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ORIGINAL REPORT

Clinical Significance of 4L Lymph Node Dissection in Left Lung Cancer

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ABSTRACT

Purpose
To investigate the prognostic impact of 4L lymph node (LN) dissection in left lung cancer and to analyze the relative risk factors for 4L LN metastasis.

Patients and Methods
We retrospectively collected data from 657 patients with primary left lung cancer who underwent surgical pulmonary resection from January 2005 to December 2009. One hundred thirty-nine patients underwent 4L LN dissection ($4L^{D+}$ group); the other 518 patients did not receive 4L LN dissection ($4L^{D-}$ group). Propensity score weighting was applied to reduce the effects of observed confounding between the two groups. Study end points were disease-free survival (DFS) and overall survival (OS).

Results
The metastasis rate of station 4L was 20.9%, which was significantly higher than those of station 7 (14.0%; $P = .048$) and station 9 (9.8%; $P < .001$). Station 4L metastasis was associated with most other LN station metastases in univariate analysis, but only station 10 LN metastasis was an independent risk factor for 4L LN metastasis (odds ratio, 0.253; 95% CI, 0.109 to 0.588; $P = .001$) in multivariate logistic analysis. The $4L^{D+}$ group had a significantly better survival than the $4L^{D-}$ group (5-year DFS, 54.8% *v* 42.7%; $P = .0376$; 5-year OS, 58.9% *v* 47.2%; $P = .0200$). After allowing potential confounders in multivariate survival analysis, dissection of 4L LN retained its independent favorable effect on DFS (hazard ratio, 1.502; 95% CI, 1.159 to 1.947; $P = .002$) and OS (hazard ratio, 1.585; 95% CI, 1.222 to 2.057; $P = .001$). Propensity score weighting further confirmed that the $4L^{D+}$ group had a more favorable DFS ($P = .0014$) and OS ($P < .001$) than the $4L^{D-}$ group.

Conclusion
Station 4L LN involvement is not rare in left lung cancer, and dissection of the 4L LN station seems to be associated with a more favorable prognosis as compared with those who did not undergo this dissection.

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INTRODUCTION

Lymph node (LN) metastasis is a major and common metastatic pathway in lung cancer, with the metastasis rate of 30% to 40%.[1] Mediastinal LN dissection is a crucial component for accurate LN staging, having important prognostic and therapeutic implications for patients with non–small-cell lung cancer (NSCLC).[2,3] The standard treatment procedure for resectable NSCLC involves lobectomy with systemic mediastinal LN dissection. However, the degree to which the mediastinal LNs should be exposed and the extent of their excision is still under debate.[4-6] Current surgical practice is partly dependent on the experience of the surgeon. Station 4L LN dissection for left lung cancer is more difficult than that for right lung cancer because of anatomic limitations caused by the aortic arch, left recurrent laryngeal nerve, and thoracic duct. Therefore, superior mediastinal LN metastasis of left lung cancer is rarely studied.[7] The International Association for the Study of Lung Cancer (IASLC) suggests that systematic nodal dissection involves the minimal excision of at least three mediastinal nodal stations, including the subcarinal node, without requirement for 4L LNs in patients with left-sided tumors.[8] Thus, we carried out this research to evaluate the clinical significance of 4L LN dissection.

ASSOCIATED CONTENT

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PATIENTS AND METHODS

Patients

Between January 2005 and December 2009, we retrospectively reviewed 707 patients undergoing left lung cancer surgery within our department. Patients who underwent surgical pulmonary resection (lobectomy or pneumonectomy) with lymphadenectomy were included. The following patients were excluded: patients with metastatic lung tumors, patients who underwent partial resection or segmentectomy, and patients who had no LN resection. Finally, 657 patients were enrolled in this study (Fig 1). Resected lung cancer samples and LNs were evaluated histopathologically by two experienced pathologists. LN stations were classified according to the LN map proposed by the IASLC,[9] and we mainly sought and removed station 1 to station 12 LNs; station 13 and station 14 LNs were not routinely resected and labeled because they were resected with the lung specimen. Tumor stage was assessed according to the eighth edition of the IASLC classification system.[10] Histologic subtypes of adenocarcinoma were classified in line with the new IASLC/American Thoracic Society/European Respiratory Society multidisciplinary lung adenocarcinoma classification.[11] The predominant pattern was defined as the pattern with the largest percentage.

Follow-Up

The follow-up data were collected by official contact with patients or their relatives by telephone or obtained from hospital records. Each hospitalized patient had complete medical records. Five patients were lost to contact after surgery in the group that underwent 4L LN dissection ($4L^{D+}$), and 103 patients in the group that did not undergo dissection ($4L^{D-}$). We compared the 108 patients who were lost to contact with the 549 patients who had complete follow-up information on the basis of the relevant covariances. The result showed that there was no statistically significant difference between the two groups ($P > .05$, Data Supplement). Routine examinations, such as a plain chest x-ray; computed tomography scan of the thorax, head, and abdomen; and ultrasound of neck and abdomen, were generally performed every 3 months for the first 2 years after surgery and every 6 months after that for 5 years. After 5 years, the patients were assessed annually. Bone scans were performed as clinically indicated on the basis of bone pain. Positron emission tomography and bronchoscopy with biopsy were performed at the treating physician's discretion. The primary end point was disease-free survival (DFS), which was calculated as the time interval from the date of surgery until the first event (relapse, metastasis, or death as a result of lung cancer) or last follow-up; overall survival (OS) served as the secondary end point, which was defined as the time interval between the date of surgery and the date of either death as a result of lung cancer or the last follow-up. Both DFS and OS were calculated in months.

The follow-up period was completed in October 2017 or to the date of death of patients. The median follow-up was 99 months (range, 4 to 153 months) for the $4L^{D+}$ group and 85 months (range, 0 to 153 months) for the $4L^{D-}$ group.

Propensity Score Weighting

Inverse probability of treatment weighting (IPTW) was used to weight participants on the basis of their estimated probability of exposure given confounders (the propensity score) to balance observed confounders between the $4L^{D+}$ group and the $4L^{D-}$ group.[12,13] Each individual has

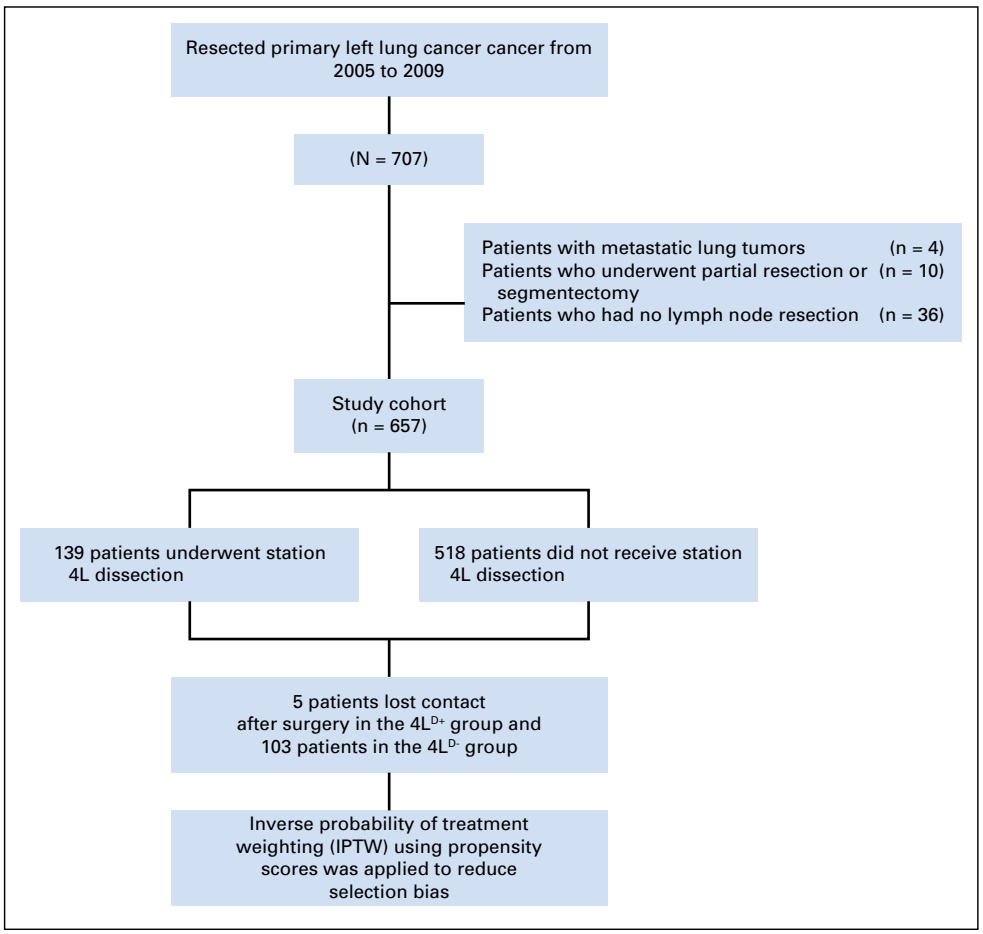

Fig 1. Patients flow diagram. IPTW, inverse probability of treatment weighting.

Table 1. Patients' Baseline Data Before and After Propensity Score Weighting

Characteristic	Entire Cohort			Propensity Score Weighting*		
	$4L^{D-}$ Group	$4L^{D+}$ Group	*P*	$4L^{D-}$ Group	$4L^{D+}$ Group	*P*
Sex			.870			.709
Male	354 (68.3)	96 (69.1)		284 (68.4)	94 (70.1)	
Female	164 (31.7)	43 (30.9)		131 (31.6)	40 (29.9)	
Age, years			.669			.962
< 65	327 (63.1)	85 (61.2)		258 (62.2)	83 (61.9)	
≥ 65	191 (36.9)	54 (38.8)		157 (37.8)	51 (38.1)	
Smoking history			.865			.615
Yes	343 (66.2)	94 (67.6)		272 (65.5)	91 (67.9)	
No	175 (33.8)	45 (32.4)		143 (34.5)	43 (32.1)	
Tumor location			.139			.989
Left upper lobe	288 (55.6)	87 (62.6)		232 (55.9)	75 (56.0)	
Left inferior lobe	230 (44.4)	52 (37.4)		183 (44.1)	59 (44.0)	
Tumor area			.845			.906
Central	158 (30.5)	45 (32.4)		123 (29.6)	39 (29.1)	
Peripheral	360 (69.5)	94 (67.6)		292 (70.4)	95 (70.9)	
Tumor size, cm (mean ± SD)	4.15 ± 2.2	4.62 ± 2.3	.028	4.30 ± 2.3	4.26 ± 2.2	.846
pT stage			.094			.869
T1	210 (40.5)	44 (31.7)		153 (36.9)	53 (39.3)	
T1a	12 (2.3)	2 (1.5)		8 (1.9)	3 (2.2)	
T1b	67 (12.9)	15 (10.8)		49 (11.8)	20 (14.9)	
T1c	131 (25.3)	27 (19.4)		96 (23.2)	30 (22.2)	
T2	206 (39.8)	56 (40.3)		169 (40.7)	52 (38.5)	
T2a	126 (24.3)	30 (21.6)		103 (24.8)	28 (20.7)	
T2b	80 (15.5)	26 (18.7)		66 (15.9)	24 (17.8)	
T3	64 (12.4)	22 (15.8)		59 (14.2)	17 (12.6)	
T4	38 (7.3)	17 (12.2)		34 (8.2)	13 (9.6)	
Histology			.705			.950
ADC	204 (39.4)	49 (35.2)		165 (39.8)	52 (38.8)	
SQ	228 (44.0)	68 (48.9)		178 (42.9)	61 (45.5)	
SCC	16 (3.1)	3 (2.2)		14 (3.4)	4 (3.0)	
Others	70 (13.5)	19 (13.7)		58 (14.0)	17 (12.7)	
Adenocarcinoma subtype			.751			.670
AIS/MIA	12 (2.3)	3 (2.1)		12 (2.9)	3 (2.2)	
Lepidic predominant	43 (8.3)	9 (6.5)		36 (8.7)	9 (6.7)	
Acinar predominant	80 (15.5)	19 (13.6)		63 (15.2)	20 (14.9)	
Papillary predominant	28 (5.4)	4 (2.9)		19 (4.6)	4 (3.0)	
Micropapillary predominant	12 (2.3)	5 (3.6)		10 (2.4)	5 (3.8)	
Solid predominant	29 (5.6)	9 (6.5)		25 (6.0)	11 (8.2)	
pTNM stage			.002			.283
I	194 (37.5)	37 (26.6)		142 (34.2)	51 (38.1)	
IA1	11 (2.1)	2 (1.4)		8 (1.9)	3 (2.2)	
IA2	48 (9.3)	13 (9.4)		36 (8.7)	18 (13.5)	
IA3	68 (13.2)	10 (7.2)		44 (10.6)	14 (10.5)	
IB	67 (12.9)	12 (8.6)		54 (13.0)	16 (11.9)	
II	137 (26.4)	29 (20.9)		112 (27.0)	27 (20.1)	
IIA	46 (8.9)	14 (10.1)		42 (10.1)	13 (9.7)	
IIB	91 (17.5)	15 (10.8)		70 (16.9)	14 (10.4)	
III	187 (36.1)	73 (52.5)		161 (38.8)	56 (41.8)	
IIIA	151 (29.2)	57 (41.0)		128 (30.8)	44 (32.8)	
IIIB	36 (6.9)	16 (11.5)		33 (7.9)	12 (9.0)	
pN stage			.034			.788
N0	291 (56.2)	67 (48.2)		228 (54.9)	77 (57.0)	
N1	72 (13.9)	14 (10.1)		52 (12.5)	14 (10.4)	
N2	155 (29.9)	58 (41.7)		135 (32.5)	44 (32.6)	

NOTE. Data presented as No. (%) unless otherwise noted.
Abbreviations: $4LD^{+}$ group, patients who underwent 4L lymph node dissection; $4L^{D-}$ group, patients who did not receive 4L lymph node dissection; AIS, adenocarcinoma in situ; ADC, adenocarcinoma; MIA, minimally invasive adenocarcinoma; SCC, small cell carcinoma; SQ, squamous cell carcinoma.
*Number of valid cases is different from the total count in the cross-tabulation table because the cell counts have been rounded. Patients with a missing value were excluded from inverse probability of treatment weighting analysis.

a different weight, from 0.58 to 2.21. If the weighting coefficient is 1.5, it will be considered as 1.5 people. The IPTW uses the weight to construct a virtual standard population, which often results in the number of valid cases being different from the total count in the cross-tabulation table because the cell counts have been rounded (Table 1). However, there will not be much difference before and after weighting, and the overall proportion is still 100% of the patients in the propensity score weighting (PSW) analysis. In addition, the patients (108) who were lost to follow-up with a missing value were excluded from IPTW analysis. Propensity scores for all patients were calculated by using a multiple logistic regression[14] with

the following covariates: age, sex, pathological T (pT) stage, smoking history, pathological N (pN) stage, histology, tumor location, tumor area, and pathological tumor-node-metastasis (pTNM) stage.

Statistical Analysis

All statistical analyses were performed using the SAS 9.4 software (SAS Institute, Cary, NC). χ^2 test was used for categorical variables, and *t* test was used for continuous variables. Multivariate analysis was performed using a logistic regression model to evaluate the relation between station 4L metastasis and risk factors. Survival was estimated by the Kaplan-Meier method and compared using the log-rank test. Multivariate Cox proportional hazards regression analysis was used to calculate the hazard ratio (HR) and 95% CI. In all analyses, two-tailed $P < .05$ was considered statistically significant.

RESULT

Baseline Data Before and After Weighting

Table 1 shows the baseline data of all of the patients (n = 657) and of the PSW patients. A total of 139 (21.2%) and 518 (78.8%) patients were assigned to the $4L^{D+}$ group and $4L^{D-}$ group, respectively. Before weighting, difference were observed in terms of pTNM stage ($P = .002$), pN stage ($P = .034$), and tumor size ($P = .028$); after weighting, the results were similar between the two groups ($P > .05$; Table 1).

Distribution of LN Involvement

Figure 2 summarizes the frequency of node involvement per station in left lung cancer. Of the 139 patients with 4L LN dissection, 29 (20.9%) had 4L involvement. The metastasis rate of station 4L (20.9%) was significantly higher than those of station 7 (14.0%; $P = .048$) and station 9 LNs (9.8%; $P < .001$), but no significant difference was observed among other node stations ($P > .05$; Fig 2).

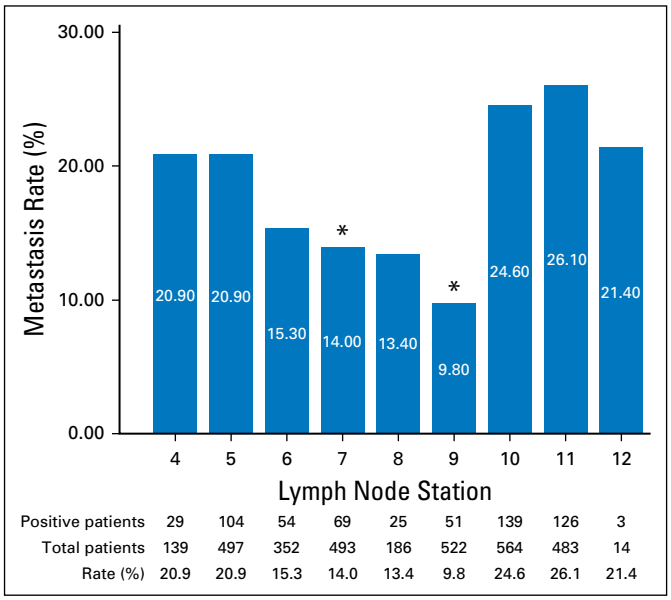

Fig 2. Metastasis rate of each lymph node station (station 4, left lower paratracheal; station 5, subaortic; station 6, para-aortic; station 7, subcarinal; station 8, paraesophageal; station 9, pulmonary-ligament; station 10, hilar; station 11, interlobar; station 12, lobar). A χ^2 test was used to compare the metastasis rate of station 4L with other lymph node stations. $*P < .001$.

Risk Factor Analysis for 4L Lymphatic Metastasis

As shown in Table 2, the 4L LN metastasis was significantly correlated with all other stations (station 5, $P < .001$; station 6, $P < .001$; station 7, $P = .005$; station 9, $P = .019$; station 10, $P < .001$; station 11, $P = .006$), except station 8 ($P = 0.660$); sex, age, smoking history, pT stage, tumor size, adenocarcinoma subtype, tumor location, and tumor area were shown to have no significant correlation with station 4L metastasis. Those statistically significant factors were further analyzed by multivariate logistic analysis, and the result revealed that station 10 metastasis was independently associated with 4L LN metastasis (OR, 0.253; 95% CI, 0.109 to 0.588; $P = .001$).

Patient Survival Before and After Weighting

At completion of the study, 335 patients died and 179 patients had recurrence or metastasis at follow-up. Seventy patients died and 34 patients had recurrence or metastasis in the $4L^{D+}$ group. Two hundred sixty-five patients died and 145 patients had recurrence or metastasis in the $4L^{D-}$ group. The 5-year DFS rates were 54.8% in the $4L^{D+}$ group and 42.7% in the $4L^{D-}$ group (median, 71.6 *v* 39.4 months). The 5-year OS rates in the two groups were 58.9% and 47.2%, respectively (median, 86.0 *v* 50.1 months). The log-rank test showed that the $4L^{D+}$ group had a significantly superior survival compared with the $4L^{D-}$ group (DFS, $P = .0376$; OS, $P = .0200$; Figs 3A and 3C). After PSW, the DFS and OS were significantly higher in the $4L^{D+}$ group compared with the $4L^{D-}$ group ($P = .0014$ and $P < .001$, respectively; Figs 3B and 3D).

Analysis of Survival Factors

Several variables, such as status of 4L LN dissection, tumor location, pT stage, histology, and pN stage, were all significant factors for DFS by univariate analysis ($P = .038$, $P = .038$, $P < .001$, $P < .001$, and $P < .001$, respectively), and status of 4L LN dissection, tumor area, pT stage, histology, and pN stage were all significant factors for OS ($P = .020$, $P = .030$, $P = .002$, $P < .001$, and $P < .001$, respectively) by univariate analysis (Table 3). Additional multivariate analysis showed that status of 4L LN dissection was an independent factor for DFS (HR, 1.502; 95% CI, 1.159 to 1.947; $P = .002$) and OS (HR, 1.585; 95% CI, 1.222 to 2.057; $P = .001$), together with pT stage, histology, and pN stage (Table 3).

DISCUSSION

The presence of tumor cell metastases is one of the most important adverse factors for prognosis in lung cancer. Considering the key role of LNs in lung cancer metastasis, thorough removal of LNs is of great importance.[2] Regarding the left lung, the Bronchogenic Carcinoma Cooperation Group of the Spanish Society of Pneumology and Chest Surgery recommended a minimal dissection of at least stations 5, 6, and 7 for left upper lobe and stations 7, 8, and 9 for left lower lobe.[15] Zurich medical university emphasized the

Table 2. Univariate and Multivariate Analysis of Correlation Between Clinicopathological Factors and Station 4L Metastasis

Variable	Univariate Analysis				Multivariate Analysis		
	No.	Station 4L Metastasis No. (%)		*P*	OR	95% CI	*P*
		Positive	Negative				
No.	139	29	110				
Sex				.069			
Male	96	16 (16.7)	80 (83.3)				
Female	43	13 (30.3)	30 (69.7)				
Age, years				.332			
< 65	85	20 (23.5)	65 (76.5)				
≥ 65	54	9 (16.7)	45 (83.3)				
Smoking history				.244			
Yes	94	17 (18.1)	77 (81.9)				
No	45	12 (26.7)	33 (73.3)				
Histology				.175			
ADC	68	10 (14.7)	58 (85.3)				
SQ	49	15 (30.6)	34 (69.4)				
SCC	3	1 (33.3)	2 (66.7)				
Others	19	3 (15.8)	16 (84.2)				
Adenocarcinoma subtype				.335			
AIS/MIA	3	0 (0)	3 (100)				
Lepidic predominant	9	1 (11.1)	8 (88.9)				
Acinar predominant	19	6 (31.6)	13 (68.4)				
Papillary predominant	4	2 (50.0)	2 (50.0)				
Micropapillary predominant	5	3 (60.0)	2 (40.0)				
Solid predominant	9	3 (33.3)	6 (66.7)				
Tumor size, cm (mean ± SD)		4.7 ± 2.1	4.6 ± 2.4	.869			
pT stage				.204			
T1	44	7 (15.9)	37 (84.1)				
T2	56	16 (28.6)	40 (71.4)				
T3	22	2 (9.1)	20 (90.9)				
T4	17	4 (23.5)	13 (76.5)				
Tumor location				.714			
Left upper lobe	87	19 (21.8)	68 (78.2)				
Left inferior lobe	52	10 (19.2)	42 (80.8)				
Tumor area				.729			
Central	42	8 (19.0)	34 (81.0)				
Peripheral	97	21 (21.6)	76 (78.4)				
Station 5 metastasis	28	10 (35.7)	18 (64.3)	< .001	2.765	0.943 to 8.103	.064
Station 6 metastasis	14	8 (57.1)	6 (42.9)	< .001	2.604	0.631 to 10.745	.186
Station 7 metastasis	17	8 (47.1)	9 (52.9)	.005	1.895	0.441 to 8.151	.391
Station 8 metastasis	7	1 (14.3)	6 (85.7)	.660			
Station 9 metastasis	10	5 (50)	5 (50)	.019	1.122	0.194 to 6.482	.897
Station 10 metastasis	32	17 (53.1)	15 (46.9)	< .001	5.175	1.855 to 14.435	.002
Station 11 metastasis	24	10 (41.7)	14 (58.3)	.006	1.427	0.419 to 4.859	.570

Abbreviations: ADC, adenocarcinoma; AIS, adenocarcinoma in situ; MIA, minimally invasive adenocarcinoma; OR, odds ratio; SCC, small cell carcinoma; SQ, squamous cell carcinoma.

removal of at least stations 4L, 5, and 6 LNs for left-sided tumors.[16] The current studies usually focus on multiple stations of LNs and summarize station 4L as the superior mediastinal LNs.[17,18] To date, there is no study involving the comparison of short- and long-outcomes of 4L nodal dissection. One explanation may be the complex anatomy of station 4L: adjacent to the aortic arch, left recurrent laryngeal nerve, and thoracic duct. These anatomic limitations make 4L dissection more difficult and increase the risk of surgery.[19] Therefore, some thoracic surgeons do not remove 4L LNs during the operation of left-sided tumors, which leads to the lack of a large sample of clinical data about the dissection of station 4L and its impact on prognosis. We therefore retrospectively reviewed the clinical significance of removing 4L LNs.

In our study, from a total of 657 patients with left lung cancer, we observed that the frequent metastatic sites of mediastinal LNs involved station 4L and 5. This finding was in line with some previous studies.[20,21] Univariate analysis revealed that 4L LN metastasis was significantly correlated with most other stations, but only station 10 metastasis was an independent risk factor for 4L LN metastasis by multivariate analysis. This may be explained by the fact that there is a transition zone between station 4L and station 10 at the tracheobronchial angle. Shimada et al[22] reported that left upper lobe tumors had more of a predilection for involvement of superior mediastinal LNs than lower lobe tumors in patients with NSCLC. In our study, we found that the metastasis of station 4L was more likely to occur in the left upper lobe, but there was no statistical significance. This may be due to the small sample size. Therefore, large prospective studies are still needed for additional research.

The results of our study revealed that the 5-year DFS and OS were significantly higher in the $4L^{D+}$ group than in the $4L^{D-}$

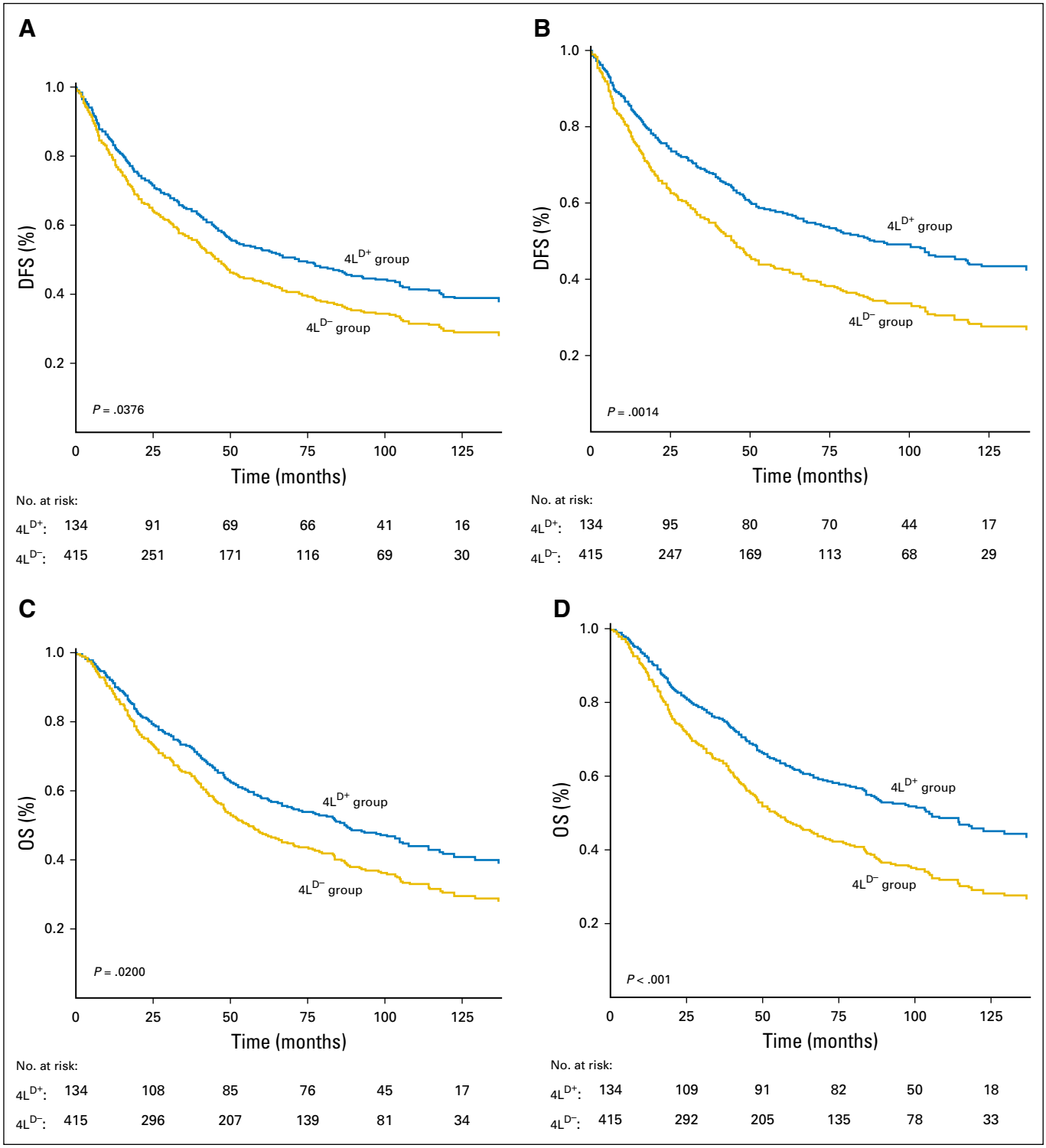

Fig 3. Kaplan-Meier curves for (A) disease-free survival (DFS) before weighting; (B) DFS after weighting; (C) overall survival (OS) before weighting; and (D) OS after weighting in the $4L^{D+}$ and $4L^{D-}$ groups. Five patients were lost to follow-up immediately after surgery in the $4L^{D+}$ group and 103 patients in the $4L^{D-}$ group.

group. Under multivariate analysis, 4L LN dissection proved to be one of the independent predictors of favorable DFS and OS. The reason may be that 4L LN dissection helps to remove localized LN metastasis and undetected micrometastases and reduce the incidence of local recurrence, which could result in better local tumor control.[16,23,24] Japanese scholars Sakao et al [25] and Kuroda et al [26] also found that dissection of 4L LNs was important for the prognosis of patients with left lung cancer. To eliminate selection bias, our study pioneers the use of the PSW method to compare the prognostic impact of pulmonary resection for left lung cancer between the $4L^{D+}$ group and the $4L^{D-}$ group. After weighting, the $4L^{D+}$ group still had a significantly higher survival rate than the

Table 3. Univariate and Multivariate Cox Regression Analysis of Prognostic Factors in Left Lung Cancer

	Univariate Analysis				Multivariate Analysis			
	DFS		OS		DFS		OS	
Predictor	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)
Sex	.423	0.909 (0.721 to 1.147)	.436	1.097 (0.869 to 1.383)	.523	1.098 (0.824 to 1.463)	.503	1.102 (0.830 to 1.462)
Age	.576	1.064 (0.855 to 1.325)	.419	1.094 (0.879 to 1.362)	.172	0.856 (0.684 to 1.070)	.179	0.858 (0.686 to 1.073)
Smoking history	.647	0.949 (0.756 to 1.190)	.663	0.951 (0.758 to 1.193)	.816	1.033 (0.783 to 1.364)	.960	1.007 (0.764 to 1.327)
Tumor location	.038	0.797 (0.643 to 0.988)	.054	0.810 (0.653 to 1.004)	.291	1.126 (0.904 to 1.402)	.614	1.058 (0.850 to 1.317)
Tumor area	.085	1.222 (0.973 to 1.535)	.030	0.776 (0.618 to 0.975)	.725	0.957 (0.751 to 1.221)	.831	1.027 (0.805 to 1.310)
pT stage	< .001	1.240 (1.108 to 1.388)	< .001	1.251 (1.118 to 1.400)	.006	1.180 (1.049 to 1.328)	.003	1.195 (1.062 to 1.345)
Histology	< .001	1.315 (1.150 to 1.504)	< .001	1.353 (1.183 to 1.548)	< .001	1.278 (1.115 to 1.465)	< .001	1.312 (1.144 to 1.505)
Station 4L dissection	.038	1.313 (1.016 to 1.697)	.020	1.356 (1.049 to 1.752)	.002	1.502 (1.159 to 1.947)	.001	1.585 (1.222 to 2.057)
pN stage	< .001	1.649 (1.468 to 1.852)	< .001	1.618 (1.441 to 1.818)	< .001	1.688 (1.496 to 1.904)	< .001	1.660 (1.471 to 1.873)

Abbreviations: DFS, disease-free survival; HR, hazard ratio; OS, overall survival.

$4L^{D-}$ group. In addition, Watanabe et al[27] pointed out that the 5-year survival rate of patients with left lung cancer with N2 disease was worse than that of patients with right-sided lesions, which may be due to insufficient LN dissection caused by anatomic restrictions. On the basis of these findings, we believe 4L LN dissection may be important. Additional prospective evaluation of the role of dissection is warranted to confirm these findings.

With the development of the technique of video-assisted thoracic surgery, surgical field visualization is also constantly improving. Some anatomic regions, such as the left paratracheal LNs (4L), which are difficult to expose by routine surgery, now can be clearly identified and resected by a thoracoscopic approach because of the magnification of the surgical field. Previous studies have demonstrated that it was feasible to dissect 4L LNs avoiding left recurrent laryngeal nerve injury.[28-31] In addition, it was reported that removal of LNs in station 4L could be achieved in 100% of patients by video-assisted mediastinal lymphadenectomy.[32] Today, many types of devices are available to make the complete and extensive dissection of LNs easier.

Our study has several limitations. First, our research is a single-center retrospective study, although PSW was used to balance the variables that may influence the outcomes between the groups. Second, the number of patients with 4L LN dissection is small, which may raise the possibility of selection bias. Third, the number of patients lost to follow-up is large. Although there was no statistically significant difference between the patients who lost contact after surgery (108) and the patients who had complete follow-up information (549) on the basis of the relevant covariances, there are still differences in loss to follow-up between the $4L^{D+}$ and $4L^{D-}$ groups. The patients lost to follow-up in the $4L^{D-}$ group were more likely to have a smoking history and more comorbidities and were older than those in the $4L^{D+}$ group. Consequently, long-term effects remain to be fully confirmed and should be studied further with a larger sample size and a multicenter randomized clinical trial.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Clinical Significance of 4L Lymph Node Dissection in Left Lung Cancer

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