Journal of Cancer Research and Clinical Oncology (2019) 145:1313–1319
https://doi.org/10.1007/s00432-019-02880-9

ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Predictors and survival impact of station 4L metastasis in left non-small cell lung cancer

Likui Fang[1] · Luming Wang[1] · Yiqing Wang[1] · Yihe Wu[1] · Peng Ye[1] · Wang Lv[1] · Jian Hu[1]

Received: 17 January 2019 / Accepted: 25 February 2019 / Published online: 16 March 2019

Abstract

Background It remains unclear about the predictors and survival impact of station 4L metastasis in left-sided non-small cell lung cancer (NSCLC). This study aims to investigate these issues to explore the significance of station 4L lymph-node dissection (LND).

Methods We retrospectively enrolled 405 patients with station 4L LND, and divided them into the positive station 4L metastasis group and the negative station 4L metastasis group. The logistic regression was performed to identify the predictors of station 4L metastasis. The survival outcomes including disease-free survival (DFS) and overall survival (OS) were analyzed in pN2 patients to explore the prognostic effect of station 4L metastasis.

Results There were 48 (11.9%) patients in the positive station 4L metastasis group and 357 (88.1%) patients in the negative station 4L metastasis group. Station 5 metastasis ($P=0.008$, OR 7.578, 95% CI 1.710–33.589), station 10 metastasis ($P=0.004$, OR 7.133, 95% CI 1.904–26.717), and cN2 ($P=0.010$, OR 5.062, 95% CI 1.473–17.392) were independent risk factors of station 4L metastasis. In pN2 patients, the positive station 4L metastasis group had inferior DFS ($P=0.019$) and OS ($P=0.006$) compared with the negative station 4L metastasis group, and station 4L metastasis was the independent risk factor for poor prognosis.

Conclusion It is of great necessity to perform station 4L LND in left NSCLC, because station 4L metastasis is not rare and has an unfavorable prognosis.

Keywords Non-small cell lung cancer · Station 4L metastasis · Lymph-node dissection · Prognosis

Introduction

Lung cancer continues to be one of the most common malignant tumors and causes most cancer-related deaths worldwide (Siegel et al. 2018; Bray et al. 2018), although much progress has been made in prevention and screening recently (Johnson et al. 2014). Non-small cell lung cancer (NSCLC) is the most frequent subtype of lung cancer, and surgery is still the major treatment method for resectable NSCLC (Reck et al. 2013). Lymph-node dissection (LND) is an important component in surgical procedure due to its crucial role in accurate staging and prognostic implication (Johnson et al. 2014; Watanabe and Asamura 2009). However, the extent of LND has remained debatable. Systematic mediastinal LND is recommended from the oncological point of view (Howington et al. 2013), while mediastinal lymph-node sampling has been proven to show similar survival outcome with complete lymphadenectomy in patients with N0 or N1 (less than hilar) NSCLC (Darling et al. 2011). Selective LND has also been controversial in spite of the concept of lobe-specific lymphatic drainage (Adachi et al. 2017; Han and Chen 2017; Liang et al. 2018).

In current clinical practice, the extent of LND has partly depended on the experience of thoracic surgeons. Because of the anatomic limitation caused by aortic arch, left recurrent laryngeal nerve, and thoracic duct, station 4L LND has been neglected by some surgeons. It is undeniable that omitting station 4L LND could reduce the risk of injury of the aortic arch, thoracic duct, and left recurrent laryngeal nerve (Sayar et al. 2016; Liang et al. 2018). However, it is seemed to be necessary to perform station 4L LND because of the relatively common involvement of

✉ Jian Hu
dr_hujian@zju.edu.cn

[1] Department of Thoracic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310003, China

this station lymph nodes (Liang et al. 2018). Therefore, this study aims to investigate the predictive factors of station 4L metastasis and its effect on survival outcomes to explore the necessity of station 4L LND in left NSCLC.

Methods

Patients' selection

We retrospectively reviewed the records of all patients who underwent left NSCLC surgery in our department from January 2013 to August 2018. Patients undergoing pulmonary resection with station 4L LND were regarded as the candidates to be enrolled. The following patients were excluded: (1) patients with distant metastasis, (2) patients who underwent neoadjuvant therapy, and (3) patients with the previous or concurrent other malignant tumors. Finally, a total of 405 patients were enrolled and their clinicopathological characteristics were collected from the hospital electronic medical records system. All patients included in the study were restaged according to the 8th edition of the American Joint Committee on Cancer (AJCC) lung cancer staging classification (Rami-Porta et al. 2017). The study protocol was approved by the Institutional Review Board of the First Affiliated Hospital of Zhejiang University, School of Medicine.

Lymph-node assessment

The preoperative evaluation of lymph nodes mainly depended on high-resolution computed tomography (CT) or contrast-enhanced CT. The lymph node was considered to be positive when its shortest axis was longer than 1 cm on CT scan. Positron-emission tomography (PET) scan was not routinely performed in the early stage NSCLC, and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was only performed in the patients who were highly suspected as N2 disease. Lymph-node stations were classified according to the International Association for the Study of Lung Cancer (IASLC) lymph-node map (Rusch et al. 2009). Mediastinal and hilar lymph nodes were systematically removed, while station 11 and station 12 LND were omitted in some early stage patients who underwent wedge resection. Station 13 and station 14 lymph nodes were not routinely labeled, because, sometimes, they were resected with pulmonary specimens. Resected lymph nodes were evaluated pathologically by at least two experienced pathologists.

Follow-up

The routine examinations after surgery were requested every 3 months for the first year and every 6 months after that for 5 years. After 5 years, the patients were still recommended to take annual examinations. The examinations included blood tumor markers testing, chest CT scan, abdominal ultrasound, and head magnetic resonance imaging (MRI). Bone scan was performed on the basis of bone pain. The follow-up information was collected by telephone or obtained from the hospital outpatient clinic records. The last follow-up time was December 2018. Disease-free survival (DFS) was defined as the time interval from the date of surgery to the first event (recurrence, metastasis, or NSCLC related death) or last follow-up. Overall survival (OS) was defined as the time interval between the date of surgery and the date of death or last follow-up. Both DFS and OS were calculated in months.

Statistical analysis

The enrolled patients were divided into the positive station 4L metastasis group and the negative station 4L metastasis group. The measurement data and numeration data of two groups were statistically analyzed with *t* test and Chi-square test, respectively. If there were clinicopathological characteristics showing significant differences between two groups, multivariate analysis was performed for those characteristics by the binary logistic regression to identify the factors predicting station 4L metastasis. To investigate the prognostic effect of station 4L metastasis, survival outcomes were compared between pN2 patients with station 4L metastasis and those without station 4L metastasis by the Kaplan–Meier method and the log-rank test. Univariate and multivariate Cox regression analyses were performed to identify the independent survival factors among the different metastatic lymph-node stations. All the above analysis was conducted by the SPSS software (version 24.0, IBM SPSS Inc. United States). Statistical significance was set at P value < 0.05 (all P values presented were two-sided).

Results

Clinicopathological characteristics

A total of 48 (11.9%) and 357 (88.1%) patients were assigned to the positive station 4L metastasis group and the negative station 4L metastasis group, respectively. The clinical and pathological characteristics of two groups are shown in Tables 1 and 2. Statistical differences were observed in terms

Table 1 Clinical characteristics of patients with or without station 4L metastasis

Variables	Station 4L metastasis		*P* value
	Positive (*N* = 48)	Negative (*N* = 357)	
Sex			0.739
Male	35 (72.9%)	252 (70.6%)	
Female	13 (27.1%)	105 (29.4%)	
Age, years			0.537
Median (range)	59.5 (43–75)	62 (32–81)	
Smoking history	29 (60.4%)	212 (59.4%)	0.891
Hypertension	11 (22.9%)	88 (24.6%)	0.793
Diabetes	1 (2.1%)	23 (6.4%)	0.381
Tuberculosis	0 (0.0%)	6 (1.7%)	0.217
CEA level, ng/mL			0.835
Median (range)	4.6 (1.1–84.4)	2.9 (0.5–448.9)	
Tumor location			0.246
LUL	35 (72.9%)	230 (64.4%)	
LLL	13 (27.1%)	127 (35.6%)	
CT characteristics			0.004
GGO	1 (2.1%)	42 (11.8%)	
Partially solid	1 (2.1%)	49 (13.7%)	
Solid	46 (95.8%)	266 (74.5%)	
cT stage			0.119
T1a	1 (2.1%)	25 (7.0%)	
T1b	5 (10.4%)	87 (24.4%)	
T1c	12 (25.0%)	66 (18.5%)	
T2a	10 (20.8%)	78 (21.8%)	
T2b	10 (20.8%)	49 (13.7%)	
T3	5 (10.4%)	35 (9.8%)	
T4	5 (10.4%)	17 (4.8%)	
cN stage			< 0.001
N0	13 (27.1%)	261 (73.1%)	
N1	4 (8.3%)	31 (8.7%)	
N2	31 (64.6%)	65 (18.2%)	

Values are *N* (percentage) unless otherwise specified

CEA carcinoembryonic antigen, *LUL* left upper lobe, *LLL* left lower lobe, *GGO* ground-glass opacity

Table 2 Pathological characteristics of patients with or without station 4L metastasis

Variables	Station 4L metastasis		*P* value
	Positive (*N* = 48)	Negative (*N* = 357)	
Anatomical type			0.936
Central	21 (43.8%)	154 (43.1%)	
Peripheral	27 (56.3%)	203 (56.9%)	
Histology			0.517
Adenocarcinoma	26 (54.2%)	188 (52.7%)	
SCC	18 (37.5%)	152 (42.6%)	
Others	4 (8.3%)	17 (4.8%)	
Cell differentiation			< 0.001
Well	0 (0.0%)	24 (6.7%)	
Moderate	7 (14.6%)	144 (40.3%)	
Poor	40 (83.3%)	170 (47.6%)	
Unknown	1 (2.1%)	19 (5.3%)	
pT stage			0.236
T1a	0 (0.0%)	26 (7.3%)	
T1b	5 (10.4%)	71 (19.9%)	
T1c	9 (18.8%)	55 (15.4%)	
T2a	15 (31.3%)	106 (29.7%)	
T2b	7 (14.6%)	40 (11.2%)	
T3	8 (16.7%)	38 (10.6%)	
T4	4 (8.3%)	21 (5.9%)	
Tumor size[a], cm			0.047
Median (range)	3.5 (1.5–11.0)	3.0 (0.3–13.0)	
Visceral pleural invasion	18 (37.5%)	82 (23.0%)	0.028
Lymphovascular invasion	12 (25.0%)	19 (5.3%)	< 0.001
Station 5 metastasis	27 (56.3%)	21 (5.9%)	< 0.001
Station 6 metastasis	18 (37.5%)	8 (2.2%)	< 0.001
Station 7 metastasis	11 (22.9%)	18 (5.0%)	< 0.001
Station 8 metastasis	4 (8.3%)	4 (1.1%)	0.007
Station 9 metastasis	4 (8.3%)	5 (1.4%)	0.011
Station 10 metastasis	20 (41.7%)	28 (7.8%)	< 0.001
Station 11 metastasis[b]	12/32 (37.5%)	21/218 (9.6%)	< 0.001
Station 12 metastasis[c]	32/43 (74.4%)	90/317 (28.4%)	< 0.001

Values are *N* (percentage) unless otherwise specified

SCC squamous cell carcinoma

[a]Tumor size was defined as the maximum diameter of the pathological specimens

[b]Station 11 lymph nodes were removed in 32 and 218 patients in two groups, respectively

[c]Station 12 lymph nodes were removed in 43 and 317 patients in two groups, respectively

of CT characteristics ($P = 0.004$), cN stage ($P < 0.001$), cell differentiation ($P < 0.001$), tumor size ($P = 0.047$), visceral pleural invasion ($P = 0.028$), and lymphovascular invasion ($P < 0.001$) between two groups. It was notable that station 4L metastasis was significantly correlated with all the other stations (station 5, $P < 0.001$; station 6, $P < 0.001$; station 7, $P < 0.001$; station 8, $P = 0.007$; station 9, $P = 0.011$; station 10, $P < 0.001$; station 11, $P < 0.001$; station 12, $P < 0.001$).

Risk factors of station 4L metastasis

Multivariate logistic analysis was further performed for those significantly different characteristics to identify the

Table 3 Multivariate analysis of correlation between risk factors and station 4L metastasis

Variables	*P* value	OR	95% CI
CT characteristics			
GGO	–	1	–
Partially solid	0.127	0.020	0.000–3.062
Solid	0.213	0.174	0.011–2.726
cN stage			
N0	–	1	–
N1	0.903	1.122	0.177–7.109
N2	0.010	5.062	1.473–17.392
Cell differentiation			
Well	0.999	0.000	–
Moderate	–	1	–
Poor	0.353	1.938	0.480–7.823
Unknown	0.530	0.247	0.003–19.312
Tumor size	0.730	0.951	0.716–1.264
Visceral pleural invasion	0.549	1.485	0.407–5.414
Lymphovascular invasion	0.839	1.172	0.254–5.407
Station 5 metastasis	0.008	7.578	1.710–33.589
Station 6 metastasis	0.518	1.766	0.314–9.930
Station 7 metastasis	0.683	1.442	0.249–8.344
Station 8 metastasis	0.466	2.716	0.185–39.857
Station 9 metastasis	0.340	4.296	0.215–86.035
Station 10 metastasis	0.004	7.133	1.904–26.717
Station 11 metastasis	0.321	2.271	0.450–11.455
Station 12 metastasis	0.262	2.211	0.553–8.841

OR odds ratio, *CI* confidence interval, *GGO* ground-glass opacity

risk factors of station 4L metastasis. As shown in Table 3, CT characteristics, cell differentiation, tumor size, visceral pleural invasion, lymphovascular invasion, station 6 metastasis, station 7 metastasis, station 8 metastasis, station 9 metastasis, station 11 metastasis, and station 12 metastasis were not statistically associated with station 4L metastasis. The results revealed that cN2 ($P=0.010$, OR 5.062, 95% CI 1.473–17.392), station 5 metastasis ($P=0.008$, OR 7.578, 95% CI 1.710–33.589), and station 10 metastasis ($P=0.004$, OR 7.133, 95% CI 1.904–26.717) were independent risk factors of station 4L metastasis.

Survival outcomes

A total of 92 patients with pN2 disease were included in survival analysis, with 48 (52.2%) assigned to the positive station 4L metastasis group ($4L^{M+}$ group) and 44 (47.8%) assigned to the negative station 4L metastasis group ($4L^{M-}$ group). Six patients were lost to contact after surgery and the follow-up information was collected in 86 patients. The median follow-up time was 21 months (range 1–69 months). The baseline data were comparable

Table 4 Baseline data of pN2 patients with or without station 4L metastasis

Variables	Station 4L metastasis		*P* value
	Positive ($N=48$)	Negative ($N=44$)	
Sex			0.618
Male	35 (72.9%)	14 (31.8%)	
Female	13 (27.1%)	30 (68.2%)	
Age, years			0.520
Median (range)	59.5 (43–75)	59.5 (45–76)	
Smoking history	29 (60.4%)	24 (54.5%)	0.569
Tumor location			0.105
LUL	35 (72.9%)	25 (56.8%)	
LLL	13 (27.1%)	19 (43.2%)	
Surgical approach			0.148
Thoracotomy	39 (81.3%)	30 (68.2%)	
VATS	9 (18.8%)	14 (31.8%)	
Surgical procedure			0.542
Lobectomy	31 (64.6%)	33 (75.0%)	
Sleeve lobectomy	7 (14.6%)	5 (11.4%)	
Pneumonectomy	10 (20.8%)	6 (13.6%)	
Anatomical type			0.869
Central	21 (43.8%)	20 (45.5%)	
Peripheral	27 (56.3%)	24 (54.5%)	
Histology			0.763
Adenocarcinoma	26 (54.2%)	25 (56.8%)	
SCC	18 (37.5%)	17 (38.6%)	
Others	4 (8.3%)	2 (4.5%)	
Cell differentiation			0.754
Moderate	7 (14.6%)	9 (20.5%)	
Poor	40 (83.3%)	34 (77.3%)	
Unknown	1 (2.1%)	1 (2.3%)	
Tumor size[a], cm			0.397
Median (range)	3.5 (1.5–11.0)	3.5 (0.8–10.0)	
pT stage			0.588
T1a	0 (0.0%)	1 (2.3%)	
T1b	5 (10.4%)	5 (11.4%)	
T1c	9 (18.8%)	5 (11.4%)	
T2a	15 (31.3%)	20 (45.5%)	
T2b	7 (14.6%)	4 (9.1%)	
T3	8 (16.7%)	7 (15.9%)	
T4	4 (8.3%)	2 (4.5%)	
pTNM stage			0.604
IIIA	36 (75.0%)	35 (79.5%)	
IIIB	12 (25.0%)	9 (20.5%)	
Adjuvant therapy	46 (95.8%)	36 (81.8%)	0.068

Values are *N* (percentage) unless otherwise specified

LUL left upper lobe, *LLL* left lower lobe, *VATS* video-assisted thoracoscopic surgery, *SCC* squamous cell carcinoma

between two groups (Table 4). The median DFS was 17 months (95% CI 6.458–27.542) and 37 months (95% CI 16.549–57.451) in the $4L^{M+}$ group and the $4L^{M-}$ group, respectively. The median OS was 28 months (95% CI 16.971–39.029) and 54 months (95% CI 25.602–82.398) in the $4L^{M+}$ group and the $4L^{M-}$ group, respectively. The log-rank test showed that the $4L^{M+}$ group had inferior DFS ($P=0.019$) and OS ($P=0.006$) compared with the $4L^{M-}$ group (Fig. 1).

Univariate Cox regression analysis showed that station 4L metastasis was the significant factor for DFS ($P=0.023$; Table 5) and OS ($P=0.009$; Table 6). Additional multivariate Cox regression analysis further proved that station 4L metastasis was the independent risk factor for DFS ($P=0.006$, HR = 2.737, 95% CI 1.344–5.577; Table 5) and OS ($P=0.004$, HR = 4.030, 95% CI 1.568–10.359; Table 6).

Discussion

Lymph-node metastasis which is a major metastatic pathway of NSCLC leads to poor prognosis (Takenaka et al. 2013). Accurate lymph-node stage not only contributes to make postoperative therapeutic strategies, but also helps to predict prognosis, so complete LND is of great importance (Whitson et al. 2007). However, the extent of LND has still been controversial. The IASLC recommended that systematic LND should involve at least three mediastinal

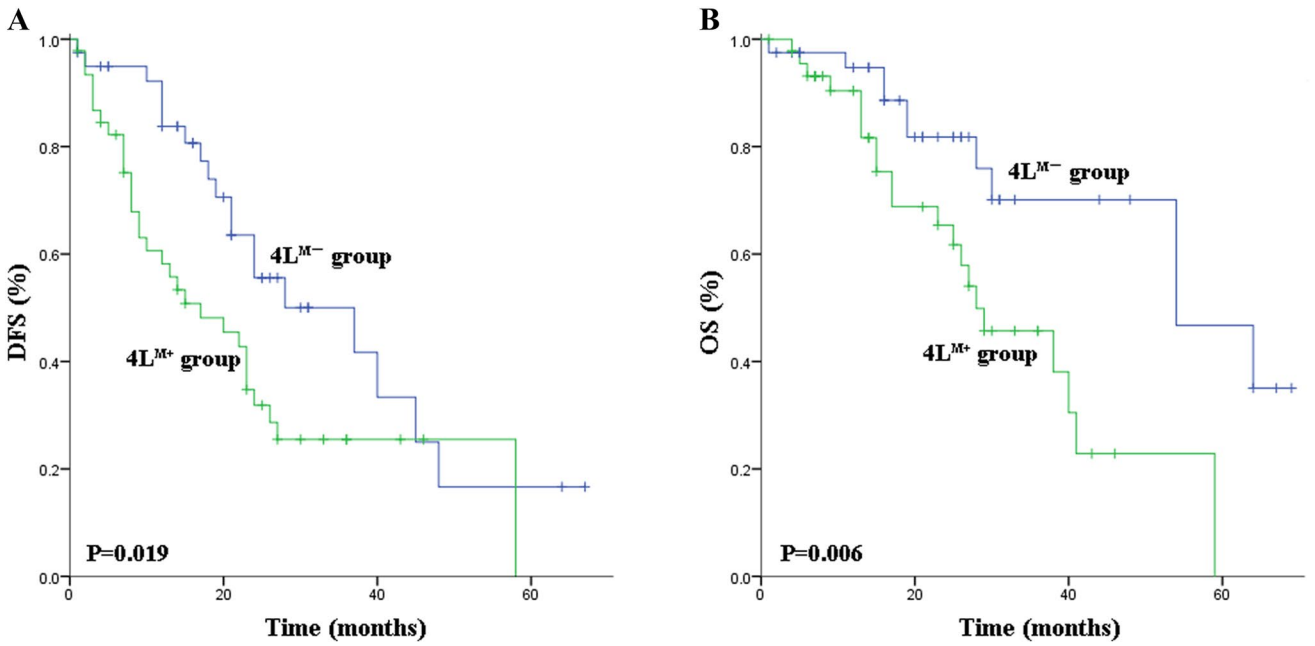

Fig. 1 Kaplan–Meier curves for **a** disease-free survival (DFS) and **b** overall survival in the $4L^{M+}$ and $4L^{M-}$ groups. $4L^{M+}$ group, positive station 4L metastasis group; $4L^{M-}$ group, negative station 4L metastasis group

Table 5 Cox regression analysis of lymph-node stations in DFS

Lymph-node station	Univariate analysis			Multivariate analysis		
	P value	HR	95% CI	*P* value	HR	95% CI
Station 4 metastasis	0.023	1.949	1.096–3.465	0.006	2.737	1.344–5.577
Station 5 metastasis	0.193	1.450	0.828–2.539	0.065	2.123	0.955–4.720
Station 6 metastasis	0.740	1.111	0.597–2.066	0.154	0.538	0.230–1.260
Station 7 metastasis	0.760	1.096	0.607–1.979	0.060	2.208	0.968–5.033
Station 8 metastasis	0.435	1.408	0.597–3.323	0.248	1.818	0.659–5.017
Station 9 metastasis	0.623	1.224	0.547–2.743	0.874	1.083	0.405–2.893
Station 10 metastasis	0.495	1.232	0.677–2.241	0.204	1.563	0.785–3.111
Station 11 metastasis	0.467	0.778	0.396–1.531	0.168	0.574	0.261–1.263
Station 12 metastasis	0.875	1.049	0.574–1.917	0.906	1.040	0.538–2.013

DFS disease-free survival, *HR* hazard ratio, *CI* confidence interval

Table 6 Cox regression analysis of lymph-node stations in OS

Lymph-node station	Univariate analysis			Multivariate analysis		
	P value	HR	95% CI	*P* value	HR	95% CI
Station 4 metastasis	0.009	2.822	1.298–6.134	0.004	4.030	1.568–10.359
Station 5 metastasis	0.243	1.521	0.753–3.073	0.086	2.438	0.882–6.742
Station 6 metastasis	0.783	0.893	0.399–2.000	0.055	0.339	0.113–1.023
Station 7 metastasis	0.290	0.647	0.289–1.448	0.823	1.137	0.368–3.513
Station 8 metastasis	0.157	2.006	0.766–5.256	0.097	3.296	0.805–13.494
Station 9 metastasis	0.836	1.118	0.389–3.217	0.742	0.770	0.162–3.658
Station 10 metastasis	0.897	0.947	0.415–2.162	0.706	1.196	0.471–3.041
Station 11 metastasis	0.442	0.703	0.287–1.723	0.408	0.644	0.227–1.828
Station 12 metastasis	0.652	0.843	0.401–1.773	0.935	0.967	0.426–2.195

OS overall survival, *HR* hazard ratio, *CI* confidence interval

lymph-node stations including the subcarinal station, without requirement for station 4L LND in left lung cancer (Rami-Porta et al. 2005). Station 4L lymph nodes were also not requested to be removed in the guideline of the European Society for Medical Oncology (ESMO) which suggested surgical evaluation of a minimum of three mediastinal lymph-node stations including the subcarinal station (Postmus et al. 2017). Although station 4L LND was not required in some guidelines, some studies indicated the clinical significance of station 4L LND in spite of its technical challenges and possible complications. Liang et al. (2018) reported that station 4L lymph nodes were commonly involved as metastases in the left upper lobe (12.0%) and left lower lobe (11.2%) by retrospectively analyzing 4511 resected NSCLC cases. Japanese researchers indicated that station 4L LND might has a beneficial effect on prognosis in left lung cancer (Sakao et al. 2006; Kuroda et al. 2015). Wang et al. (2018) suggested that patients undergoing station 4L LND seemed to have a significantly higher survival rate than those who did not undergo this dissection and found that station 10 metastasis was an independent risk factor for station 4L metastasis.

On the basis of previous studies, it has still been unclear about the preoperative predictors and prognostic implication of station 4L metastasis. In this study, from a total of 405 patients with station 4L LND, we observed that the incidence of station 4L metastasis was not rare (11.9%), which was high enough to warrant attention. To identify the predictors of station 4L metastasis, we compared the clinical and pathological factors between the positive station 4L metastasis group and the negative station 4L metastasis group, and performed multivariable analysis for those statistically different factors. The results revealed that station 4L metastasis was not only associated with station 10 metastasis, but also correlated with cN2 and station 5 metastasis. These findings implied that the status of station 4L lymph nodes should be assessed adequately in left NSCLC, especially in those with cN2, station 5 metastasis, and station 10 metastasis.

The location of N2 was reported to have a prognostic impact in NSCLC (Clement-Duchene et al. 2018), and our study further analyzed the prognosis of station 4L metastasis in pN2 patients. We found that the $4L^{M-}$ group had favorable DFS and OS compared with the $4L^{M+}$ group. Station 4L metastasis was further proven to be an independent predictive factor of poor prognosis by Cox regression analysis. In addition, Feng et al. (2014) and Billiet et al. (2016) reported that station 4L was one of the most common recurrent sites after surgery by analyzing the patterns of locoregional relapses in patients with N2 disease. One of the reasonable explanations might be the complex anatomy of station 4L which led to incomplete resection of station 4L lymph nodes. However, with the rapid development of minimal invasive techniques, some complex anatomic regions could be exposed easily and identified clearly under the thoracoscope. There were several studies in recent years reporting the clinical feasibility and safety of station 4L LND (Yoo et al. 2011; Kim et al. 2016; Nagashima 2016). According to these findings, we believe that it is of great necessity to perform station 4L LND in left NSCLC.

Our study has some limitations. First, this is a single-center retrospective research that inevitably has the selection bias. Second, the number of patients with pN2 is small, which may influence the outcomes between the groups. Consequently, the results in this study remain to be further confirmed by a multi-center randomized clinical trial.

Author contributions Drs. JH and LF contributed to the conception and design of the work. Dr. LF and contributed to conception, design, data analysis, and editing the manuscript. Drs. LF, LW, YW, and YW contributed to data acquisition, statistical analysis, and interpretation of the data. Drs. PY and WL contributed to the revision of the manuscript.

Funding This study was funded by Major Science and Technology Projects of Zhejiang Province (2014C03032), Key Disciplines

of Traditional Chinese Medicine in Zhejiang Province (2017-XK-A33), National Key R&D Program of China (2017YFC0113500), and National Natural Science Foundation of China (31700690). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest regarding the publication of this paper.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

Adachi H, Sakamaki K, Nishii T et al (2017) Lobe-specific lymph node dissection as a standard procedure in surgery for non-small cell lung cancer: a propensity score matching study. J Thorac Oncol 12(1):85–93

Billiet C, De Ruysscher D, Peeters S et al (2016) Patterns of locoregional relapses in patients with contemporarily staged stage III-N2 NSCLC treated with induction chemotherapy and resection: implications for postoperative radiotherapy target volumes. J Thorac Oncol 11(9):1538–1549

Bray F, Ferlay J, Soerjomataram I et al (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68(6):394–424

Clement-Duchene C, Luc A, Casse JM et al (2018) Survival impact of stations of pathological lymph nodes in N2 non-small cell lung cancer in a French Hospital. Ann Surg Oncol 25(5):1262–1268

Darling GE, Allen MS, Decker PA et al (2011) Randomized trial of mediastinal lymph node sampling versus complete lymphadenectomy during pulmonary resection in the patient with N0 or N1 (less than hilar) non-small cell carcinoma: results of the American College of Surgery Oncology Group Z0030 Trial. J Thorac Cardiovasc Surg 141(3):662–670

Feng W, Fu XL, Cai XW et al (2014) Patterns of local-regional failure in completely resected stage IIIA(N2) non-small cell lung cancer cases: implications for postoperative radiation therapy clinical target volume design. Int J Radiat Oncol Biol Phys 88(5):1100–1107

Han H, Chen H (2017) Selective lymph node dissection in early-stage non-small cell lung cancer. J Thorac Dis 9(7):2102–2107

Howington JA, Blum MG, Chang AC et al (2013) Treatment of stage I and II non-small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 143(5 Suppl):e278S–e313S

Johnson DH, Schiller JH, Bunn PA Jr (2014) Recent clinical advances in lung cancer management. J Clin Oncol 32(10):973–982

Kim HJ, Kim YH, Choi SH et al (2016) Video-assisted mediastinoscopic lymphadenectomy combined with minimally invasive pulmonary resection for left-sided lung cancer: feasibility and clinical impacts on surgical outcomesdagger. Eur J Cardiothorac Surg 49(1):308–313

Kuroda H, Sakao Y, Mun M et al (2015) Lymph node metastases and prognosis in left upper division non-small cell lung cancers: the impact of interlobar lymph node metastasis. PLoS One 10(8):e0134674

Liang RB, Yang J, Zeng TS et al (2018) Incidence and distribution of lobe-specific mediastinal lymph node metastasis in non-small cell lung cancer: data from 4511 resected cases. Ann Surg Oncol 24:3300–3307

Nagashima T (2016) Thoracoscopic left mediastinal lymph node dissection. Ann Transl Med 4(1):10

Postmus PE, Kerr KM, Oudkerk M et al (2017) Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 28(suppl 4):iv1–iv21

Rami-Porta R, Wittekind C, Goldstraw P et al (2005) Complete resection in lung cancer surgery: proposed definition. Lung Cancer 49(1):25–33

Rami-Porta R, Asamura H, Travis WD et al (2017) Lung cancer—major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer J Clin 67(2):138–155

Reck M, Heigener DF, Mok T et al (2013) Management of non-small-cell lung cancer: recent developments. Lancet 382(9893):709–719

Rusch VW, Asamura H, Watanabe H et al (2009) The IASLC lung cancer staging project: a proposal for a new international lymph node map in the forthcoming seventh edition of the TNM classification for lung cancer. J Thorac Oncol 4(5):568–577

Sakao Y, Miyamoto H, Yamazaki A et al (2006) The spread of metastatic lymph nodes to the mediastinum from left upper lobe cancer: results of superior mediastinal nodal dissection through a median sternotomy. Eur J Cardiothorac Surg 30(3):543–547

Sayar A, Citak N, Buyukkale S et al (2016) The incidence of hoarseness after mediastinoscopy and outcome of video-assisted versus conventional mediastinoscopy in lung cancer staging. Acta Chir Belg 116(1):23–29

Siegel RL, Miller KD, Jemal A (2018) Cancer statistics, 2018. CA Cancer J Clin 68(1):7–30

Takenaka T, Katsura M, Shikada Y et al (2013) Outcome of surgical resection as a first line therapy in T3 non-small cell lung cancer patients. World J Surg 37(11):2574–2580

Trujillo-Reyes JC, Martínez-Téllez E, Rami-Porta R et al (2018) Combination video-assisted mediastinoscopic lymphadenectomy and transcervical thoracoscopy. Multimed Man Cardiothorac Surg. https://doi.org/10.1510/mmcts.2018.004

Wang YN, Yao S, Wang CL et al (2018) Clinical significance of 4L lymph node dissection in left lung cancer. J Clin Oncol 36(29):2935–2942

Watanabe S, Asamura H (2009) Lymph node dissection for lung cancer: significance, strategy, and technique. J Thorac Oncol 4(5):652–657

Whitson BA, Groth SS, Maddaus MA (2007) Surgical assessment and intraoperative management of mediastinal lymph nodes in non-small cell lung cancer. Ann Thorac Surg 84(3):1059–1065

Yoo DG, Kim YH, Kim DK et al (2011) Clinical feasibility and surgical benefits of video-assisted mediastinoscopic lymphadenectomy in the treatment of resectable lung cancer. Eur J Cardiothorac Surg 40(6):1483–1486