involved in tumors of

Table VII. *Lymph node involvement to the mediastinum according to tumor location*

	Mediastinal lymph node location									
Location	*No. 1*	*No. 2*	*No. 3*	*No. 4*	*No. 5*	*No. 6*	*No. 7*	*No. 8*	*No. 9*	*N2/3*
RUL (122)	5 (4.1)	3 (2.5)	17 (13.9)	4 (3.3)			2 (1.6)			18 (14.8)
RML (31)	2 (6.5)	1 (3.2)	5 (16.1)				5 (16.1)			7 (22.6)
RLL (64)	3 (4.7)		3 (4.7)				8 (12.5)		2 (3.1)	11 (17.2)
LUL (83)		3 (3.6)	2 (2.4)	6 (7.2)	5 (6.0)	6 (7.2)	4 (4.8)			15 (18.1)
LLL (37)				1 (2.7)	1 (2.7)	1 (2.7)	3 (8.1)	1 (2.7)	1 (2.7)	5 (13.5)

Numbers in parentheses indicate percentage. *RUL,* Right upper lobe; *RML,* right middle lobe; *RLL,* right lower lobe; *LUL,* left upper lobe; *LLL,* left lower lobe.

Table VIII. *Lymph node involvement to the hilum and lung according to tumor location*

	Hilar intrapulmonary lymph node location					
Location	*No. 10*	*No. 11*	*No. 12*	*No. 13*	*No. 14*	*N1**
RUL (122)	5 (4.1)	8 (6.6)	9 (7.4)	8 (6.6)	3 (2.5)	22 (18.0)
RML (31)	3 (9.7)	6 (19.4)	3 (9.7)	1 (3.2)	1 (3.2)	9 (29.0)
RLL (64)	4 (6.3)	9 (14.1)	6 (9.4)	4 (6.3)	1 (1.6)	24 (37.5)
LUL (83)	7 (8.4)	6 (7.2)	11 (13.3)	7 (8.4)	4 (4.8)	23 (27.7)
LLL (37)	1 (2.7)	2 (5.4)	3 (8.1)	2 (5.4)	1 (2.7)	6 (16.2)

Numbers in parentheses indicate percentage. *RUL,* Right upper lobe; *RML,* right middle lobe; *RLL,* right lower lobe; *LUL,* left upper lobe; *LLL,* left lower lobe.

*Patients with both mediastinal and hilar/intrapulmonary metastases were included.

Table IX. *Characteristics of 14 patients with skipping metastases*

Primary lesion (lobe)	*No. of patients*	*Metastatic site (No.)*	*Histologic type (No.)*
RUL	6	No. 3 (6)	AD (5), LG (1)
		No. 1 (1)	
RML	3	No. 3 (2)	AD (3)
		No. 2 (1)	
		No. 7 (1)	
RLL	1	No. 7 (1)	AD (1)
LUL	3	No. 6 (2)	AD (2), SQ (1)
		No. 5 (1)	
		No. 7 (1)	
LLL	1	No. 7 (1)	AD (1)
Total	14		

AD, Adenocarcinoma; *LG,* large cell carcinoma; *SQ,* squamous cell carcinoma; *RUL,* right upper lobe; *RML,* right middle lobe; *RLL,* right lower lobe; *LUL,* left upper lobe; *LLL,* left lower lobe.

the upper lobe, whereas the subcarinal (No. 7) nodes were involved in tumors of the lower lobe.

Skipping metastases (Table IX). Of the 56 cases of N2/N3 disease, 14 were skipping metastases (25%). Histologically, 12 of the 14 skipping metastases occurred in adenocarcinomas and one each occurred in large cell carcinoma and squamous cell carcinoma. On the right side, the most common site of involvement of skipping metastasis was the pretracheal (No. 3) nodes in eight patients, followed by the subcarinal (No. 7) nodes in two and by nodes Nos. 1 and 2 in one patient each. The pretracheal node was involved only in tumors of the right upper and middle lobes and not in tumors of the lower lobe. On the left side, the para-aortic (No. 6) and Botallo's (No. 5) nodes were involved only in tumors of the upper lobe, whereas the subcarinal (No. 7) nodes were involved in tumors of both lobes, although the number of patients was limited.

M1 disease. Nine patients had minute carcinomatous nodules incidentally found in the same lobe as the main tumor at the time of pathologic examination. These nodules were apparently remote from the main lesion and only a few millimeters in diameter. We categorized these carcinomatous lesions as M1 disease. The nodal status of the nine patients was as follows: N0 in three, N1 in one, and N2 in five. Four of them had recurrence (2 locoregional, 2 distant). All of the patients with recurrence died of cancer. The remaining five patients remained alive without disease.

Recurrence. Cancer recurrence was analyzed only for 213 patients who were operated on 5 or more years previously. Fifty-nine patients (27.7%) showed cancer recurrence, 7 showed second primary lung carcinoma after operation, and 4 were lost to follow-up. Among the patients with recurrence, 40 (67.8%) had distant relapse, 17 (28.8%) had locore-

Table X. *First relapse site in patients with cancer recurrence in 213 patients with a follow-up period of 5 years or more*

	No.	
Locoregional		19
Supraclavicular lymph node	10	
Lung	4	
Bronchial stump	2	
Pleural effusion	2	
Mediastinal lymph node	1	
Distant		42
Lung	14	
Bone	13	
Brain	6	
Liver	3	
Adrenal gland	1	
Miscellaneous	5	

Table XI. *Cancer recurrence according to tumor histologic type in 213 patients with a follow-up period of 5 years or more*

Histologic type	*With recurrence*	*Without recurrence*	*Total*
Adenocarcinoma	53 (31.9)	113 (68.1)	166 (100)
Squamous cell carcinoma	2 (7.7)	24 (92.3)	26 (100)
Large cell carcinoma	2 (28.6)	5 (71.4)	7 (100)
Adenosquamous carcinoma	2 (66.7)	1 (33.3)	3 (100)
Total	59 (29.2)	143 (70.8)	202 (100)

The numbers in parentheses indicate percentage. Statistically significant (χ^2, $p = 0.0375$).

gional relapse, and two (3.4%) had both simultaneously. The initial site of recurrence is presented in Table X. The intervals from the initial operation to the discovery of recurrence varied from 83 to 2978 days. In 11 cases (5.2%), recurrence was found 5 years or more after resection of the primary tumor. These were all adenocarcinomas. Table XI shows the prevalence of recurrence according to histologic type; adenocarcinoma had a significantly higher prevalence of recurrence compared with the other histologic types (χ^2 test, $p = 0.0375$). In Table XII, the prevalence of recurrence is shown according to histologic type for patients with resected stage I disease. In this smaller category, there was no significant difference between the different histologic types (χ^2 test, $p = 0.3095$).

Prognosis. The survival curve for all 337 patients is shown in Fig. 1. The 5- and 10-year survival rates were 77.2% and 59.5%, respectively. Survival curves were drawn according to nodal status (Fig. 2). As shown in Table XIII, significant differences were found among the 5- and 10-year survival rates in each nodal category

Table XII. *Cancer recurrence in stage I disease according to histologic type*

Histologic type	*With recurrence*	*Without recurrence*	*Total*
Adenocarcinoma	24 (19.8)	97 (80.2)	121 (100)
Squamous cell carcinoma	1 (4.3)	22 (95.7)	23 (100)
Large cell carcinoma	1 (25)	3 (75)	4 (100)
Adenosquamous carcinoma	0 (0)	1 (100)	1 (100)
Total	26 (17.4)	123 (82.6)	149 (100)

The numbers in parentheses indicate percentage.

Table XIII. *Survival rates based on nodal status (percent)*

	Nodal status			
Survival	*N0*	*N1*	*N2*	*N3*
5-Year survival	91.9	61.8	44.5	0.0
10-Year survival	86.9	27.5	0.0	0.0

($p < 0.0001$). Survival curves of patients with and without lymph node involvement are shown according to histologic type in Figs. 3 and 4, respectively. There was no statistically significant difference in survival between the different histologic types.

Survival was further compared in patients with and without lymph node involvement according to tumor diameter: tumors 2.0 cm or less in diameter and those more than 2.0 cm in diameter (Figs. 5 and 6). No significant difference was seen in survival according to tumor diameter. In the 56 patients with N2/3 disease, the prognosis of patients with lymph node involvement in only one mediastinal lymph node location was compared with the prognosis in those with lymph node involvement in two or more locations. Patients in whom only one location was involved showed no survival advantage.

Discussion

One of the important findings in the current study was the relatively high prevalence of lymph node involvement despite the small size of the primary tumor: 26.1% in tumors 3.0 cm or less in diameter and 19.5% in those 2.0 cm or smaller. However, several points were also of clinical interest. First, larger tumors were associated with a significantly higher prevalence of lymph node involvement. Second, with regard to lymph node involvement, there was no significant difference between adenocarcinomas and squamous cell carcinomas both originating at the periphery, although the latter have been reported to grow more locally.[17] This observation indicated that even squa-

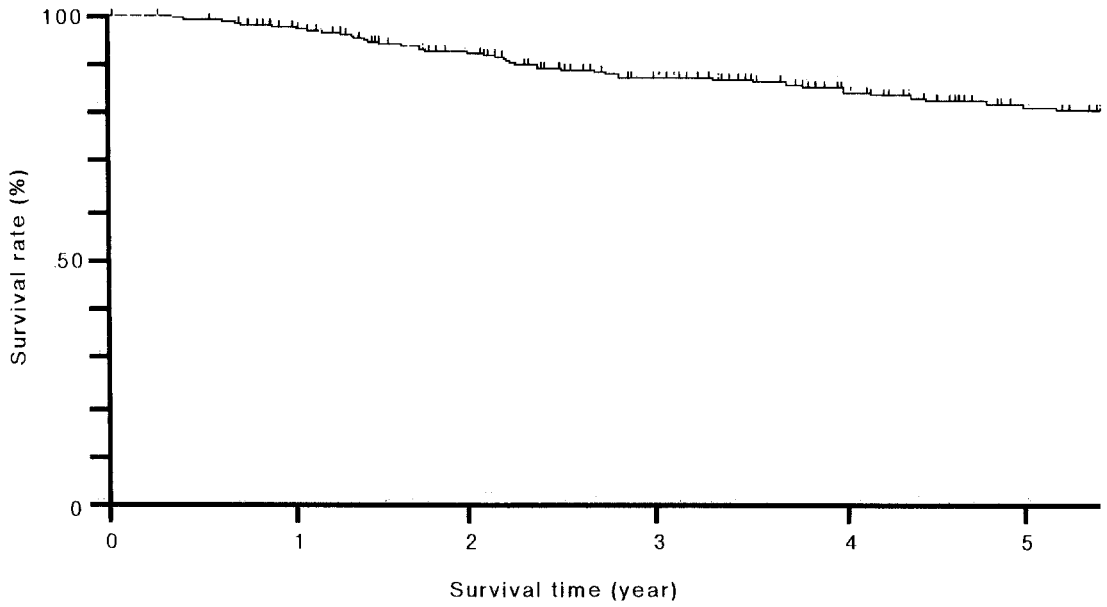

Fig. 1. Survival curve for all 337 patients with lung carcinoma 3.0 cm or less in diameter.

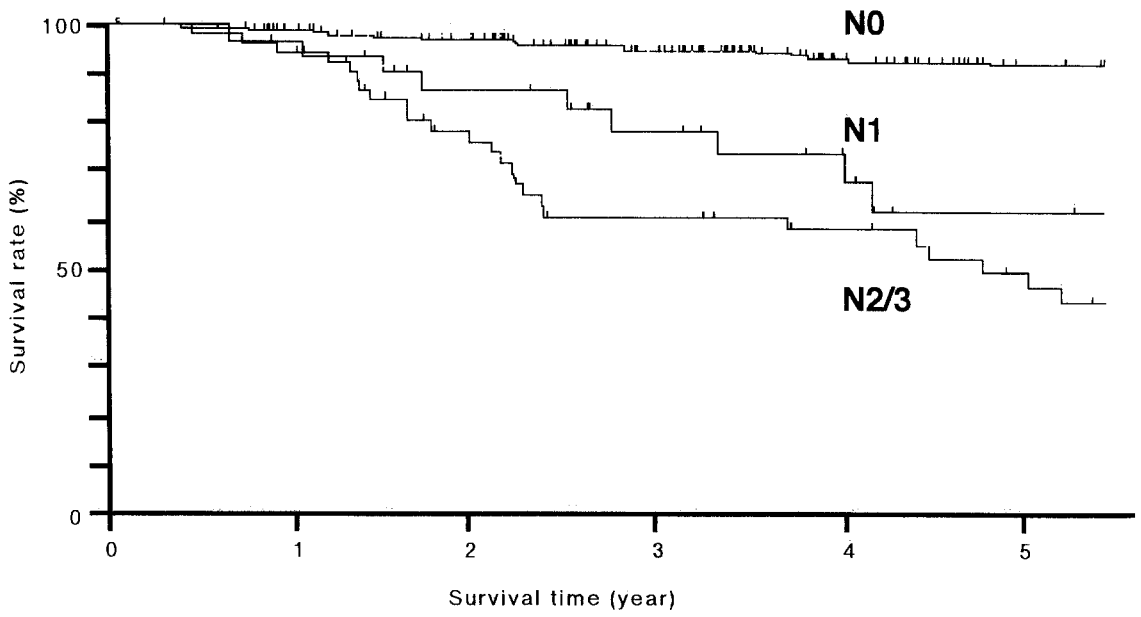

Fig. 2. Survival curves based on nodal status (N0, N1, N2/3). Statistically significant difference was observed (log-rank test, $p < 0.0001$).

mous cell carcinomas, if they originate at the peripheral lung, might have clinical characteristics similar to those of adenocarcinomas arising at the same location, which may account for the cytopathologic similarities of these two histologic types.[17] However, the difference in the tendency to lymph node involvement between the two histologic types might become clearer if a large enough number of patients with squamous cell carcinoma is studied.

A third point of clinical interest is that lymph node involvement was very rare among squamous cell carcinomas 2.0 cm or less in diameter. This rarity of lymphatic spread might justify not performing lymphadenectomy. Fourth, the location of the involved

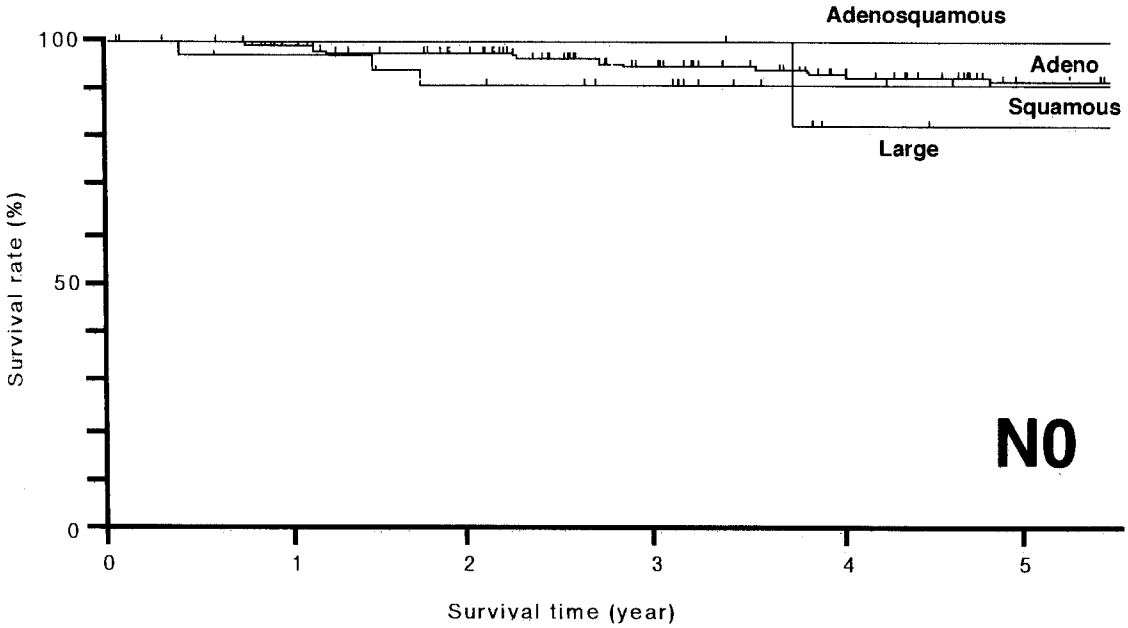

Fig. 3. Survival curves based on histologic type in patients without any lymph node involvement. There was no statistically significant difference (log-rank test, $p = 0.9046$). *Adeno,* Adenocarcinoma; *Large,* large cell.

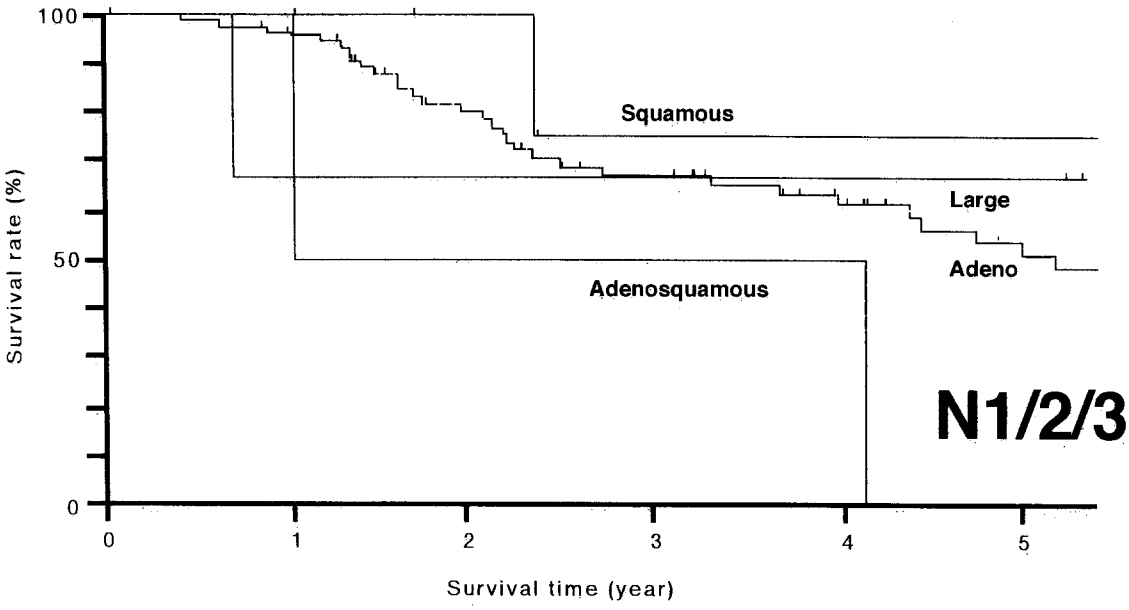

Fig. 4. Survival curves based on histologic type in patients with lymph node involvement at hilum/mediastinum. There was no statistically significant difference (log-rank test, $p = 0.1964$). *Adeno,* Adenocarcinoma; *Large,* large cell.

lymph node was determined primarily by the lobe in which the primary tumor was located. Especially on the right side, this rule was clear. This was probably because the metastasis occurred in the direction of the lymphatic stream. Only the middle lobe had two mediastinal locations in favor of lymph node involvement (Nos. 3 and 7), which indicates that the middle lobe has the two major lymphatic drainage pathways common for both the upper and lower lobes.

Skipping metastasis also has considerable clinical

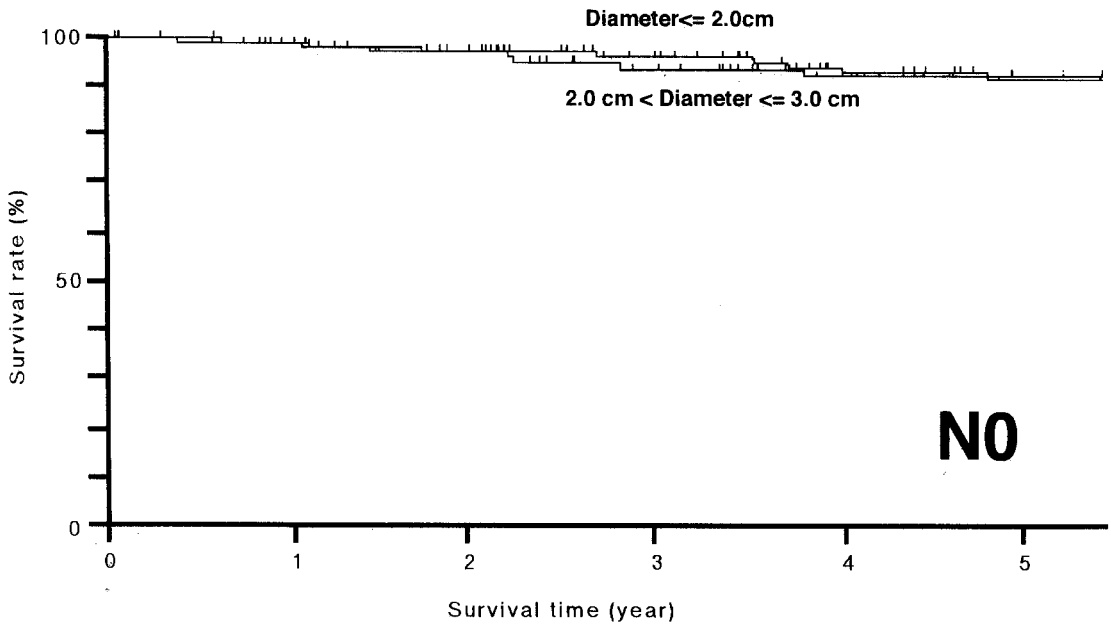

Fig. 5. Survival curves based on tumor diameter (tumors 2.0 cm or less in diameter versus those larger than 2.0 cm) in patients without lymph node involvement. There was no statistically significant difference (log-rank test, $p = 0.7561$).

significance when we weigh strategies for lymphadenectomy in such small-sized carcinomas. In our series, 25% of N2 involvement occurred in a skipping manner (mediastinal involvement without hilar involvement). This rate is close to those reported previously: 27% by Martini and colleagues,[18] 28.6% by Ishida and colleagues,[19] and 31.5% by Naruke.[20] Two points were of clinical significance: (1) this "skipping" spread occurred almost exclusively in adenocarcinomas and (2) a special location of the lymph nodes was affected in the skipping involvement, and this was determined by the location of the primary tumor. For example, in tumors of the right upper lobe, skipping involvement occurred exclusively in the upper mediastinum. Therefore we should not overlook the sampling or dissection of such "sentinel" nodes, even for staging.

Another important finding was the better survival in the current series compared with those in previous series, including our own. Especially for resected T1 N0 M0 tumors, whereas the previously reported 5-year survival rate has ranged from 70% to 83%,[21-24] the present series showed a survival rate of 92.6%. Although squamous cell carcinoma of hilar origin was not included in the present series, this may not have significantly affected the results, because this group also showed a good prognosis. The most probable explanation for the better survival in the present series might involve patient selection, because all of the patients underwent complete lymphadenectomy and were categorized according to subsequent pathologic examination. T1 N0 tumors, which were diagnosed by operative palpation alone without mediastinal dissection or by sampling only a limited number or location of nodes, were all excluded from the present series. These might inevitably include more advanced latent or subclinical N2 diseases. The better clinical outcome might be a result of the exclusion of aberrant advanced disease and of the purification of each TNM category. Our results may reflect prognostic data based on the most purified T1 N0 M0 population, which indicates the importance of accurate staging by complete lymphadenectomy. However, the prognostic impact of this factor could not be clearly determined in the setting of the current study.

Cancer recurrence after resection, especially for resected stage I disease, has been analyzed in several previous reports with different comments. In the current series, there was no significant histologic propensity for cancer recurrence in patients with stage I disease, although adenocarcinoma showed a significantly higher recurrence rate in the entire group. Pairolero and associates[25] also demonstrated that there was no significant difference in the overall rate of recurrence among the various cell types. On

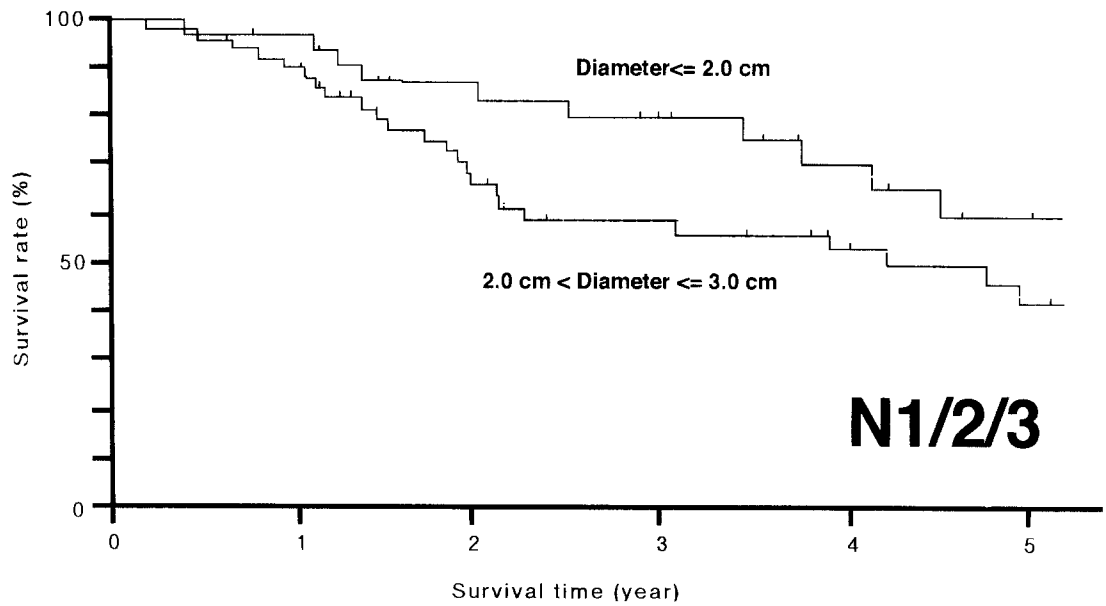

Fig. 6. Survival curves based on tumor diameter in patients with lymph node involvement. There was no statistically significant difference (log-rank test, $p = 0.1121$).

the other hand, a significantly higher rate of recurrence was found for those with nonsquamous histologic makeup, compared with squamous histologic makeup, in a series of studies by the Lung Cancer Study Group.[26, 27] Because we excluded squamous cell carcinoma of hilar origin, the locoregional recurrence rate may have been reduced. However, it should be remembered that peripheral squamous cell carcinoma has a tendency for recurrence similar to that of peripheral adenocarcinoma. In terms of the first relapse site, all of the previous reports have recognized a common site of recurrence at distant organs for 56% to 75% of all instances of recurrence.[25, 27]

What, then, should the surgical strategy for small, peripheral lung carcinomas be? Concerning the extent of resection for the primary tumor, a randomized study by the Lung Cancer Study Group in T1 N0 carcinomas has provided at least one answer.[2, 3] Both a threefold increase in locoregional failure and a small but significant reduction in survival in the limited resection group favored lobectomy. For systematic mediastinal lymphadenectomy, a randomized trial by Izbicki and colleagues[4] showed no survival benefit. The current results, however, still favor lymphadenectomy of the hilum and mediastinum, regardless of histologic type, because of the high prevalence of lymph node involvement in tumors 3.0 cm or less in diameter, with a goal of accurate staging and possible cure. Lymphadenectomy to a smaller extent might be an option for patients with squamous cell carcinomas with a diameter 2.0 cm or less, inasmuch as lymph node involvement was rare in these tumors. Furthermore, because of the rarity of skipping metastasis in squamous cell carcinoma, if the hilar node is free from tumor cells in a frozen section during the operation, mediastinal lymphadenectomy might not be necessary. In nonsquamous carcinoma, we still support the need for lymphadenectomy and recommend that the extent of the dissection not be minimized.

The current results address whether small, peripheral lung carcinomas are candidates for VATS. Definite indications for major VATS in lung cancer have not yet been determined. Roviaro and associates[8] reported that a "small peripheral lesion in stage I" might be a candidate for VATS. Lewis[10] reported a strategy in which wedge or sublobar resection was done in tumors 2.0 cm or less in diameter, whereas lobectomy was done in larger tumors and those located more deeply. In the report by Kirby and Rice,[9] lobectomies were done for stage I non-small-cell carcinoma in patients with good risk conditions because of their "pilot study" setting. However, are major pulmonary resection and lymphadenectomy technically feasible? Reports by other groups and our own experiences have shown that VATS lobectomy can be done under conditions of good lobulation, minimal adhesion, minimal an-

atomic anomaly, and good cardiopulmonary function that will allow one-lung ventilation. A detailed description of video-assisted lymphadenectomy has not yet been reported. Our experience with open thoracotomy, however, suggests that lymphadenectomy can be difficult, particularly in nodes at the special locations such as the hilum and subcarina (No. 7); the latter requires considerable retraction. Therefore we should realize that because the surgical technique for complete video-assisted lymphadenectomy has not yet been established, it is unlikely that it is done as it is done with open thoracotomy.

In conclusion, we think the basic strategy for lymphadenectomy in patients with small, peripheral non-small-cell carcinomas should be as follows.

1. Complete hilar/mediastinal lymphadenectomy should be routinely done regardless of tumor histologic type as long as patients are at good risk and are thought to be able to tolerate this surgical procedure.
2. In squamous cell histologic types, the prevalence of nodal involvement was low in tumors 2.0 cm or less in diameter. Mediastinal nodal involvement was also less common, if the hilar node was free from carcinoma cells. Therefore mediastinal lymphadenectomy might be dispensable, if the tumor is less than 2.0 cm in diameter or if the hilar node is proved to be tumor-free on pathologic examination of the frozen section during operation.

Considering the technical limitations of the current VATS procedures, especially in the performance of meticulous lymphadenectomy, we think that the present results suggest that performance of VATS lobectomy with less than complete lymphadenectomy would not be recommended, even if the tumors are T1. Furthermore, because cN0 status in 43 of 305 patients was converted to pN2 after operation, evaluation by preoperative mediastinoscopy is strongly recommended for the better selection of future VATS candidates.

REFERENCES

1. Pearson FAG. Current status of surgical resection for lung cancer. Chest 1994;106:337s-9s.
2. Ginsberg RJ, Rubinstein R, for the Lung Cancer Study Group. A randomized comparative trial of lobectomy vs. limited resection for patients with T1N0 non-small cell lung cancer [Abstract]. Lung Cancer 1991;7(Suppl):83.
3. Ginsberg RJ, Rubinstein L. The comparison of limited resection to lobectomy for T1N0 non-small cell lung cancer: LCSG 821. Chest 1994;106:318s-9s.
4. Izbicki JR, Thetier O, Habekost M, et al. Radical systematic mediastinal lymphadenectomy in non-small cell lung cancer: a randomized controlled trial. Br J Surg 1994;81:229-35.
5. Wakabayashi A. Expanded applications of diagnostic and therapeutic thoracoscopy. J Thorac Cardiovasc Surg 1991;102:721-3.
6. Landreneau RJ, Mack M, Hazelrigg SR, et al. Video-assisted thoracic surgery: basic technical concepts and intercostal approach strategies. Ann Thorac Surg 1992;54:800-7.
7. Lewis RJ, Sisler GE, Caccavale RJ. Imaged thoracic lobectomy: should it be done? Ann Thorac Surg 1992;54:80-3.
8. Roviaro G, Varoli F, Rebuffat C, et al. Major pulmonary resections: pneumonectomies and lobectomies. Ann Thorac Surg 1993;56:779-83.
9. Kirby TJ, Rice TW. Thoracoscopic lobectomy. Ann Thorac Surg 1993;56:784-6.
10. Lewis RJ. The role of video-assisted thoracic surgery for carcinoma of the lung: wedge resection to lobectomy by simultaneous individual stapling. Ann Thorac Surg 1993;56:762-8.
11. The World Health Organization. Histological typing of lung tumors. 2nd ed. Geneva: World Health Organization, 1981.
12. Naruke T, Suemasu K, Ishikawa S. Lymph node mapping and curability at various levels of metastasis in resected lung cancer. J Thorac Cardiovasc Surg 1978;76:832-9.
13. Hermanek P, Sobin LH, eds. UICC TNM classification on malignant tumours. 4th ed, 2nd rev. Berlin: Springer, 1992.
14. Martini N, Melamed MR. Multiple primary lung cancers. J Thorac Cardiovasc Surg 1975;70:606-12.
15. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457-81.
16. Mantel N. Evaluation of survival data and two new rank order statistics arising in its consideration. Cancer Chemother Rep 1966;50:163-70.
17. Shimosato Y. Pulmonary neoplasms. In: Sternberg SS, ed. Diagnostic surgical pathology. New York: Raven, 1989:785-827.
18. Martini N, Flehinger BJ, Zaman MB, Beattie EJ. Results of resection in non-oat cell carcinoma of the lung with mediastinal lymph node metastases. Ann Surg 1983;198:386-97.
19. Ishida T, Yano T, Maeda K, Kaneko S, Tateishi M, Sugimachi K. Strategy for lymphadenectomy in lung cancer three centimeters or less in diameter. Ann Thorac Surg 1990;50:708-13.
20. Naruke T. Significance of lymph node metastases in lung cancer. Semin Thorac Cardiovasc Surg 1993;5:210-8.
21. Naruke T, Goya T, Tsuchiya R, Suemasu K. Prognosis and survival in resected lung carcinoma based on the new international staging system. J Thorac Cardiovasc Surg 1988;96:440-7.
22. Martini N, Beattie EJ. Results of surgical treatment in stage I lung cancer. J Thorac Cardiovasc Surg 1977;74:499-505.
23. Williams DE, Pairolero PC, Davis CS, et al. Survival of patients surgically treated for stage I lung cancer. J Thorac Cardiovasc Surg 1981;82:70-6.
24. Mountain CF. A new international staging system for lung cancer. Chest 1986;89(Suppl):225s-33s.
25. Pairolero PC, Williams DE, Bergstralh EJ, Piehler JM, Bematz PE, Payne WS. Postsurgical stage I bronchogenic carcinoma: morbid implications of recurrent disease. Ann Thorac Surg 1984;38:331-8.
26. Thomas PA, Piantadosi S. Postoperative T1N0 non-small cell lung cancer: squamous versus nonsquamous recurrences. J Thorac Cardiovasc Surg 1987;94:349-54.
27. Feld R, Rubinstein LV, Weisenberger TH. Sites of recurrence in resected stage I non-small-cell lung cancer: a guide for future studies. J Clin Oncol 1984;2:1352-8.