LOBE-SPECIFIC EXTENT OF SYSTEMATIC LYMPH NODE DISSECTION FOR NON–SMALL CELL LUNG CARCINOMAS ACCORDING TO A RETROSPECTIVE STUDY OF METASTASIS AND PROGNOSIS

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Background: **Complete lymphadenectomy of the mediastinum is advised for patients with lung cancer to provide prognostic information and possible survival benefit. The proper extent of dissection should be further defined.** ***Method:*** **The lymphatic metastatic patterns according to the primary site and prognoses were retrospectively analyzed in 166 patients with non–small cell carcinoma who underwent at least lobectomy with hilar and mediastinal lymphadenectomy. All patients had histologically proven mediastinal metastasis (pN2).** ***Results:*** **Among 54 right upper lobe tumors the most common site of metastasis was the lower pretracheal station (74%), whereas metastases to the subcarinal station were seen only in 13%. Among 8 patients with right middle lobe tumors and 41 patients with right lower lobe tumors, both superior mediastinal and subcarinal stations were involved. The 34 left upper segment tumors metastasized to the aorticopulmonary window most commonly (71%) and to the subcarina only in 12% of cases. Inversely, the 10 left lingular tumors metastasized to the subcarina most commonly (50%) and to the aorticopulmonary window only in 20% of cases. Among 44 left lower lobe tumors the subcarinal station was most common for metastasis (58%), with infrequent metastases to the aorticopulmonary window. The 5-year survival for all 166 patients was 35%. Patients with single-station and single-node metastases had a significantly better prognosis than those with more extensive metastases. Right lower lobe tumors with superior mediastinal metastasis carried a particularly poor 5-year survival of only 4.1%.** ***Comment:*** **Subcarinal lymphadenectomy is not always necessary for tumors of the right upper lobe and left upper segment. For tumors of other lobes both superior mediastinal dissection and subcarinal dissection are advised. However, superior mediastinal metastasis should be recognized as an indicator of poor prognosis in tumors of both lower lobes. (J Thorac Cardiovasc Surg 1999;117:1102-11)**

Lymph node dissection for lung cancer is both an old and a new issue in the thoracic surgical community. Complete hilar and mediastinal lymphadenectomy, which is also called *radical systematic mediastinal lymph node dissection*, is a local surgical option that seeks to achieve better local control, with subsequent improvement in survival, as well as a complete nodal staging of the lung carcinoma. In fact, it is widely recognized that precise information regarding nodal status obtained by systematic dissection provides the most reliable information regarding prognosis and also enables optimal postoperative treatment, the evaluation of protocol eligibility, and comparisons among different institutions. The prognostic impact (improvement of local control and postoperative survival) has yet to be determined, however, although retrospective studies have suggested that systematic mediastinal dissection may improve the prognosis.[1,2] Recently Izbicki and associates[3] performed a randomized controlled trial in which they compared systematic mediastinal lymphadenectomy with mediastinal lymph node sampling for 169 patients with non–small cell lung cancer without overt lymph node

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Table I. *Patient characteristics*

	No.	*%*
Sex		
Male	123	74.1
Female	43	25.9
Histologic type		
Adenocarcinoma	96	57.8
Squamous cell carcinoma	55	33.1
Large cell carcinoma	13	7.8
Adenosquamous carcinoma	2	1.3
Tumor size (cm)		
≤2.0	19	11.4
2.0-3.0	147	88.6
Postoperative T status (pT)		
T1	42	25.3
T2	87	52.4
T3	37	22.3
Preoperative N status (cN)		
N0	67	40.4
N1	30	18.1
N2	66	39.7
N3	3	1.8
Tumor location		
Right upper lobe	54	32.5
Right middle lobe	8	4.8
Right lower lobe	41	24.7
Left upper lobe	44	26.5
Left lower lobe	19	11.5
Operation		
Pneumonectomy	48	28.9
Bilobectomy	14	8.4
Lobectomy	104	62.7
Curability		
Complete	150	90.4
Incomplete	16	9.6

Table II. *Lymph node location*

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

involvement. They found no difference between the 2 groups in disease-free survival or overall survival; however, their subset analysis in patients with limited mediastinal lymph node metastases suggested that a systematic lymphadenectomy may improve the prognosis. These results are not yet conclusive and require confirmation. The attitude of surgeons toward possible mediastinal lymph node metastasis in lung carcinomas therefore currently varies from institution to institution. Surgical options include nodal sampling only,[4] radical systematic lymph node dissection,[1,2,5] and ultraradical lymph node dissection of bilateral mediastinum through a median sternotomy.[6]

The concept of systematic lymph node dissection of the mediastinum for thoracic malignant tumors originates in the report by Cahan in 1960.[7,8] He proposed a lobectomy instead of pneumonectomy, which was then a standard surgical option, with en bloc resection of the mediastinum for patients at poor risk, and called this procedure *radical lobectomy.* His original technique for dissection was accepted as optimal and has been performed ever since by thoracic surgeons, although it was not based on a detailed analysis of metastasis at each mediastinal location (lymph node mapping became available 10 years later).[9] With the accumulation of data, a reevaluation of the mediastinal dissection, especially in terms of extent, may be necessary.

In this study we retrospectively reviewed the prevalences of lymph node metastases at each mediastinal site among patients with N2 disease, especially with respect to the lobe of the primary tumor. We examined the prognosis of patients with respect to metastases at certain sites in the mediastinum. On the basis of these results we tried to determine the proper lobe-specific extent of mediastinal dissection.

Patients and methods

During the 10-year period from 1987 to 1997, 1610 patients underwent pulmonary resection for lung cancer at the National Cancer Center Hospital in Tokyo. Among these we retrospectively analyzed the pattern of lymph node metastasis and the prognosis in 166 patients with a non–small cell histologic type as a lung carcinoma and histologically proven mediastinal lymph node metastasis (pN2) after a careful pathologic examination of all the dissected lymph nodes. All the tumors were resected by pulmonary resection (at least lobectomy) and systematic hilar and mediastinal lymph node dissection as described elsewhere[10] and were categorized as either T1, T2, or T3.[11] The following were criteria for exclusion from this study: tumors with small cell or low-grade malignant histologic type; T4 tumors, including those with

Table III. *Lymph node metastases among 54 patients with right upper-lobe tumors*

	Metastases		*Single-station metastases*		*Single-node metastases*	
Lymph node station	*No.*	*%*	*No.*	*%*	*No.*	*%*
1	15	27.8	1	1.9	1	1.9
2	4	7.4	2	3.7	1	1.9
3	40	74.1	21	38.9	12	22.2
4	16	9.6	9	16.7	9	16.7
7	7	13.0	1	1.9	1	1.9
Right hilar and intrapulmonary nodes	30	55.6	—	—	—	—
Total	54	100	34	63.0	24	44.4

malignant effusion and pleural dissemination; tumors with distant metastatic disease; resection procedures less than lobectomy for the primary tumor (segmentectomy or wedge resection); and lack of hilar and mediastinal lymphadenectomy. Excluded patients comprised 18% of the total. The patients ranged in age from 29 to 83 years (median 60.5 years). One hundred twenty-three patients were male and 43 were female. Most of the patients underwent a physical examination, chest radiography, chest computed tomographic scan, bone scintigraphy, and abdominal ultrasonography for staging and the evaluation of resectability before the operation. The clinical characteristics of these 166 patients are presented in Table I. Resected specimens were examined histologically, and their histologic type was determined according to the World Health Organization classification[12] as adenocarcinoma, squamous cell carcinoma, large cell carcinoma, or adenosquamous carcinoma.

Analysis of lymph node metastasis. The extent of lymph node metastasis was precisely recorded station by station. The median number of lymph nodes resected and examined was 21 per patient (range 5-50 per patient). The locations of intrapulmonary (stations 13 and 14, N1), hilar (stations 10-12, N1), and mediastinal (stations 1-9, N2) lymph nodes were expressed according to the lymph node map for lung cancer proposed previously (Table II).[9] Mediastinal stations were categorized as superior mediastinal (stations 1 and 4), aortic (stations 5 and 6), and inferior mediastinal (stations 7-9). The number of metastatic nodes and their percentage were determined according to the lobe in which the primary tumor was located. For tumors of the left upper lobe the metastases were further analyzed independently according to the upper and lingular segments.

Mode of lymph node metastasis. Special types of lymph node metastasis to the mediastinum were also defined. A metastasis was considered to be a *skip metastasis* if any of the mediastinal lymph nodes were involved by the tumor without hilar or intrapulmonary node metastasis. *Single-station metastasis* was defined as when only a single station in the mediastinum was involved, regardless of hilar node metastasis. *Single-node metastasis* was defined as when only a single node in the mediastinum was involved.

Recurrence and prognosis. Cancer recurrence was carefully divided into 2 categories according to the site of initial recurrence: locoregional and distant. *Locoregional recurrence* was defined as any recurrent disease within the ipsilateral hemithorax, mediastinum, or supraclavicular lymph nodes. All other sites of recurrence were referred to as *distant metastases.* The cause of death was recorded as either cancer related, related to other disease, or unknown. The survival was calculated by the Kaplan-Meier life table method[13] and comparisons were made by a log rank test[14] in which the initial day of treatment was the day of the operation. A death that was not due to cancer was considered to be a censored case. A χ^2 test was used to compare the prevalence.

Results

Lymph node metastases according to location of the primary tumor

Right upper lobe. The most common site of involvement for tumors of the right upper lobe (n = 54 patients; Table III) was the lower pretracheal station (station 3), at which 40 patients (74%) had metastases. The pretracheal station was also the most common site for single-station (39%) and single-node (22%) metastases. Overall, 53 of 54 patients (98.1%) had metastases in at least 1 of the superior mediastinal stations from 1 through 4. In contrast, the subcarinal station (station 7) was involved in only 7 patients (13%), 6 of whom had both subcarinal and superior mediastinal node involvement (multiple-station involvement). Only 1 patient (1.9%) showed metastasis to the subcarinal station without superior mediastinal involvement, and this patient showed hilar node involvement.

Right middle lobe. The superior mediastinal and subcarinal stations were equally involved by tumors of the right middle lobe (n = 8 patients; Table IV). Among these the subcarinal node was involved most commonly (n = 7 patients, 88%), followed by the lower pretracheal station (n = 6 patients, 75%). Single-station metastases occurred in only 3 patients (38%); 2 of these occurred in the subcarinal station and 1 occurred in the pretracheal station.

Right lower lobe. The most common site of metasta-

Table IV. *Lymph node metastases among 8 patients with right middle-lobe tumors*

	Metastases		*Single-station metastases*		*Single-node metastases*	
Lymph node station	*No.*	*%*	*No.*	*%*	*No.*	*%*
1	3	37.5	0	0	0	0
2	0	0	0	0	0	0
3	6	75	1	12.5	0	0
4	1	12.5	0	0	0	0
7	7	87.5	2	25	2	25
Right hilar and intrapulmonary nodes	7	87.5	—	—	—	—
Total	8	100	3	37.5	2	25

Table V. *Lymph node metastases among 41 patients with right lower-lobe tumors*

	Metastases		*Single-station metastases*		*Single-node metastases*	
Lymph node station	*No.*	*%*	*No.*	*%*	*No.*	*%*
1	12	29.3	2	4.9	1	2.4
2	1	2.4	0	0	0	0
3	27	65.9	8	19.5	3	7.3
4	6	14.6	1	2.4	1	2.4
7	24	58.5	10	24.4	9	22.0
8	0	0	0	0	0	0
9	4	9.8	0	0	0	0
Right hilar and intrapulmonary nodes	36	87.8	—	—	—	—
Total	41	100	21	51.2	14	34.1

Table VI. *Lymph node metastases among 44 patients with left upper-lobe tumors*

	Metastases		*Single-station metastases*		*Single-node metastases*	
Lymph node station	*No.*	*%*	*No.*	*%*	*No.*	*%*
1	1	2.3	0	0	0	0
2	8	18.2	1	2.3	0	0
3	6	13.6	0	0	0	0
4	12	27.3	4	9.1	1	2.3
5	26	59.1	11	25	9	20.5
6	14	31.8	4	9.1	3	6.8
7	9	20.5	5	11.4	5	11.4
Left hilar and intrapulmonary nodes	37	84.1	—	—	—	—
Total	44	100	25	56.8	18	40.9

sis for tumors of the right lower lobe (n = 41 patients; Table V) was the lower pretracheal station (station 3, n = 27 patients, 75%), followed by the subcarinal station (n = 24 patients, 59%). One of the superior mediastinal stations from 1 through 4 was involved in 31 patients (76%). Furthermore, metastasis occurred most commonly at the subcarinal station in patients with single-station metastasis (n = 10/21 patients, 48%). The remaining cases of single-station metastasis (n = 11/21 patients, 52%) occurred in superior mediastinal stations 1 through 4. This indicates the existence of lymphatic pathways from the lower lobe to the superior mediastinum that do no pass through the subcarinal station.

Left upper lobe. The most common site of metastasis in tumors of the left upper lobe (n = 44 patients; Table VI) was the aorticopulmonary window (n = 26 patients, 59%), followed by the para-aortic station (n = 14 patients, 32%). Involvement of the subcarinal or lower

Table VII. *Lymph node metastases among 34 patients with upper-segment tumors and 10 patients with lingular-segment tumors*

	Metastases (%)				*Single-station metastases (%)*				*Single-node metastases (%)*			
	Upper segment (n = 34)		*Lingular segment (n = 10)*		*Upper segment (n = 34)*		*Lingular segment (n = 10)*		*Upper segment (n = 34)*		*Lingular segment (n = 10)*	
Lymph node station	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*	*No.*	*%*
1	1	2.9	0	0	0	0	0	0	0	0	0	0
2	6	17.6	2	20	1	2.9	0	0	0	0	0	0
3	6	17.6	0	0	0	0	0	0	0	0	0	0
4	10	29.4	2	20	2	5.9	2	20	0	0	1	10
5	24	70.6	2	20	10	29.4	1	10	8	23.5	1	10
6	11	32.4	3	30	3	8.8	1	10	2	5.9	1	10
7	4	11.8	5	50	1	2.9	4	40	1	2.9	4	40
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
Left hilar and intrapulmonary nodes	30	88.2	7	70	—	—	—	—	—	—	—	—
Total	34	100	10	100	17	50	8	80	11	32.4	7	70

Table VIII. *Lymph node metastases among 19 patients with left lower-lobe tumors*

	Metastases		*Single-station metastases*		*Single-node metastases*	
Lymph node station	*No.*	*%*	*No.*	*%*	*No.*	*%*
1	0	0	0	0	0	0
2	1	5.3	0	0	0	0
3	2	10.5	0	0	0	0
4	8	42.1	3	15.8	3	15.8
5	3	15.8	1	5.3	0	0
6	1	5.3	0	0	0	0
7	11	57.9	5	26.3	3	15.8
8	1	5.3	0	0	0	0
9	5	26.3	2	10.5	2	10.5
Left hilar and intrapulmonary nodes	7	36.8	—	—	—	—
Total	19	100	11	57.9	8	42.1

mediastinal stations was relatively rare (21% and 0%, respectively). Single-station metastasis occurred in 25 patients (57%); the station of the aorticopulmonary window was most often involved (n = 11 patients, 25%). The subcarinal station was involved less commonly (n = 9 patients, 21%), and single-station metastasis was seen in 5 of those patients. None of the stations in the lower mediastinum were involved.

Left upper segment versus lingular segment. Forty-four patients with tumors of the upper lobe (Table VII) were further analyzed according to the segment of the primary tumor; there were 34 tumors in the upper segment and 10 in the lingular segment. There were distinctive differences in the pattern of lymphatic spread between tumors of the upper and lingular segments. Among tumors of the upper segment the most common site of metastasis was the aorticopulmonary window (n = 24 patients, 71%), followed by the para-aortic station (n = 11 patients, 32%). Involvement of the subcarinal station was seen in only 4 patients (12%), 3 of whom had multiple-station metastases. Only 1 patient (2.9%) had metastasis only at the subcarinal station. In contrast, the most common site of metastasis for tumors of the lingular segment was the subcarinal station (n = 4 patients, 40%). The aorticopulmonary window and para-aortic stations were involved in only 20% and 30% of cases, respectively.

Left lower lobe. The most common site of metastasis for tumors of the left lower lobe (n = 19 patients; Table VIII) was the subcarinal station (n = 11 patients, 58%),

Table IX. *Single-station and single-node metastases by station site*

Single-station metastases					*Single-node metastases*			
Right		*Left*			*Right*		*Left*	
No.	*%*	*No.*	*%*	*Station No.*	*No.*	*%*	*No.*	*%*
3	3.2	—	—	1	2	3.0	—	—
2	2.1	1	1.1	2	1	1.5	0	0
30	31.9	—	—	3	15	22.7	—	—
10	10.6	7	7.4	4	10	15.2	4	6.1
—	—	12	12.8	5	—	—	9	13.6
—	—	4	4.3	6	—	—	3	4.5
17	18.1	6	6.4	7	12	18.2	8	12.1
0	0	0	0	8	0	0	0	0
0	0	2	2.1	9	0	0	2	3.0
62	66.0	32	34.0	Subtotal	40	60.6	26	39.4
94	100			Total	66	100		

followed by the tracheobronchial station (n = 8 patients, 42%). The aorticopulmonary window and para-aortic stations, which were commonly involved in left upper lobe tumors, were not often involved (16% and 5.3%, respectively). One of the superior mediastinal or aortic stations was involved in 11 patients (58%). Single-station metastases occurred in 11 patients (58%). Although the most common site for single-station metastasis was the subcarinal station (n = 5 patients, 26%), aortic stations were also involved in 4 patients (21%).

Single-station and single-node metastases. Single-station metastases (Table IX) occurred in 94 patients (57%). Regarding the site of single-station metastasis, the lower pretracheal (n = 30 patients, 48%) and subcarinal (n = 17 patients, 28%) stations were common among tumors on the right side, whereas the aorticopulmonary window station (n = 12 patients, 38%) was common among tumors on the left side. In 66 patients (40%) the metastasis was limited to a single lymph node of the mediastinum (single-node metastasis; Table IX). Among tumors on the right side the lower pretracheal node was the most common site of single-node metastasis (n = 15 patients, 23%), followed by the subcarinal node (n = 12 patients, 18%). Among tumors on the left side the aorticopulmonary window (n = 9 patients, 14%) was the most common site, followed by the subcarinal node (n = 8 patients, 12%).

Skip metastases. Skip metastases occurred in 42 (25%) of the 166 patients. According to histologic examination, adenocarcinoma (55%) was the most common histologic type that metastasized in a skip manner, followed by squamous cell carcinoma (36%) and large cell carcinoma (9.5%).

Recurrence. One hundred six patients (64%) had cancer recurrence after resection. Detailed data regarding recurrence were not available for 6 patients. The initial recurrence site was analyzed in the remaining 100 cases: 61 patients (61%) had distant relapse, 33 patients (33%) had locoregional relapse, and 6 patients (6%) had both simultaneously. The initial sites of recurrence are presented in Table X. As a local site of recurrence the supraclavicular node (41%) was the most common, whereas the lung (37%) was the most common site for distant recurrence. The intervals between the initial operation and the discovery of recurrence varied from 83 to 2978 days. In 11 patients (5.2%) recurrence was found 5 years or longer after resection of the primary tumor. These 11 patients all had adenocarcinomas.

Table X. *Mode of recurrence in 100 patients with recurrence*

Mode of recurrence	*Location*	*No.*
Locoregional (n = 39*)	Supraclavicular node	16
	Mediastinal node	11
	Pleural effusion or dissemination	6
	Bronchial stump	4
	Intrapulmonary metastasis	2
Distant (n = 67*)	Lung	25
	Brain	16
	Bone	14
	Liver	9
	Adrenal	2
	Others	1

*Six patients with simultaneous local and distant recurrences are included.

Prognosis. The survival curve for all 166 patients is shown in Fig 1. The overall 5-year survival was 35%. Patients with single-station metastases had a significantly better prognosis than did those with multiple-

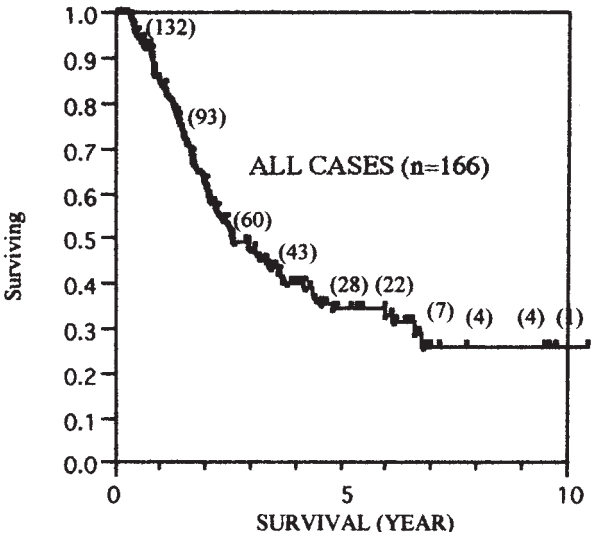

Fig 1. Survival curve for all 166 patients with lung carcinoma with mediastinal lymph node metastasis. Five-year survival was 35%. Numbers in *parentheses* indicate number of patients still at risk at every postoperative year.

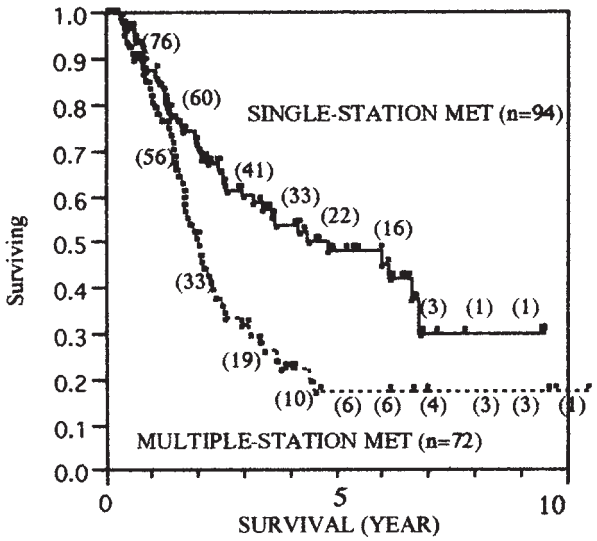

Fig 2. Survival curves of patients with single-station metastases *(MET)* and multiple-station metastases. Five-year survivals for patients with single-station metastases and multiple-station metastases were 48% and 18%, respectively. Statistically significant difference between groups was observed (log rank test, *P* = .0006). Numbers in *parentheses* indicate number of patients still at risk at every postoperative year.

station metastases (*P* = .0006; Fig 2). Patients with single-node metastases in the mediastinum also had a significantly better prognosis than did those with multiple-node metastases (P = .0002; Fig 3). Five-year survivals for those with single-node and single-station metastases were 55% and 48%, respectively.

Subcarinal node metastases. The prognoses of patients with and without metastases at the subcarinal station were compared for right upper lobe tumors (Fig 4). There was no significant difference in survival between these 2 groups of patients.

Upper mediastinal metastasis. The prognoses of patients with and without superior mediastinal node metastasis were also compared for right lower lobe tumors (Fig 5). Although no statistically significant difference in survival was observed, the survival of those with superior mediastinal node metastasis was quite poor, with a 5-year survival of 4.1%.

Discussion

Lymph node dissection of the pulmonary hilum and mediastinum combined with lobectomy (radical lobectomy) was first introduced by Cahan[7] as an alternative to pneumonectomy, which was respected as a standard mode of surgery in those days; radical lobectomy was originally indicated as a limited procedure for patients at poor risk. Cahan[7] stated, "We do not at present elect to do a radical lobectomy for cancer of the lung as the treatment of choice." He first postulated that the extent of dissection should be based on the lobe in which the primary tumor was located. He also stated that bilobectomy should be performed for tumors of the right middle or lower lobe. His proposal regarding the extent of dissection was not based on a detailed analysis of the prevalence of involvement in each mediastinal location, however, although he had experience with this surgical technique in 48 patients with lung cancer (n = 34 patients), metastasis (n = 9 patients), and benign conditions (n = 5 patients). Data became available only after surgeons adopted his technique, applied it practically, and described the metastatic status according to the lymph node map. It is also important to note that the original report of Cahan[7] did not differentiate between N1 and N2 nodes. It is quite surprising that he was able to propose such a good extent of dissection with the information available at that time.

The optimal extent of lymph node dissection should be based on the prevalence of metastases to each mediastinal station and on the prognosis. Dissection of the station with the least possibility of metastasis increases the morbidity and mortality as well as the operative time and blood loss while providing the least efficacy. Because the lymphatic drainage route, and therefore the prevalence of metastasis, is particular to the anatomic location of the primary tumor (lobe), an

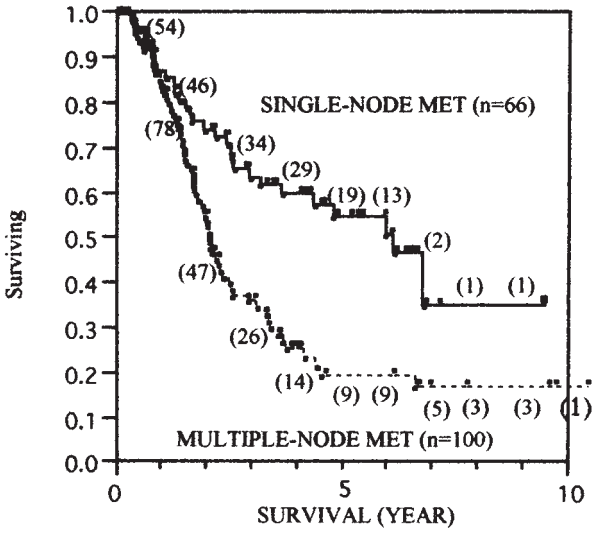

Fig 3. Survival curves of patients with single-node metastases *(MET)* and multiple-node metastases. Five-year survivals for patients with single-node metastases and multiple-node metastases were 55% and 20%, respectively. Statistically significant difference between groups was observed (log rank test, $P = .0002$). Numbers in *parentheses* indicate number of patients still at risk at every postoperative year.

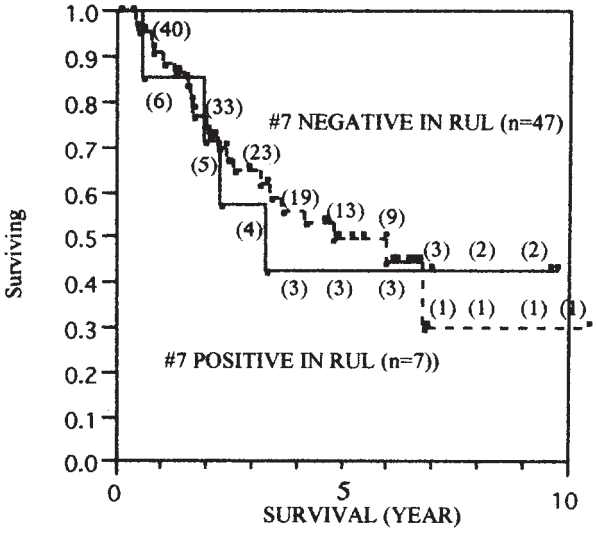

Fig 4. Survival curves of patients with and without subcarinal node (station 7) metastases among 54 patients with right upper lobe *(RUL)* tumors. There was no statistically significant difference between groups (log rank test, $P = .97$). Numbers in *parentheses* indicate number of patients still at risk at every postoperative year.

Table XI. *Recommendations regarding the extent of lymph node dissection according to the lobe of the primary site of the tumor*

		Lymph node location				
Primary site (lobe or segment)	*Study*	*Superior mediastinal (1-4)*	*Aortic (5-6)*	*Subcarinal (7)*	*Lower mediastinal (8-9)*	*Hilar and inter lobar (10-11)*
Right upper lobe	Cahan[7]	Yes	—	No	No	Yes
	Current study	Yes	—	No	No	Yes
Right middle and lower lobe	Cahan[7]	No	—	Yes	Yes	Yes
	Current study	Yes	—	Yes	Yes	Yes
Left upper segment	Cahan[7]	Yes	Yes	No	No	Yes
	Current study	Yes*	Yes	No	No	Yes
Left lingular segment	Cahan[7]	Yes	Yes	No	No	Yes
	Current study	Yes*	Yes	Yes	No	Yes
Left lower lobe	Cahan[7]	No	No	Yes	Yes	Yes
	Current study	Yes*	Yes	Yes	Yes	Yes

*Because the highest mediastinal and lower pretracheal nodes are not usually accessible by left lateral thoracotomy, these nodes are not dissected.

analysis of lymphatic involvement according to the primary site is indispensable for determining the optimal extent of dissection. The important points of this study are as follows:

1. Dissection of the subcarinal node is not always necessary for tumors of the right upper lobe and the left upper segment because single-station metastases to this station occur rarely (1.9% and 2.9%, respectively). In this case dissection is indicated only when involvement of the superior mediastinal station is noted by a frozen-section examination during the operation.

2. The right middle and lower lobes can be resected by lobectomy, not by bilobectomy, with complete eradication of the lymphatic drainage route.

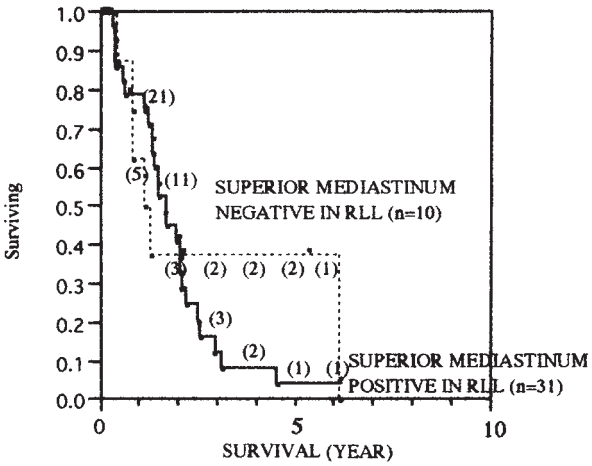

Fig 5. Survival curves of patients with and without superior mediastinal node metastasis (from station 1 through station 4) in 41 right lower lobe tumors. Five-year survival for patients with superior mediastinal metastasis was 4.1%. There was no statistically significant difference (log rank test, $P = .55$). Numbers in *parentheses* indicate the number of patients still at risk at every 1 year after surgery.

3. Although the subcarinal station was commonly involved in tumors of the lower lobe of both sides, the lower station of the superior mediastinum or aortic station was also involved without subcarinal involvement in a significant number of cases (right side, 42%; left side 42%).

4. Indeed, the higher prevalence of metastasis in superior mediastinal stations seems unusual for right lower lobe tumors. Looking at our results in detail, however, we find that both single-node metastases and single-station metastases were more common in the subcarinal station than in the pretracheal station. This finding indicates that the subcarinal station was the principal first-step site of mediastinal spread of the tumor cells and that lower pretracheal node involvement by lower lobe tumors could be regarded as the sign of considerable advancement of the disease. In this series many advanced cases were included, maybe by chance, and this could account for the higher prevalence of lower pretracheal metastases. This speculation corresponds with the extremely poor prognosis (a survival of 4.l%) for patients with superior mediastinal metastases of right lower lobe tumors (Fig 5).

5. In light of these findings, superior mediastinal dissection is preferable for tumors of both lower lobes because of the relatively higher prevalence. However, the prognosis was extremely poor even after systematic dissection, and this procedure is least likely to improve survival.

Table XI shows the extents of dissection recommended according to our results and those in Cahan's original proposal.[7] Surprisingly, there were only small differences between these suggestions, and our data basically support Cahan's original recommendations.[7]

Another important finding in this study was that patients with single-station and single-node metastases had a significantly better prognosis than those with multiple-station and multiple-node metastases: 5-year survivals were 48% and 55%, respectively. The better prognosis of patients with single-station metastases has been reported elsewhere.[5,15] These findings indicate that patients with N2 disease are a heterogeneous population with a considerably varied prognosis and that patients with single-station or single-node metastasis should be recognized as having "minimal N2 disease," with a different clinical course after surgical treatment than that of those with other types of N2 disease. This minimal N2 disease was otherwise categorized as N0 or N1 disease if systematic lymph node dissection was not performed. Patients with minimal N2 disease would theoretically best benefit from systematic lymph node dissection, however, because minimal N2 disease has the greatest chance of being a pure localized disease and cancer cells in the mediastinal nodes could be eradicated by systematic lymph node dissection without being overlooked. The better survival of these patients with dissected minimal N2 disease suggests a prognostic advantage of systematic lymph node dissection. Because a previous randomized study by Izbicki and coworkers[3] included only 24.7% patients with N2 disease, who would best benefit from lymphadenectomy, it is unclear whether that study would have been able to detect an improvement in survival. Their subset analysis among patients with N2 disease found that patients undergoing systematic lymph node dissection had a significantly better prognosis than did those undergoing sampling alone, and this seems to be compatible with our speculations.

Most of the tumor recurrences after surgical treatment were at distant organs, as noted in many previous reports.[16-18] This indicates that many cases of N2 disease are already systemic disease at the time of the operation, with subclinical or latent systemic metastases (micrometastases). The purpose of postoperative or preoperative adjuvant chemotherapy is to control these distant lesions, although the significance has yet to be determined. Systematic lymph node dissection is a purely local therapeutic option that has no impact on controlling systemic micrometastases. Because there is currently no diagnostic tool for detecting subclinical micrometastases, however, we cannot differentiate

between minimal N2 disease (local disease) and N2 disease with systemic micrometastases. When surgical resection is indicated, regardless of whether it is a primary or an adjuvant operation, systematic lymph node dissection of the extent discussed here should therefore be performed.

This retrospective analysis yielded a lobe-specific extent for systematic lymph node dissection according to the prevalence at each mediastinal station. The results support the extent originally proposed by Cahan,[7] with only minor changes. Questions regarding mediastinal lymph node dissection must always be answered according to whether survival is actually improved. Considering that patients with N2 disease can best benefit from lymph node dissection, a future trial must be large enough to include patients with minimal N2 disease, because only they might have a chance for cure. Otherwise, the results may always remain inconclusive. Finally, mediastinoscopy has the advantage in evaluating nodes on the contralateral side that are not easily assessed during surgery. Therefore, regardless of results of this study, the importance of staging mediastinoscopy remains unchanged for the purpose of better selection of surgical candidates by exclusion of N3 or N2 spread of the disease.

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