Original Article

Treatment patterns and clinical outcomes of resectable central non-small cell lung cancer patients undergoing sleeve lobectomy: a large-scale, single-center, real-world study

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Background: In the treatment of central-type non-small cell lung cancer (NSCLC), sleeve lobectomy (SL) has emerged as the surgical treatment of choice over pneumonectomy (PN). This retrospective study evaluates the clinical profiles and prognostic elements impacting survival and recurrence rates in patients who underwent SL.

Methods: We retrospectively analyzed 288 patients who underwent SL from January 2010 to December 2023. Survival analysis was performed using the Kaplan-Meier method, and survival curves were subsequently drawn. Factors predicting SL outcomes were investigated through univariate and multivariable Cox regression analyses.

Results: Univariate and multivariable analyses consistently demonstrated significant variations in overall survival (OS) and disease-free survival (DFS) among subgroups receiving neoadjuvant therapy (NT), which also stood out as independent prognostic factors. Patients undergoing NT showed enhanced OS [hazard ratio (HR) =0.4652, 95% confidence interval (CI): 0.3042–0.7116, P=0.004] and DFS (HR =0.5182, 95% CI: 0.3243–0.8279, P=0.01). Earlier pT stages were associated with better prognosis (P<0.05). Significant differences in both OS and DFS were noted across pN stages, with earlier stages indicating improved prognosis; this was a significant independent factor for DFS (P<0.001). Similar significant trends were observed across pathological Tumor-Node-Metastasis (pTNM) stages, with earlier stages linked to better outcomes. Additionally, body mass index (BMI) was identified as an independent prognostic factor for both OS and DFS. Clinical T stage independently influenced DFS. No significant prognostic disparities were observed in other clinical characteristics (P>0.05).

Conclusions: NT significantly improves the prognosis for NSCLC patients undergoing SL. Pathological staging is proven to be more indicative of prognosis than clinical staging. Understanding the staging of lymph nodes (LNs) is crucial for predicting the long-term recurrence risk in patients with NSCLC who undergo SL treatment. Mediastinal and hilar LN dissection is especially important in minimizing this risk and improving prognosis.

Keywords: Non-small cell lung cancer (NSCLC); sleeve lobectomy (SL); overall survival (OS); disease-free survival (DFS)

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Introduction

The American Cancer Society projects state that by 2024, lung cancer will still be one of the most common malignant tumors in the US, both in terms of incidence and fatality (1). Historically, pneumonectomy (PN) has been the primary treatment for central non-small cell lung cancer (NSCLC). However, this surgical approach is often associated with significant postoperative complications and mortality (2-4). Sleeve lobectomy (SL) was established as feasible in the 1950s and has since gained considerable attention (5). SL is particularly beneficial for patients with compromised cardiopulmonary function who are unsuitable for PN. In comparison to PN, SL preserves more lung function and markedly enhances long-term survival rates (6-9). SL has now become the standard surgical method for certain cases of central NSCLC that involve the main bronchus.

Lobectomy is considered the gold standard for treating resectable NSCLC (10). In central NSCLC, where the tumor invades the bronchus, conventional lobectomy may not ensure negative margins. The challenge and uniqueness of SL involve resecting a segment of the affected bronchus and anastomosing its ends, which carries a heightened risk of bronchial complications and may affect short-term survival (11-13). With improvements in surgical techniques, recent studies indicate that SL's perioperative complications are comparable to those of conventional lobectomy and do not compromise prognosis (13,14). Neoadjuvant therapy (NT) and clinical staging are significant prognostic factors in conventional lobectomy (15,16). Although SL is now a standard procedure for certain central lung cancer patients, reports on SL populations remain scarce and prospective randomized trials are unlikely to occur in the future.

Consequently, the purpose of this study is to review important prognostic markers in a sizable cohort and investigate the clinical and pathological features of patients receiving SL. Prognostic analysis of SL utilizing the most thorough data available is the primary focus of this largest real-world single-center study to date, as far as we are aware. This manuscript is written in accordance with the STROBE reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-685/rc).

Highlight box

Key findings

- Pathological staging according to the 9th Tumor-Node-Metastasis edition is more predictive of non-small cell lung cancer (NSCLC) sleeve lobectomy (SL) patient prognosis than clinical staging.

What is known and what is new?

- Sleeve lobectomy of NSCLC requires anastomosis of the bronchi or pulmonary artery, leaving subgroup prognostic analyses for these rare populations unreported.
- Our study is the world's largest known single-center real-world study on subgroup prognostic analysis of NSCLC patients underwent SL.

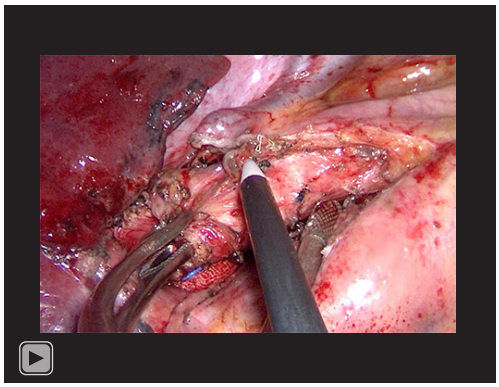
What is the implication, and what should change now?

- Neoadjuvant therapy significantly improves the prognosis for NSCLC patients who underwent SL, and mediastinal and hilar lymph node dissection is especially important in minimizing long-term recurrence risk and improving prognosis in NSCLC patients with SL.

Methods

Patients

From January 2010 to December 2023, 288 patients with primary central NSCLC who had SL surgery were retrospectively studied. Inclusion criteria included: (I) diagnosis of primary lung NSCLC; (II) undergoing SL surgery with negative resection margins; (III) no history of other systemic malignant tumors. Exclusion criteria comprised: (I) absence of clinical data; (II) positive resection margins; (III) patients receiving neoadjuvant radiotherapy. All patients were diagnosed pathologically via bronchoscopy or percutaneous puncture. Preoperative evaluations consisted of chest computed tomography (CT), brain magnetic resonance imaging (MRI)/CT, abdominal ultrasound, bone emission CT (ECT), or positron emission tomography-CT (PET-CT) to exclude distant metastases. Surgical decisions were made following multidisciplinary discussions involving thoracic surgery, oncology, and respiratory medicine, and were based on the informed consent of the patients. Based on the 9th edition guidelines (17), the tumor staging was evaluated. The Ethics



Video 1 This video shows uniportal VATS sleeve lobectomy of right upper lobe after neoadjuvant chemoimmunotherapy. VATS, video-assisted thoracic surgery.

Committee of National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College approved this study (No. 24/340-4620) and individual consent for this retrospective analysis was waived, and it was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Surgical strategy and NT

NT was employed after multidisciplinary consultations involving respiratory oncology experts and thoracic surgery specialists, with patient consent. NT is administered when tumors exceed 4 cm, or when resection is hindered by extensive N2 involvement, multi-station N2 involvement, or invasion of critical thoracic structures (16,18). Using CT-guided percutaneous biopsy or endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) (19), histological typing was performed prior to NT. Each therapy cycle lasted 21 days and programmed cell death-ligand 1 (PD-L1) tumor proportion score (TPS) testing was used preferentially. NT involves chemotherapy or a combination of chemotherapy and PD-L1 inhibitors. The first patient enrolled in neoadjuvant chemotherapy was in 2010, and the first patient enrolled in neoadjuvant chemotherapy combined with PD-L1 was in 2017). After every two cycles of NT, lesions were reassessed by CT/PET-CT scans. The timing of surgery was determined by thoracic surgeons, which took place 3 to 4 weeks after the last NT. Lymph node (LN) dissection and video-assisted thoracoscopic surgery (VATS) could be performed during the operation.

Conditions for SL include: (I) patient tolerance of surgical resection as confirmed by cardiopulmonary function evaluation; (II) adequate space between the bronchial opening of the affected lung lobe and the carina for anastomosis; (III) R0 surgical margins. After resecting the afflicted lung lobe and a section of the damaged bronchus, the SL procedure (20) closes the bronchial stump through anastomosis. Open thoracotomy may be utilized instead of VATS in certain cases (*Video 1*). After confirming negative margins at the proximal and distal ends of the bronchus/pulmonary artery using intraoperative frozen section analysis, 3-0 and 5-0 Johnson & Johnson Prolene sutures, respectively, are utilized to sew the bronchial and pulmonary artery anastomoses. A water leak test is conducted post-anastomosis to ensure integrity, and systematic mediastinal or lobar LN dissection is performed. Two chest tubes are placed postoperatively to assist lung expansion and fluid drainage. Hematological tests are started on the day of surgery and repeated every three days. A chest X-ray is necessary on the first postoperative day and before removing the drainage tube to ensure proper lung re-expansion. In addition, a bronchoscopy is conducted on the first day after surgery to evaluate the healing of the anastomosis.

Surgical margins and postoperative pathological examinations are reviewed by two senior experts. All paraffin sections are stained with hematoxylin-eosin. Removing all tumor cells from a specimen is considered a pathologic complete response (PCR), while a major pathologic response (MPR) rate is achieved when there are 10% or less viable tumor cells observed in the postoperative pathology report (21).

Follow-up strategy, data collection, and statistical analysis

Overall survival (OS) is defined as the time from diagnosis to death or last follow-up. Disease-free survival (DFS) is defined as the time from diagnosis to recurrence or last follow-up. In terms of median dates of survival and no recurrence, respectively, we get median DFS time and median survival time. The median time between recurrences is used to determine the median follow-up time. Data were extracted independently by two researchers, with discrepancies resolved by a third. The hospital records were combed through for pertinent clinical data, which included demographics and cancer-related details. Regular examinations were planned for 1, 3, 6, and 12 months after surgery, and then semiannually until May 2024 as

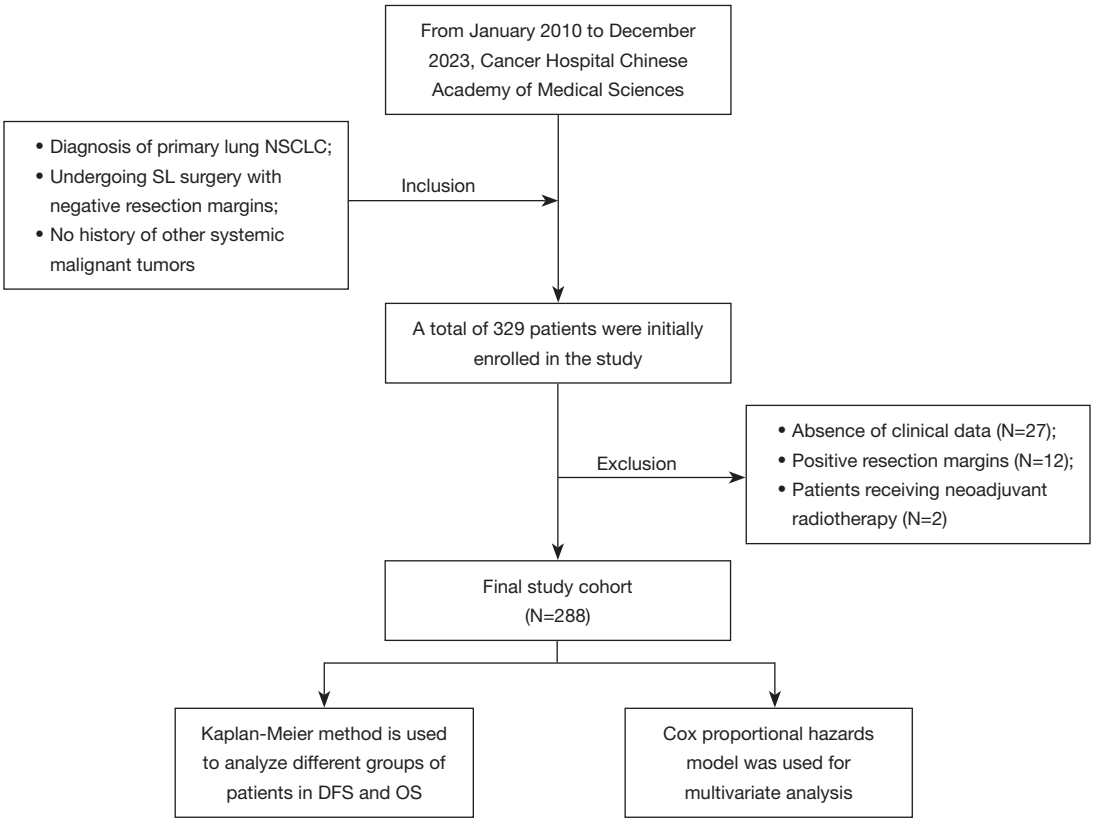


Figure 1 Study flowchart. NSCLC, non-small cell lung cancer; SL, sleeve lobectomy; DFS, disease-free survival; OS, overall survival.

part of the postoperative follow-up that included both in-person and phone appointments. Follow-up examinations included chest, abdominal, and cranial enhanced CT scans, abdominal ultrasound, and ultrasound of the neck and supraclavicular LNs. PET-CT was performed as required. Postoperative bronchoscopy was not used as a routine follow-up examination. If a patient presents with symptoms such as fever or chest tightness, a bronchopleural fistula is clinically considered, then a bronchoscopy is performed.

Subgroup cutoffs were established for some variables on the basis of previously recommended trial-group assignments. Group variables are typically represented as percentages. Continuous variables are typically reported as means ± standard deviations (SDs). We generated survival curves using the Kaplan-Meier method and compared them between treatment groups using a log-rank test. Hazard rate (HR) between groups were estimated using the Cox's proportional hazards model. After variables with a $P<0.05$ in univariate analysis, variables were analyzed using in multivariate analysis. The statistical analyses, unless specified differently, were all two-tailed and performed using SPSS version 27.0. Graphs were generated using GraphPad Prism version 9.0, unless indicated otherwise in the text.

Results

Patient information

Between January 2010 and December 2023, a total of 288 patients underwent SL, which involved the dissection of mediastinal LN. The flowchart of the study is shown in *Figure 1*. The cohort consisted of 263 male patients (91.3%). Among these, 232 patients (80.6%) were smokers, and 219 patients (76.0%) had right-sided tumors. Of the 85 patients (29.5%) who received NT before surgery, 42 patients received neoadjuvant chemotherapy and 43 patients received neoadjuvant chemotherapy and immunotherapy. Clinical stages I, II, and III were represented by 35.4%, 22.9%, and 41.7% of patients, respectively. In postoperative T staging, 233 patients (80.9%) were classified as T1–2, and 123 patients (42.7%) showed no LN metastasis

(N0). Pathological stages I, II, and III were reported for 27.8%, 43.1%, and 22.6% of patients, respectively. In the NT group, 19 patients (6.6% of the total) achieved a clinical stage of T0N0. Squamous cell carcinoma (SCC) was diagnosed in 226 cases (78.5%). On average, 5.92±1.37 LN stations were dissected, while the mean number of LNs dissected was 21.12±9.09. The surgeries performed consisted of open surgery (n=227, 78.8%) and VATS (n=61, 21.2%). The average postoperative length of stay (LOS) was 12.42±6.33 days, with an average duration of chest tube placement of 8.34±5.87 days. The average postoperative drainage volume was 1,814±1,181 mL (*Table 1*).

OS and DFS

Kaplan-Meier curve for subgroup analysis: the OS time for the patients was 57.64±36.84 months. As of May 2024, 171 patients (59.4%) were still alive, while 117 patients (40.6%) had died. A total of 135 patients (46.9%) were followed up for over 5 years, with a median follow-up time of 84.0 months. The average DFS time was 54.51±37.86 months. By May 2024, 91 patients had experienced local recurrence or distant metastasis, while 128 patients had not experienced recurrence within 5 years.

Prognostic factor analysis

Differences in OS [NT, HR =0.4652, 95% confidence interval (CI): 0.3042–0.7116, P=0.004, *Figure 2A*] and DFS (NT, HR =0.5182, 95% CI: 0.3243–0.8279, P=0.01, *Figure 2B*) were observed among patients receiving NT. Patients receiving NT exhibited improved 5-year OS (yes *vs.* no, 76.7% *vs.* 58.9%, *Table 2*) and 5-year DFS (yes *vs.* no, 78.3% *vs.* 64.2%, *Table 3*). OS and DFS in different clinical stage are shown (*Figure 3A-3F*), among them, only the DFS of different cT stages was different (P<0.001, *Figure 3D*), with lower stages associated with better DFS. The differences in OS and DFS among different pathological stages are shown in *Figure 4*. Differences in OS and DFS were also seen across different pT stages (OS: P=0.01, *Figure 4A*; DFS: P<0.001, *Figure 4D*), with lower stages indicating a better prognosis, especially T0N0 and pT1, which demonstrated superior 5-year OS (94.7% and 70.3%, *Table 2*) and 5-year DFS (66.7% and 77.2%, *Table 3*). Similarly, different pN stages showed prognostic variability in OS (P<0.001, *Figure 4B*) and DFS (P<0.001, *Figure 4E*), with lower stages yielding better outcomes, notably pN0 with enhanced 5-year OS (81.0%, *Table 2*) and 5-year DFS (88.0%, *Table 3*). Distinct disparities in OS and DFS were evident across different pathological Tumor-Node-Metastasis (pTNM) stages (OS: P<0.001, *Figure 4C*; DFS: P<0.001, *Figure 4F*), with stage I presenting the most favorable 1-, 3-, and 5-year OS (98.8%, 88.0%, and 82.2%, *Table 2* and *Figure 4C*) and DFS (97.5%, 94.7%, and 90.0%, *Table 3* and *Figure 4F*) rates. The differences in OS and DFS between different body mass index (BMI), pathological type, and tumor size are shown (*Figure 5*). There were differences in OS between different BMI subgroups (*Figure 5A*), with higher BMI having better OS. There were differences in DFS among different pathological types (*Figure 5E*), ADC is associated with poor DFS. Tumor size was correlated with OS (≤3 cm, HR =0.6756, 95% CI: 0.4695–0.9722, P=0.03, *Figure 5C*) and DFS (≤3 cm, HR =0.4974, 95% CI: 0.3298–0.7503, P=0.001, *Figure 5F*), with smaller tumors (≤3 cm) showing better 5-year OS (65.6%, *Table 2*) and 5-year DFS (75.9%, *Table 3*) outcomes. There were no notable variations in survival rates among different BMI and pathological types (P>0.05, *Figure 5B*,*5D*).

Survival analysis

Various clinical characteristics were used to conduct the Cox proportional hazards model study. The results of the univariate analysis showed that the following factors—tumor size, BMI, NT, pT, pN, and pTNM—influenced OS (*Table 2*). DFS was associated with BMI, NT, cT, pT, pN, pTNM, pathological type, and tumor size (*Table 3*).

Multivariate analysis demonstrated that BMI and receiving NT were significant factors affecting OS (*Table 4*, *Figure 6A*). BMI, receiving NT, cT, and pN were significant for DFS (*Table 4*, *Figure 6B*).

Discussion

For central NSCLC involving the trachea and/or artery, SL has been identified as safe and effective in certain patients, serving as a potential alternative to PN (22-24). SL preserves more lung function compared to PN and does not increase tumor recurrence (6,25), leading to its increasing use and development in thoracic surgery. Previous research has primarily compared PN and SL; however, prognostic analysis of SL subgroups remains scarce. In this retrospective analysis of 288 patients undergoing SL, the association between different subgroups and long-term prognosis was examined. It was found that NT could

Table 1 Baseline demographics of patients' basic characteristics

Factor	Total (N=288)
Age, years, mean ± SD	59.42±9.38
BMI, kg/m^2, mean ± SD	24.30±3.15
Sex, n (%)	
Male	263 (91.3)
Female	25 (8.7)
Smoking history, n (%)	
No	56 (19.4)
Yes	232 (80.6)
Tumor location, n (%)	
Left	69 (24.0)
Right	219 (76.0)
NT, n (%)	
No	203 (70.5)
NC	42 (14.6)
NC + Imo	43 (14.9)
cT stage, n (%)	
cT1	36 (12.5)
cT2	200 (69.4)
cT3	38 (13.2)
cT4	14 (4.9)
cN stage, n (%)	
cN0	137 (47.6)
cN1	43 (14.9)
cN2a	55 (19.1)
cN2b	53 (18.4)
cTNM stage, n (%)	
I	102 (35.4)
II	66 (22.9)
III	120 (41.7)
pT stage, n (%)	
pT1	116 (40.3)
pT2	117 (40.6)
pT3	25 (8.7)
pT4	11 (3.8)
T0N0	19 (6.6)
pN stage, n (%)	
0 (T0N0)	123 (42.7)
1	106 (36.8)
2a	38 (13.2)
2b	21 (7.3)
pTNM stage, n (%)	
I	80 (27.8)
II	124 (43.1)
III	65 (22.6)
T0N0	19 (6.6)
Pathological type, n (%)	
SCC	226 (78.5)
ADC	30 (10.4)
Other	32 (11.1)
Differentiated degree, n (%)	
Poorly	94 (32.6)
Moderately	152 (52.8)
High	20 (6.9)
Unknown	22 (7.6)
Operative approach	
Open	227 (78.8)
VATS	61 (21.2)
Pathological tumor size, cm, mean ± SD	3.14±1.68
LNs, n, mean ± SD	21.12±9.09
LN station, n, mean ± SD	5.92±1.37
LOS, d, mean ± SD	12.42±6.33
Drainage tube removal time, d, mean ± SD	8.34±5.87
Postoperative drainage volume, mL, mean ± SD	1,814±1,181
OS, m, mean ± SD	57.64±36.84
DFS, m, mean ± SD	54.51±37.86

SD, standard deviation; BMI, body mass index; NT, neoadjuvant therapy; NC, neoadjuvant chemotherapy; NC + Imo, neoadjuvant chemotherapy and immunotherapy; c, clinical; p, pathological; T, tumor; N, node; M, metastasis; SCC, squamous cell carcinoma; ADC, adenocarcinoma; VATS, video-assisted thoracoscopic surgery; LN, lymph node; LOS, length of hospital; d, days; m, months; OS, overall survival; DFS, disease-free survival.

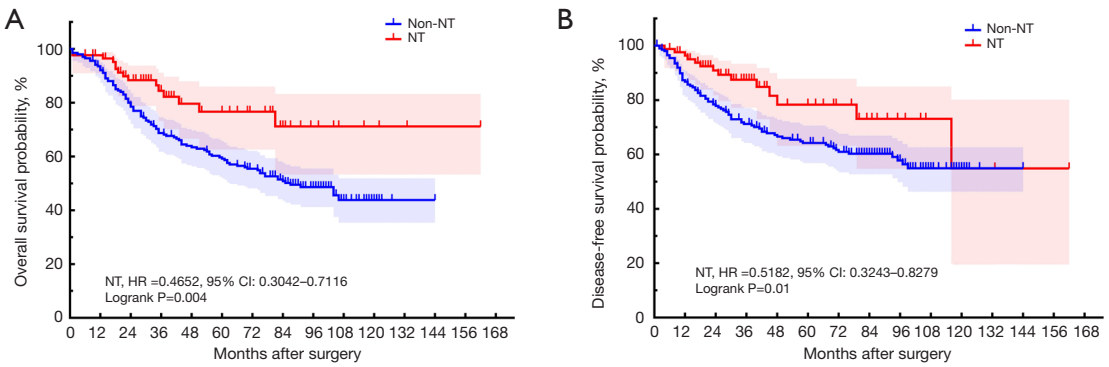


Figure 2 Kaplan-Meier survival curves. (A) OS among patients receiving NT and Non-NT. (B) DFS among patients receiving NT and non-NT. NT, neoadjuvant therapy; HR, hazard ratio; CI, confidence interval; OS, overall survival; DFS, disease-free survival.

Table 2 Univariate analysis for the prognosis of 288 patients of overall survival

Factor	Total (N=288), n (%)	OS rate, %			OS, HR (95% CI)	P
		1-year	3-year	5-year		
Age, years						0.55
<60	131 (45.5)	93.8	72.0	63.3	Reference	
≥60	157 (54.5)	94.2	72.9	62.8	1.116 (0.774–1.611)	
BMI, kg/m^2						0.007
<18.5	11 (3.8)	81.8	54.5	32.7	Reference	
≥18.5 to <25	161 (55.9)	95.0	67.8	58.5	0.478 (0.230–0.996)	0.049
≥25	116 (40.3)	93.9	80.8	72.2	0.318 (0.149–0.683)	0.003
Sex						0.16
Male	263 (91.3)	94.7	74.1	64.7	Reference	
Female	25 (8.7)	92.0	57.3	46.9	1.503 (0.843–2.679)	
Smoking history						0.62
No	56 (19.4)	87.5	68.1	55.3	Reference	
Yes	232 (80.6)	96.1	73.6	64.8	0.893 (0.566–1.409)	
Tumor location						0.21
Left	69 (24.0)	94.1	70.8	62.4	Reference	
Right	219 (76.0)	94.0	73.1	63.3	0.780 (0.525–1.159)	
NT						0.005
No	203 (70.5)	93.1	68.4	58.9	Reference	
Yes	85 (29.5)	97.6	84.4	76.7	0.454 (0.264–0.784)	
cT stage						0.10
cT1	36 (12.5)	91.7	69.9	66.4	Reference	
cT2	200 (69.4)	96.0	75.5	66.6	1.117 (0.608–2.052)	0.72
cT3	38 (13.2)	89.3	60.1	45.3	1.996 (0.975–4.087)	0.059
cT4	14 (4.9)	92.9	69.8	49.9	1.514 (0.595–3.848)	0.38

Table 2 (*continued*)

Table 2 (*continued*)

Factor	Total (N=288), n (%)	OS rate, %			OS, HR (95% CI)	P
		1-year	3-year	5-year		
cN stage						0.17
cN0	137 (47.6)	96.4	77.8	70.4	Reference	
cN1	43 (14.9)	88.4	60.7	54.3	1.500 (0.881–2.552)	0.13
cN2a	55 (19.1)	88.9	73.1	63.2	1.229 (0.741–2.037)	0.42
cN2b	53 (18.4)	96.3	68.4	52.1	1.632 (1.023–2.601)	0.40
cTNM stage						0.23
I	102 (35.4)	95.1	75.8	68.7	Reference	
II	66 (22.9)	92.4	70.6	68.5	0.885 (0.522–1.502)	0.65
III	120 (41.7)	92.4	71.0	55.6	1.297 (0.864–1.947)	0.20
pT stage						0.04
pT1	116 (40.3)	95.7	75.4	70.3	Reference	
pT2	117 (40.6)	92.2	72.0	59.5	1.456 (0.972–2.183)	0.06
pT3	25 (8.7)	92.0	53.7	48.3	1.861 (0.997–3.476)	0.051
pT4	11 (3.8)	81.8	61.4	30.3	2.217 (0.993–4.947)	0.05
T0N0	19 (6.6)	94.7	94.7	94.7	0.241 (0.033–1.756)	0.16
pN stage						<0.001
0 (T0N0)	123 (42.7)	97.6	87.6	81.0	Reference	
1	106 (36.8)	91.4	63.8	52.1	2.528 (1.604–3.983)	<0.001
2a	38 (13.2)	89.5	58.7	45.8	3.121 (1.792–5.436)	<0.001
2b	21 (7.3)	85.0	55.0	48.9	4.119 (2.175–7.802)	<0.001
pTNM stage						<0.001
I	80 (27.8)	98.8	88.0	82.2	Reference	
II	124 (43.1)	94.3	70.9	60.8	1.871 (1.134–3.087)	0.01
III	65 (22.6)	84.5	51.7	38.8	3.752 (2.240–6.284)	<0.001
T0N0	19 (6.6)	94.7	94.7	94.7	0.358 (0.048–2.667)	0.31
Pathological tumor size						0.048
≤3 cm	144 (50.0)	95.1	74.5	65.6	Reference	
>3 cm	144 (50.0)	91.6	70.7	57.1	1.449 (1.003–2.095)	
Pathological type						0.07
SCC	226 (78.5)	94.2	74.5	65.7	Reference	
ADC	30 (10.4)	90.0	60.7	43.6	1.815 (1.077–3.057)	0.02
Other	32 (11.1)	90.4	70.3	63.1	1.272 (0.734–2.205)	0.39
Differentiated degree						0.32
Poorly	94 (32.6)	90.4	67.2	58.9	Reference	
Moderately	152 (52.8)	95.4	74.7	64.6	0.750 (0.508–1.108)	0.14
High	20 (6.9)	95.0	78.5	63.4	0.590 (0.251–1.385)	0.22
Unknown	22 (7.6)	95.0	75.0	69.6	0.605 (0.273–1.344)	0.21

OS, overall survival; HR, hazard ratio; CI, confidence interval; BMI, body mass index; NT, neoadjuvant therapy; c, clinical; p, pathological; T, tumor; N, node; M, metastasis; SCC, squamous cell carcinoma; ADC, adenocarcinoma.

Table 3 Univariate analysis for the prognosis of 288 patients of disease-free survival

Factor	Total N=288, n (%)	DFS rate, %			DFS, HR (95% CI)	P
		1-year	3-year	5-year		
Age, years						0.64
<60	131 (45.5)	86.5	76.5	69.7	Reference	
≥60	157 (54.5)	92.1	75.0	66.9	1.102 (0.727–1.671)	
BMI, kg/m^2						0.006
<18.5	11 (3.8)	80.0	70.0	42.0	Reference	
≥18.5 to <25	161 (55.9)	89.1	70.5	63.1	0.532 (0.229–1.237)	0.14
≥25	116 (40.3)	92.9	83.2	77.3	0.325 (0.134–0.788)	0.01
Sex						0.40
Male	263 (91.3)	90.9	77.0	68.8	Reference	
Female	25 (8.7)	76.0	61.8	61.8	1.338 (0.672–2.667)	
Smoking history						0.63
No	56 (19.4)	85.1	73.9	61.7	Reference	
Yes	232 (80.6)	91.5	76.0	69.4	0.881 (0.526–1.476)	
Tumor location						0.87
Left	69 (24.0)	88.2	76.5	67.0	Reference	
Right	219 (76.0)	91.0	75.4	68.5	1.039 (0.642–1.680)	
NT						0.02
No	203 (70.5)	86.8	71.2	64.2	Reference	
Yes	85 (29.5)	96.3	87.5	78.3	0.513 (0.290–0.910)	
cT stage						0.002
cT1	36 (12.5)	88.2	81.8	73.6	Reference	
cT2	200 (69.4)	92.7	78.4	72.0	1.245 (0.594–2.610)	0.56
cT3	38 (13.2)	75.6	55.3	47.7	3.302 (1.416–7.241)	0.005
cT4	14 (4.9)	84.6	76.9	54.9	1.699 (0.555–5.200)	0.35
cN stage						0.06
cN0	137 (47.6)	92.4	80.7	73.6	Reference	
cN1	43 (14.9)	85.7	69.6	62.3	1.600 (0.871–2.939)	0.13
cN2a	55 (19.1)	88.4	75.9	67.8	1.375 (0.776–2.437)	0.27
cN2b	53 (18.4)	86.4	67.3	59.2	1.999 (1.185–3.373)	0.009
cTNM stage						0.06
I	102 (35.4)	93.9	82.4	74.4	Reference	
II	66 (22.9)	84.6	70.9	70.9	1.373 (0.758–2.485)	0.29
III	120 (41.7)	88.6	72.5	61.4	1.783 (1.090–2.916)	0.02

Table 3 (*continued*)

Table 3 (*continued*)

Factor	Total N=288, n (%)	DFS rate, %			DFS, HR (95% CI)	P
		1-year	3-year	5-year		
pT stage						0.001
pT1	116 (40.3)	95.6	80.7	77.2	Reference	
pT2	117 (40.6)	86.7	71.7	64.9	2.183 (1.337–3.563)	0.002
pT3	25 (8.7)	75.3	54.7	45.9	3.038 (1.517–6.028)	0.002
pT4	11 (3.8)	70.7	70.7	35.4	3.467 (1.416–8.491)	0.007
T0N0	19 (6.6)	100	100	66.7	0.363 (0.049–2.689)	0.32
pN stage						<0.001
0 (T0N0)	123 (42.7)	97.5	92.9	88.0	Reference	
1	106 (36.8)	88.2	65.2	57.1	4.070 (2.255–7.344)	<0.001
2a	38 (13.2)	80.6	65.7	54.3	4.422 (2.185–8.951)	<0.001
2b	21 (7.3)	65.8	44.5	33.4	11.505 (5.783–22.887)	<0.001
pTNM stage						<0.001
I	80 (27.8)	97.5	94.7	90.0	Reference	
II	124 (43.1)	90.9	70.8	66.3	4.279 (2.007–9.121)	<0.001
III	65 (22.6)	77.1	59.9	39.5	9.980 (4.660–21.378)	<0.001
T0N0	19 (6.6)	100	100	67.7	0.880 (0.109–7.067)	0.90
Pathological tumor size						0.002
≤3 cm	144 (50.0)	93.5	80.3	75.9	Reference	
>3 cm	144 (50.0)	85.6	71.0	60.9	2.011 (1.303–3.102)	
Pathological type						0.03
SCC	226 (78.5)	91.7	77.1	70.0	Reference	
ADC	30 (10.4)	75.9	59.6	49.1	2.059 (1.175–3.605)	0.01
Other	32 (11.1)	87.3	80.1	72.1	0.845 (0.406–1.761)	0.65
Differentiated degree						0.39
Poorly	94 (32.6)	87.7	71.7	66.7	Reference	
Moderately	152 (52.8)	88.5	75.4	66.5	0.937 (0.600–1.463)	0.77
High	20 (6.9)	95.0	85.0	77.3	0.538 (0.190–1.525)	0.24
Unknown	22 (7.6)	95.2	84.6	78.9	0.487 (0.172–1.380)	0.17

DFS, disease-free survival; HR, hazard ratio; CI, confidence interval; BMI, body mass index; NT, neoadjuvant therapy; c, clinical; p, pathological; T, tumor; N, node; M, metastasis; SCC, squamous cell carcinoma; ADC, adenocarcinoma.

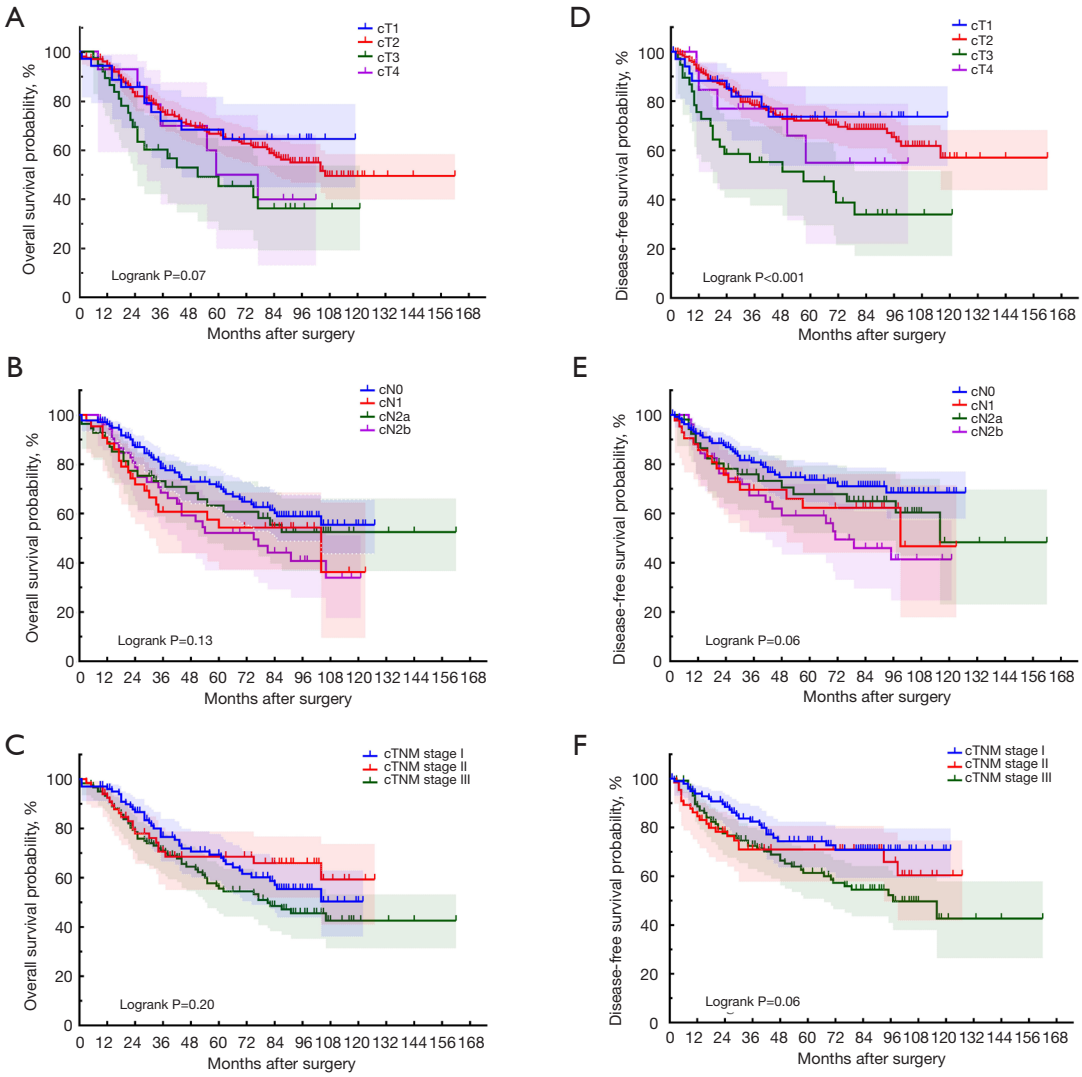


Figure 3 Kaplan-Meier survival curves. (A) OS between different clinical T stages subgroups. (B) OS between different clinical N stages subgroups. (C) OS between different clinical TNM stages subgroups. (D) DFS between different clinical T stages subgroups. (E) DFS between different clinical N stages subgroups. (F) DFS between different clinical TNM stage subgroups. TNM, Tumor-Node-Metastasis; OS, overall survival; DFS, disease-free survival.

enhance the prognosis of SL patients, and factors such as pathological staging and BMI were linked to patient prognosis. This study employs the 9th TNM staging system and is the greatest real-world, single-center investigation of SL subgroup prognosis that we are aware of.

In the past few decades of SL development, SL has exhibited higher rates of local recurrence compared to the PN group (26). Yildizeli *et al.* (27) reported that in patients undergoing SL, higher LN staging (N1–2) was identified as an independent risk factor for OS, while higher N staging (N2 *vs.* N0–1) and higher TNM staging (III *vs.* I–II) were associated with poorer DFS. Our subgroup analysis results align with prior studies, indicating that higher pathological staging correlates with poorer prognosis in SL patients, as determined through Cox univariate analysis, and pN is an independent factor influencing DFS. Finally, it was noted that patients with a N2b stage had a worse prognosis compared to those with a N2a stage, which provides more evidence that the 9th TNM staging system is suitable for SL patients. Deslauriers *et al.* (24) reported that compared to PN, SL enhanced OS in the patient population. Both SL and lobectomy preserve more normal

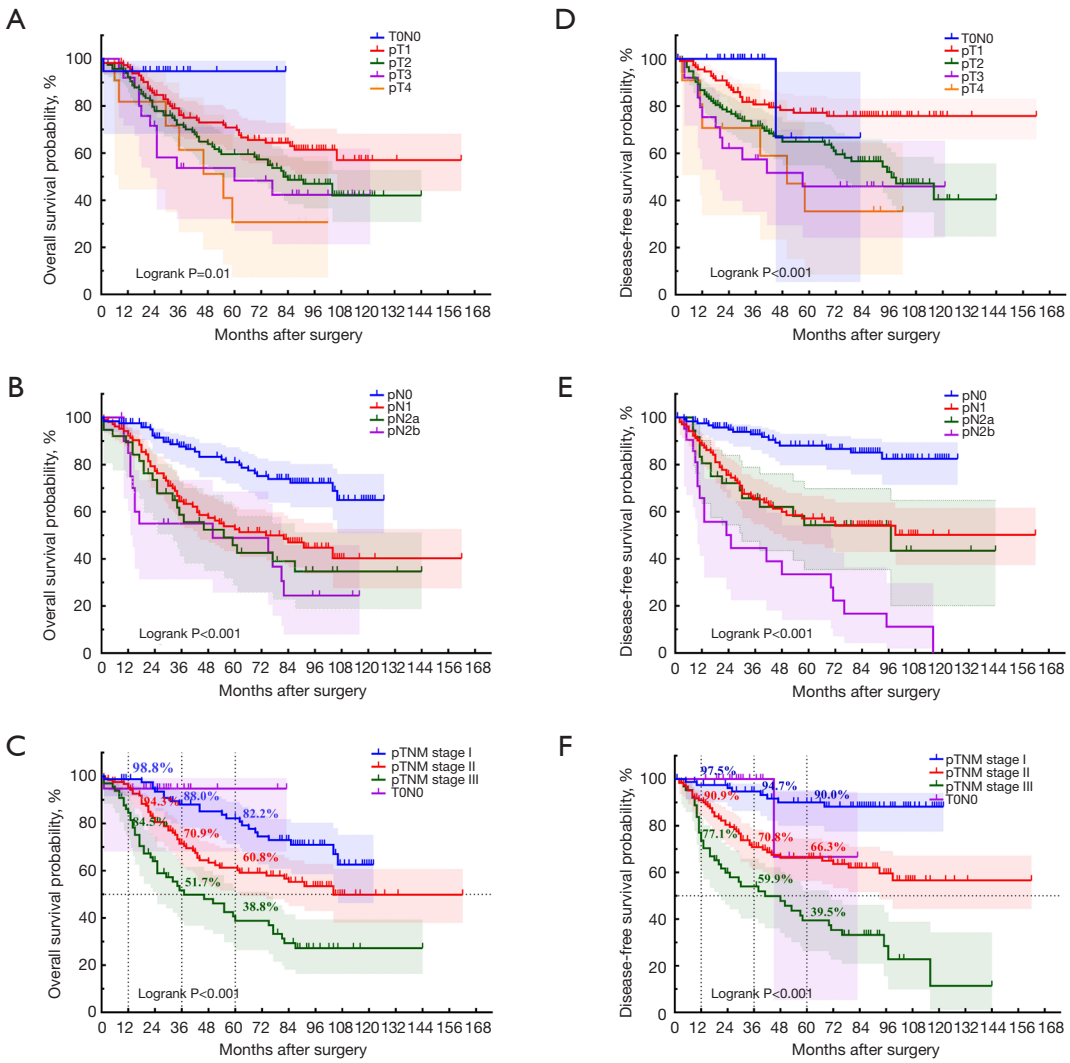


Figure 4 Kaplan-Meier survival curves. (A) OS between different pathological T stages subgroups. (B) OS between different clinical N stages subgroups. (C) OS between different pathological TNM stages subgroups. (D) DFS between different pathological T stages subgroups. (E) DFS between different pathological N stages subgroups. (F) DFS between different pathological TNM stage subgroups. TNM, Tumor-Node-Metastasis; OS, overall survival; DFS, disease-free survival.

lung tissue than pulmonary lobectomy, thereby improving postoperative quality of life with comparable 5-year OS rates (8). Literature reports suggest that post-SL 5-year OS rates vary between 52.0% and 56.6% (4,28-30). Our study revealed a 5-year survival rate of 63.1% in the SL patient cohort, indicating an improvement in survival rates relative to previous studies, potentially due to advances in treatment methods and the inclusion of neoadjuvant patients.

By blocking immune checkpoint pathways like programmed death-1 (PD-1)/PD-L1, tumors that are not surgically removed can avoid immune surveillance. Antibodies that block this pathway, such as PD-L1 inhibitors, represent a new strategy for improving the prognosis of resectable NSCLC patients. Central NSCLC patients undergoing SL after NT have demonstrated that SL is safe and feasible, does not increase tumor recurrence rates, and enhances long-term prognosis (18,31,32). Neoadjuvant combined immunotherapy has been linked to favorable outcomes in the SL cohort (33). Independently affecting factors, our study found that SL patients who received NT before surgery had better OS and DFS results (as shown by univariate Cox analysis). Although immune

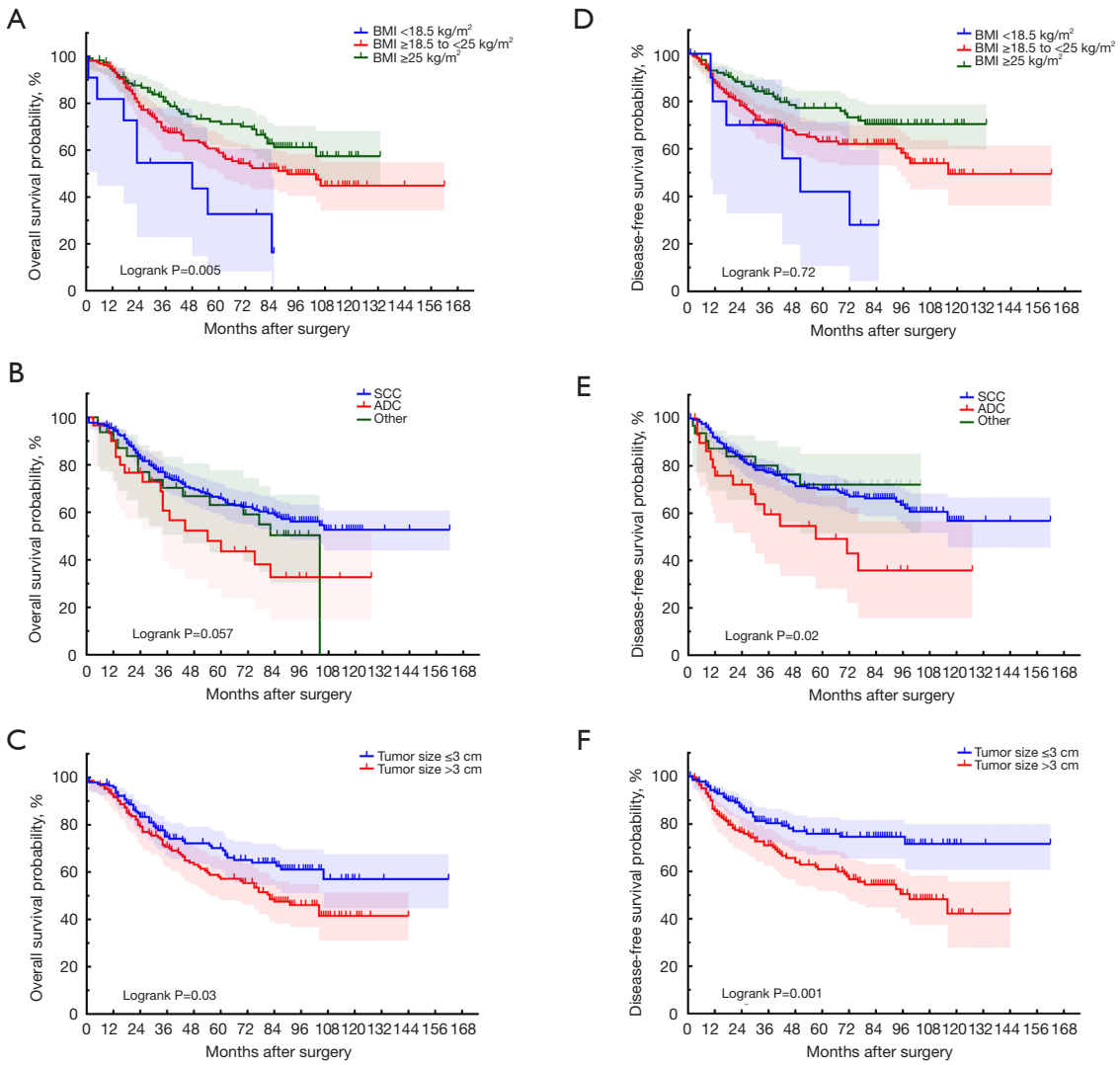


Figure 5 Kaplan-Meier survival curves. (A) OS between different BMI subgroups. (B) OS between different pathological pattern subgroups. (C) OS between tumor size ≤3 and >3 cm subgroups. (D) DFS between different BMI subgroups. (E) DFS between different pathological pattern subgroups. (F) DFS between tumor size ≤3 and >3 cm subgroups. BMI, body mass index; SCC, squamous cell carcinoma; ADC, adenocarcinoma; OS, overall survival; DFS, disease-free survival.

checkpoint inhibitors have shown efficacy in various cancer types, they have just recently been approved by the Food and Drug Administration (FDA) for treating NSCLC. Antibody therapy targeting PD-L1 prior to surgery has been proven to enhance long-term prognosis in operable stage III NSCLC patients (34,35), and can elevate survival rates in NSCLC patients. Results from CHEKMATE 159 were the first to demonstrate that preoperative treatment with nivolumab-based PD-L1 monotherapy was safe and feasible compared to surgery alone, and could increase the pathological response rate in resectable (36). The NADIM study confirmed the safety and efficacy of nivolumab-based NT for stage IIIA NSCLC, improving DFS and long-term prognosis (37). Subsequently, CHECKMATE 816 also confirmed that nivolumab-based PD-L1 monotherapy combined with platinum-based chemotherapy significantly enhanced the prognosis of resectable NSCLC patients at stages IB–IIIA (38). Recent studies have similarly demonstrated that immunotherapy combined with chemotherapy as NT followed by SL is safe and feasible,

Table 4 Multivariate cox analysis for the prognosis of 288 patients

Factor	OS		DFS	
	HR (95% CI)	P	HR (95% CI)	P
BMI, kg/m^2		0.01		0.006
<18.5	Reference		Reference	
≥18.5 to <25	0.486 (0.224–1.053)	0.06	0.645 (0.254–1.641)	0.35
≥25	0.321 (0.143–0.720)	0.006	0.307 (0.116–0.815)	0.01
NT		0.005		0.01
No	Reference		Reference	
Yes	0.428 (0.238–0.770)		0.444 (0.237–0.834)	
cT stage	–	–		0.03
cT1	–	–	Reference	
cT2	–	–	0.614 (0.261–1.445)	0.26
cT3	–	–	1.366 (0.511–3.652)	0.53
cT4	–	–	0.484 (0.103–2.276)	0.35
pN stage	–	–		0.02
0	–	–	Reference	
1	–	–	2.104 (0.849–5.212)	0.10
2a	–	–	2.965 (0.848–10.373)	0.08
2b	–	–	8.215 (1.959–34.438)	0.004

OS, overall survival; HR, hazard ratio; CI, confidence interval; DFS, disease-free survival; BMI, body mass index; NT, neoadjuvant therapy; c, clinical; p, pathological; T, tumor; N, node.

improving tumor pathological response and long-term survival (18,39). Similarly, our study found that NT with PD-L1 combined with platinum-based chemotherapy or chemotherapy alone in the SL cohort can improve OS and DFS in stages I–III NSCLC.

The relationship between BMI and survival rates in NSCLC is complex, as extreme body conditions may influence treatment efficacy and tolerability. Being underweight (BMI <18.5 kg/m^2) is associated with poorer outcomes (40), and within a limited range, higher BMI is linked to improved patient survival. Our research findings also indicate that a BMI <18.5 kg/m^2 correlates with poor OS and DFS in SL patients, representing a marker of poor prognosis in NSCLC mortality. Adenocarcinoma (ADC) and SCC differ significantly at the molecular, pathological, and clinical levels, necessitating distinct diagnostic, prognostic, and treatment approaches that lead to personalized treatment outcomes (41). Immune checkpoint inhibitors exhibit varying effects in ADC and SCC, while targeted therapies such as anti-vascular endothelial growth factor (VEGF) bevacizumab and epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) have been shown to enhance survival in lung ADC patients (42). Our study observed that SCC is a prevalent pathological type in central lung cancer, with no significant differences in OS between SCC, ADC, and other pathological types; however, ADC is linked to poorer DFS.

Several limitations should be acknowledged. First, the study's statistical power was low and selection bias could have been introduced due to the small sample size and retrospective nature. Second, the overall population undergoing SL was relatively small and included patients receiving NT, with some subgroups not reaching median survival times. Third, lung cancer's invasion of the bronchus can lead to obstructive pneumonia, thus impacting clinical tumor staging. Consequently, there are likely discrepancies between clinical and pathological staging. The study provided a comprehensive description of accurate pathological staging.

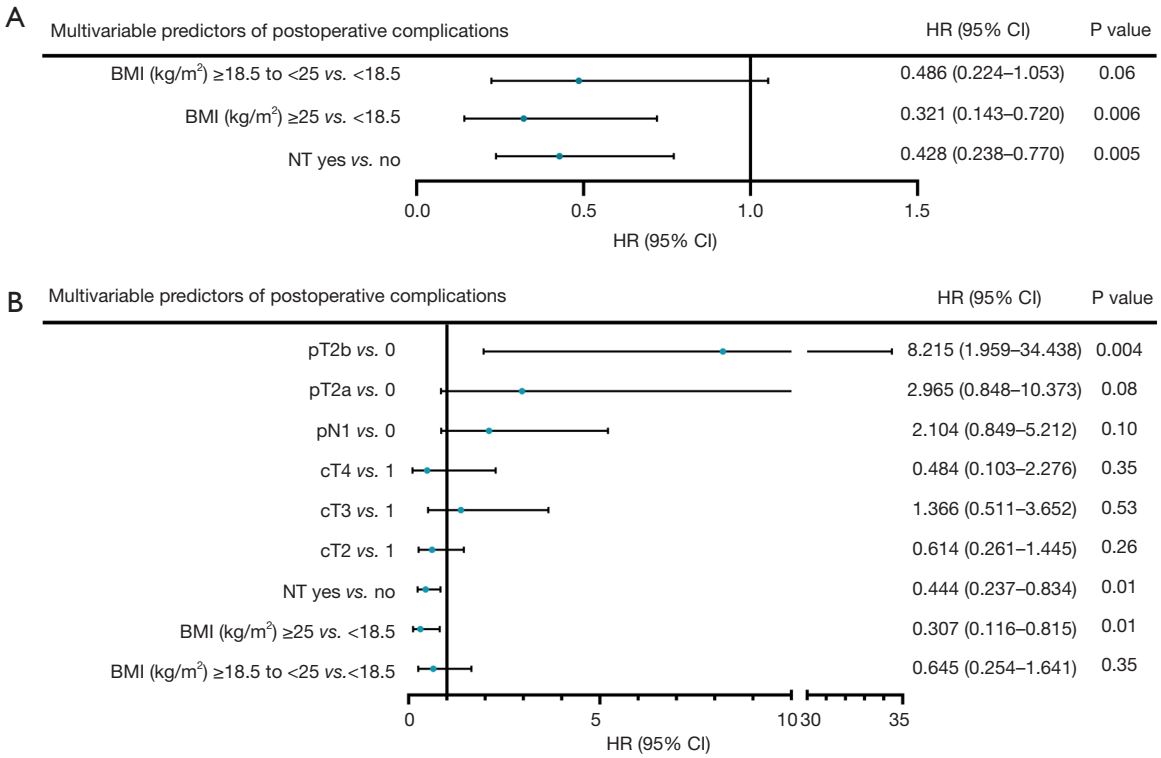


Figure 6 COX multivariate regression analysis. (A) Multivariate regression analysis of variables affecting OS in the total population. (B) Multivariate regression analysis of variables affecting DFS in the total population. HR, hazard ratio; CI, confidence interval; BMI, body mass index; NT, neoadjuvant therapy; OS, overall survival; DFS, disease-free survival.

Conclusions

In summary, the findings of this study indicate that postoperative pathological staging according to the 9th edition is more predictive of SL patient prognosis than clinical staging. It is worth noting that the prognosis of SL patients in the study cohort was greatly improved by NT, highlighting the significance of taking into account BMI and LN dissection.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-685/rc

Data Sharing Statement: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-685/dss

Peer Review File: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-685/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-685/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Medical Ethics Committee of National Cancer Center/National

Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (No. 24/340-4620) and individual consent for this retrospective analysis was waived.

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