



OPEN Choice of wedge resection for selected T1a/bN0M0 non-small cell lung cancer

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Recently, several studies have reported that the survival benefit of wedge resection might not be inferior to that of lobectomy in early-stage NSCLC patients, but there is no unified definition of the details or cutoff value. Patients with early-stage NSCLC with a tumour size ≤ 2.0 cm were chosen from the SEER database. The influence of confounding factors was minimized by 1:1 propensity score matching (PSM). Kaplan–Meier curves and Cox proportional hazards models were used to evaluate the overall survival (OS) and lung cancer-specific survival (LCSS) of patients undergoing lobectomy and wedge resection. A total of 3891 patients with early-stage NSCLC with tumour size ≤ 2.0 cm were enrolled, of whom 2839 underwent lobectomy and 1052 underwent wedge resection. Both before and after PSM, lobectomy significantly improved OS and LCSS compared with wedge resection in the unstratified study population. In the tumour size ≤ 1 cm group, lobectomy had better OS and LCSS than wedge resection ($P < 0.05$) before PSM; after PSM, there was no significant difference in OS ($P = 0.16$) and LCSS ($P = 0.17$). In Grade I patients, before PSM, lobectomy was superior to wedge resection in LCSS ($P = 0.038$), while there was no significant difference in OS ($P = 0.16$); after PSM, there were no significant differences in either OS ($P = 0.78$) or LCSS ($P = 0.11$). For early-stage NSCLC patients with a tumour size ≤ 1 cm or with a tumour size ≤ 2 cm and with Grade I, there was no significant difference in survival between wedge resection and lobectomy.

Keywords Lobectomy, Wedge resection, Non-small cell lung cancer, Overall survival, Lung cancer specific survival

Lung cancer is the leading cause of cancer death and the second most common cancer in the world¹. Non-small cell lung cancer (NSCLC) is the main type of lung cancer, accounting for 85% of all lung cancers², and the 5-year survival rate is less than 30%³. Radical surgical resection is the first choice for early NSCLC⁴. Surgical methods for early NSCLC include lobectomy, segmentectomy and wedge resection⁵. The latter two were collectively referred to as sublobar resection⁶. Among sublobar resections, wedge resection is more common in clinical practice due to the difficulty of segmentectomy⁷.

Nearly 3 decades ago, the Lung Cancer Study Group reported a prospective randomized controlled trial (LC5G821) in which lobectomy was the best option for the treatment of patients with early-stage NSCLC⁸. However, with the widespread use of high-resolution computed tomography (HRCT) and lung cancer screening programs, which have made it common to detect lesions of NSCLC of a small size at an early stage^{9–11}, lobectomy seems to be overtreatment⁶. In several studies, scholars have reported that in patients with lung cancer with a maximum tumour diameter of 2.0 cm or less and a proportion of consolidation tumours, the survival of patients who undergo sublobar resection does not lead to a poor prognosis and preserves more lung function without serious complications^{12–14}. Wedge resection has the advantages of easy operation, short operation time, less trauma and low incidence of postoperative complications^{15,16} and is more common than segmentectomy in clinical practice. Hence, we tried to explore the role of wedge resection in early-stage NSCLC.

Generally, the choice of surgical approach for NSCLC patients with a tumour size of 2 cm or less remains controversial in clinical practice. This study compared the survival benefits of lobectomy and wedge resection in early-stage NSCLC patients with a tumour size ≤ 2.0 cm, providing a basis for the selection of surgical methods for early-stage NSCLC patients.

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Result

Baseline characteristics of the study population

A total of 3891 patients were enrolled in the study, of whom 2839 underwent lobectomy and 1052 underwent wedge resection. Given that the age data from the SEER database were a continuous variable, we used X-tile software to determine the best cutoff ages of 61 years and 78 years in our study population to facilitate grouping and processing (Supplementary Fig. 1). Most patients were characterized as follows: 62–78 years old (60.4%), female (60.7%), married (57.8%), primary site in the upper lobe (61.4%), right side (60.2%), pathologically confirmed adenocarcinoma (69.9%), Grade II (44.7%), and tumour size 1–2 cm (81.6%). The lobectomy group differed from the wedge resection group in terms of age, laterality, histological type, grade and tumour size. Wedge resection was used more often than lobectomy in the population of patients aged >78 years or with tumours less than or equal to 1 cm. After PSM, the χ^2 test did not show any significant difference between the two groups, which was balanced and comparable (Table 1).

Survival analysis of the total population

The Kaplan–Meier method was used to plot survival curves for NSCLC patients with tumour size ≤ 2 cm. Before PSM, lobectomy had superior OS ($p < 0.0001$) and LCSS ($p < 0.0001$) compared to wedge resection (Fig. 1a and b). After PSM, we observed the same results (Fig. 1c and d). When univariate Cox regression analysis was performed in the total population, age, sex, marital status, histologic type, grade, tumour size, and surgery were all significantly correlated with the OS and LCSS of patients. In the subsequent multivariate Cox regression analysis, all of these factors were confirmed to be independent risk factors. For patients with NSCLC within 2 cm, wedge resection was an independent risk factor for OS (HR, 1.690; 95% CI, 1.499–1.905; $P < 0.001$) and LCSS (HR, 1.806; 95% CI, 1.502–2.172; $P < 0.001$) (Table 2).

Variable	Before PSM				After PSM			
	Lobectomy N = 2839(%)	Wedge resection N = 1052(%)	P	SMD	Lobectomy N = 1005(%)	Wedge resection N = 1005(%)	P	SMD
Age			<0.001	0.306			0.947	0.015
< 62	897 (31.6)	226 (21.5)			217 (21.6)	222 (22.1)		
62–78	1700 (59.9)	651 (61.9)			640 (63.7)	633 (63.0)		
> 78	242 (8.5)	175 (16.6)			148 (14.7)	150 (14.9)		
Sex			1	<0.001			0.891	0.008
Female	1724 (60.7)	639 (60.7)			609 (60.6)	605 (60.2)		
Male	1115 (39.3)	413 (39.3)			396 (39.4)	400 (39.8)		
Marital status			1	0.001			0.964	0.004
Married	1642 (57.8)	608 (57.8)			593 (59.0)	591 (58.8)		
Not-married	1197 (42.2)	444 (42.2)			412 (41.0)	414 (41.2)		
Primary site			0.505	0.043			0.932	0.017
Upper lobe	1742 (61.4)	649 (61.7)			621 (61.8)	613 (61.0)		
Middle lobe	188 (6.6)	59 (5.6)			55 (5.5)	57 (5.7)		
Lower lobe	909 (32.0)	344 (32.7)			329 (32.7)	335 (33.3)		
Laterality			0.001	0.124			0.822	0.012
Left	1082 (38.1)	465 (44.2)			430 (42.8)	436 (43.4)		
Right	1757 (61.9)	587 (55.8)			575 (57.2)	569 (56.6)		
Histologic type			<0.001	0.202			0.916	0.019
LUAD	2054 (72.3)	664 (63.1)			649 (64.6)	650 (64.7)		
LUSC	493 (17.4)	231 (22.0)			222 (22.1)	216 (21.5)		
Others	292 (10.3)	157 (14.9)			134 (13.3)	139 (13.8)		
Grade			0.004	0.131			0.375	0.079
I	919 (32.4)	373 (35.5)			355 (35.3)	356 (35.4)		
II	1318 (46.4)	421 (40.0)			414 (41.2)	414 (41.2)		
III	580 (20.4)	249 (23.7)			233 (23.2)	226 (22.5)		
IV	22 (0.8)	9 (0.9)			3 (0.3)	9 (0.9)		
Tumour size			<0.001	0.319			1	<0.001
≤ 1 cm	424 (14.9)	293 (27.9)			258 (25.7)	258 (25.7)		
1–2 cm	2415 (85.1)	759 (72.1)			747 (74.3)	747 (74.3)		

Table 1. Baseline demographic characteristics of patients with T1a/b N0M0 non-small cell lung cancer ($n = 3891$).

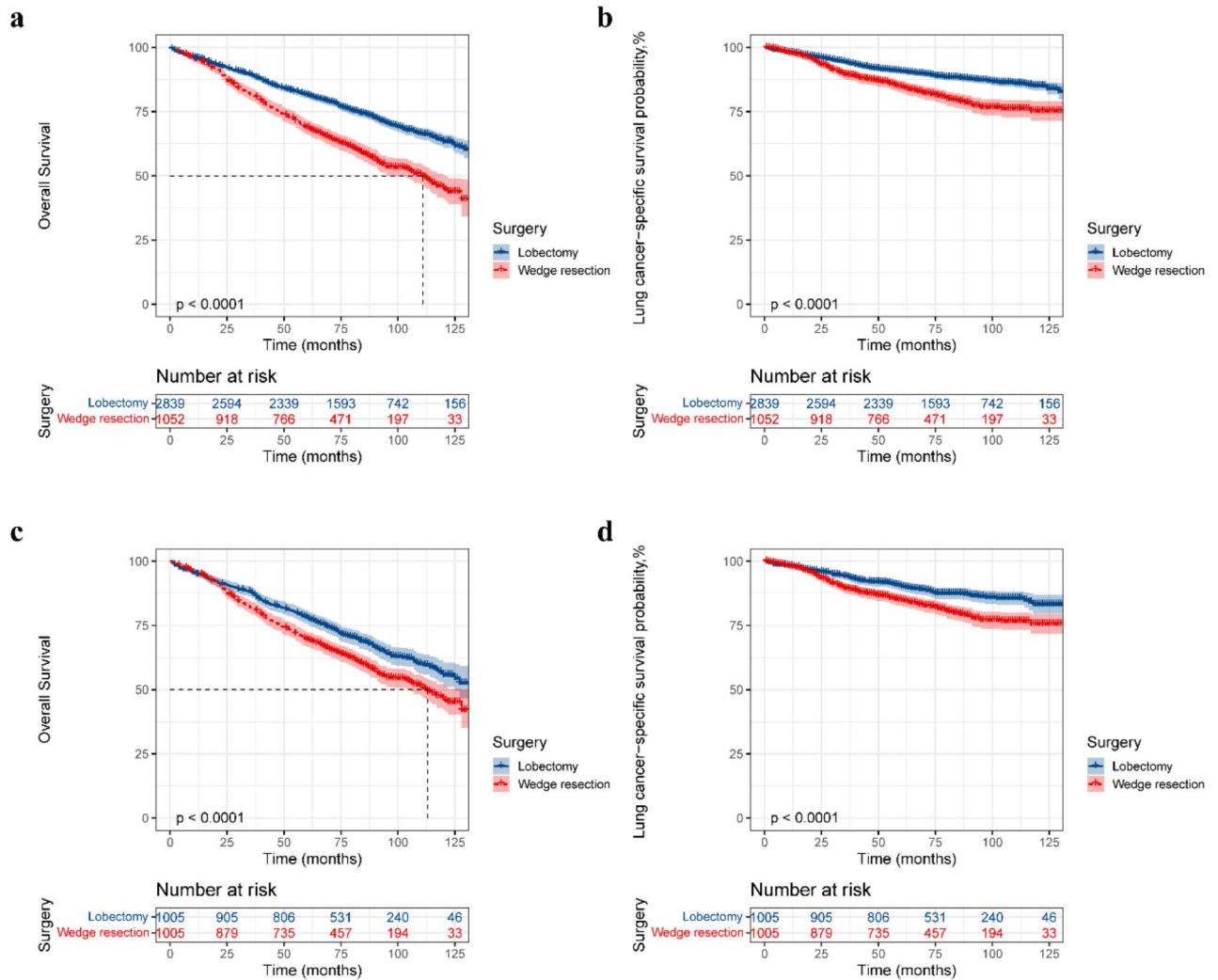


Fig. 1. Kaplan-Meier survival curve of overall patients (a) Before PSM, overall survival; (b) Before PSM, lung cancer-specific survival; (c) After PSM, overall survival; (d) After PSM, lung cancer-specific survival.

Subgroup analysis of people with tumour size ≤ 1 cm and better-differentiated tumours (Grade I)

To further investigate the impact of the surgical approach on survival in smaller, well-differentiated tumours, patients with a tumour size ≤ 1 cm and those with Grade I tumour differentiation were selected for subgroup analysis. Baseline characteristics of patients with tumour size ≤ 1 cm and Grade I patients are demonstrated in Supplementary Tables 1 and 2, and the lobectomy and wedge resection groups after PSM were balanced and comparable. Survival curve results suggested that OS ($P=0.001$) and LCSS ($P=0.015$) were better with lobectomy than wedge resection before PSM in those with tumour size ≤ 1 cm (Fig. 2a and b), while no significant OS ($P=0.16$) and LCSS ($P=0.17$) were seen between lobectomy and wedge resection after PSM differences (Fig. 2c and d). In Grade I patients, prior to PSM, lobectomy was superior to wedge resection in terms of LCSS ($P=0.038$), while no significant difference was seen in OS ($P=0.16$) (Fig. 3a and b). After PSM, no significant difference in OS ($P=0.78$) or LCSS ($P=0.11$) was observed between lobectomy and wedge resection (Fig. 3c and d). Further calculation of adjusted risk ratios (AHR) for different surgical modalities in the subgroups based on multivariate Cox analysis also showed that OS and LCSS in the wedge resection group were worse than those in the lobectomy group before PSM, but there was no significant difference in the impact on survival between the two groups after PSM (Table 3).

Discussion

In 1995, the GCSG821 trial provided strong evidence that lobectomy was the gold standard for early-stage lung cancer⁸, but recently, the best surgical approach for lung cancer has become controversial due to advances in diagnostic techniques following with the increasing number of smaller pulmonary nodules being detected^{9–11}. Although in many studies the survival of early NSCLC patients treated with wedge resection is slightly inferior to that of those treated with segmentectomy and lobectomy, the 5-year survival rate of early NSCLC patients

Variable	OS				LCSS			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
<i>Age</i>								
< 62	Reference		Reference		Reference		Reference	
62–78	2.054(1.762, 2.395)	<0.001	1.860(1.593, 2.172)	<0.001	1.622(1.298, 2.026)	<0.001	1.482(1.183, 1.856)	<0.001
> 78	4.035(3.346, 4.866)	<0.001	3.288(2.713, 3.984)	<0.001	3.080(2.328, 4.075)	<0.001	2.528(1.896, 3.370)	<0.001
<i>Sex</i>								
Female	Reference		Reference		Reference		Reference	
Male	1.638(1.466, 1.831)	<0.001	1.667(1.484, 1.873)	<0.001	1.757(1.479, 2.087)	<0.001	1.774(1.482, 2.122)	<0.001
<i>Marital status</i>								
Married	Reference		Reference		Reference		Reference	
Not-married	1.424(1.274, 1.592)	<0.001	1.433(1.276, 1.609)	<0.001	1.414(1.191, 1.680)	<0.001	1.444(1.207, 1.727)	<0.001
<i>Primary site</i>								
Lower lobe	Reference		Reference		Reference		Reference	
Middle lobe	0.786(0.601, 1.028)	0.078	0.919(0.697, 1.210)	0.546	0.753(0.494, 1.148)	0.187	0.870(0.565, 1.339)	0.527
Upper lobe	1.140(1.009, 1.289)	0.036	1.026(0.907, 1.161)	0.682	1.112(0.921, 1.342)	0.271	0.965(0.797, 1.167)	0.710
<i>Laterality</i>								
Left	Reference		Reference		Reference		Reference	
Right	0.924(0.825, 1.035)	0.171	0.979(0.872, 1.100)	0.724	0.964(0.809, 1.149)	0.682	1.014(0.846, 1.214)	0.884
<i>Histologic type</i>								
LUAD	Reference		Reference		Reference		Reference	
LUSC	1.911(1.683, 2.169)	<0.001	1.191(1.041, 1.363)	0.011	1.479(1.203, 1.817)	<0.001	0.848(0.683, 1.052)	0.134
Others	0.890(0.732, 1.083)	0.245	0.940(0.768, 1.150)	0.546	0.796(0.585, 1.082)	0.146	0.807(0.588, 1.107)	0.184
<i>Grade</i>								
I	Reference		Reference		Reference		Reference	
II	2.127(1.834, 2.467)	<0.001	1.920(1.646, 2.239)	<0.001	2.538(1.980, 3.253)	<0.001	2.413(1.871, 3.112)	<0.001
III	2.878(2.449, 3.382)	<0.001	2.326(1.959, 2.761)	<0.001	3.963(3.053, 5.143)	<0.001	3.589(2.732, 4.716)	<0.001
IV	2.409(1.379, 4.209)	0.002	2.133(1.209, 3.764)	0.009	3.291(1.437, 7.537)	0.005	3.061(1.314, 7.129)	0.009
<i>Tumour size</i>								
≤ 1 cm	Reference		Reference		Reference		Reference	
1–2 cm	1.316(1.127, 1.537)	<0.001	1.252(1.069, 1.466)	0.005	1.637(1.263, 2.123)	<0.001	1.541(1.183, 2.006)	0.001
<i>Surgery</i>								
Lobectomy	Reference		Reference		Reference		Reference	
Wedge resection	1.752(1.560, 1.967)	<0.001	1.690(1.499, 1.905)	<0.001	1.769(1.480, 2.114)	<0.001	1.806(1.502, 2.172)	<0.001

Table 2. OS and LCSS in univariate and multivariate analyses.

treated with wedge resection can reach more than 80% in lung cancer with diameter within 2 cm¹⁷ and up to 95% in lung cancer with diameter within 1 cm¹⁸. Wedge resection is the first choice for adenocarcinoma in situ and minimally invasive adenocarcinoma¹⁹. Recently, several studies have suggested that the survival benefit of wedge resection might not be inferior to that of lobectomy in early-stage NSCLC patients with unique features, such as smaller tumour size and consolidation tumour ratio^{12,13,18,20}. In our study, for early-stage NSCLC patients with a tumour size ≤ 2 cm, wedge resection had the poorer OS and LCSS than lobectomy, whereas for early-stage NSCLC patients with a tumour size ≤ 1 cm or with a tumour size ≤ 2 cm and with Grade I, wedge resection was noninferior to lobectomy in OS and LCSS.

Many studies have evaluated the survival difference between lobectomy and sublobar resection in NSCLC patients with tumours of 2 cm or less in diameter, and lobectomy has been found to be superior to sublobar resection^{21–24}. There are also studies that directly compared the survival difference between wedge resection and lobectomy for NSCLC lesions measuring less than 2 cm and concluded that lobectomy is superior to wedge resection^{7,20,21}. This is consistent with our conclusions obtained when comparing survival between wedge resection and lobectomy in the total study population of tumours measuring 2 cm or less. However, several studies have suggested that tumour size and the consolidation tumour ratio (CTR) are significantly related to the prognosis of early lung cancer^{25–27}. With the increase in tumour size and CTR, tumour aggressiveness and malignancy increase^{28–30}, and smaller tumour size and CTR may indicate suitability for limited resection. A prospective randomized controlled trial (CALGB140503) reported that for NSCLC lesions measuring less than or equal to 2 cm, sublobar resection offers a similar survival to lobectomy and is more conducive to preservation of lung function¹². The JCOG0804 trial reported that in patients with peripheral lung cancer with a maximum tumour diameter of 2.0 cm or less and a proportion of consolidation tumours of 0.25 or less detected by high-resolution CT, the 5-year recurrence-free survival rate of patients who underwent sublobar resection was up

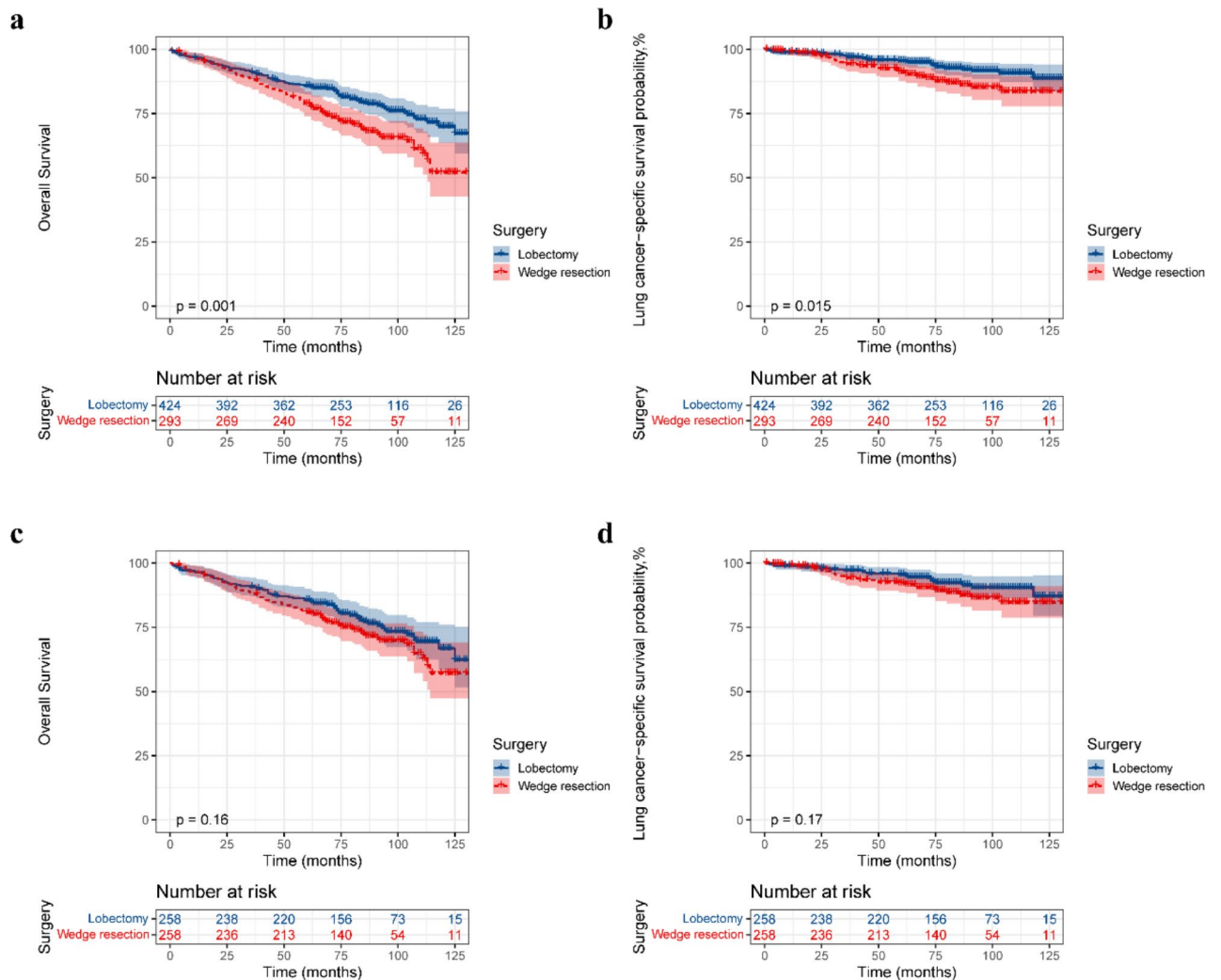


Fig. 2. Kaplan-Meier survival curves for patients with Tumour size ≤ 1 cm (a) Before PSM, overall survival; (b) Before PSM, lung cancer-specific survival; (c) After PSM, overall survival; (d) After PSM, lung cancer-specific survival.

to 99.7% with no serious complications¹³. JCOG0802 reported that for patients with NSCLC smaller than 2 cm, segmentectomy had superior overall survival compared to lobectomy¹⁴. Inspired by the relatively good prognosis of early-stage NSCLC patients with tumour size ≤ 2 cm and with small CTR treated with sublobar resection, we considered a common logic: smaller tumours were treated adequately with limited resections²¹. Wedge resection has the advantages of easy operation, short operation time, less invasiveness to damage chest wall anatomy and low incidence of postoperative complications^{15,16} and is more common than segmentectomy in clinical practice. Hence, we tried to explore the role of wedge resection in early stage NSCLC with tumours of 1 cm or less in diameter. The results suggest that the survival of early NSCLC patients treated with wedge resection is not inferior to that of patients treated with lobectomy in tumours ≤ 1 cm. Zhou's¹⁸ and Hu's²⁰ studies were consistent with our results. However, a study based on the SEER database concluded that the survival benefit of wedge resection was significantly inferior to that of lobectomy in patients with either 0–1 cm or 1–2 cm NSCLC lesions, and wedge resection should be recommended only in patients with no other choice²¹. However, in their study, the baseline of patients between the wedge resection group and lobectomy group was not completely balanced²¹. The choice of surgical method for early-stage NSCLC is also closely related to the primary tumour location. Lobectomy is widely used for early-stage NSCLC, whereas wedge resection is more likely to be reserved for patients with peripheral lung cancer (located in the outer third of the lung parenchyma) without evidence of metastasis³¹. Although there may be inevitable selection bias due to the different primary tumour site, both wedge resection and lobectomy aim to ensure adequate surgical margins³¹. In addition, the treatment of lymph nodes in the two surgical methods is often different, which also has an impact on survival. A high proportion of patients who undergo wedge resection do not receive combined lymph node treatment^{32,33}. Even if a patient underwent lymph node biopsy, lymph node dissection of the remaining lobes could not be performed³⁴. These may account for the high local recurrence rate of wedge resection³⁴. Lobectomy is often combined with mediastinal lymph node dissection on the basis of anatomical resection³¹. Systematic lymph

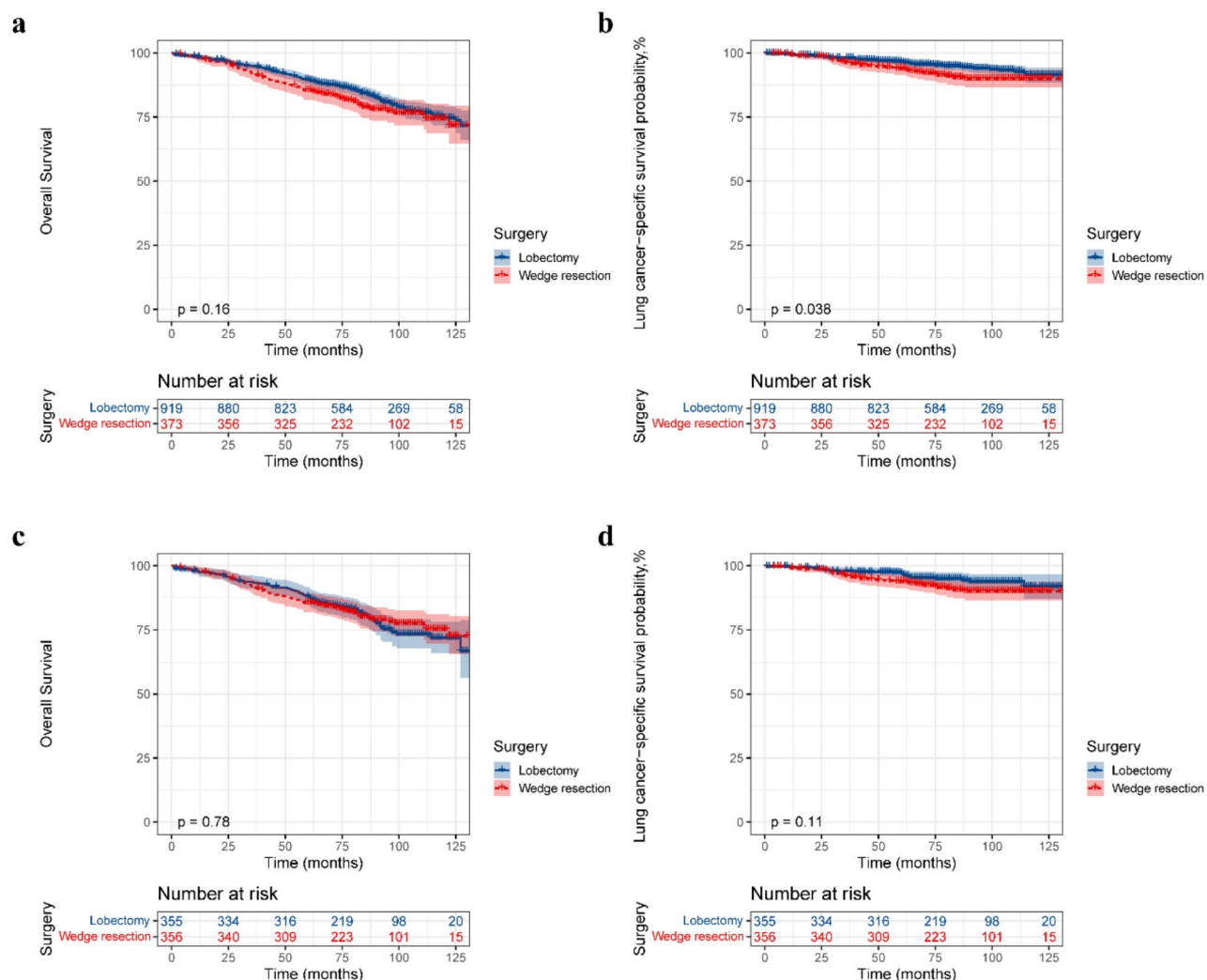


Fig. 3. Kaplan-Meier survival curves for patients with Grade I (a) Before PSM, overall survival; (b) Before PSM, lung cancer-specific survival; (c) After PSM, overall survival; (d) After PSM, lung cancer-specific survival.

Variables	Before PSM		After PSM	
	Wedge resection vs. Lobectomy		Wedge resection vs. Lobectomy	
	AHR (95% CI)	P	AHR (95% CI)	P
<i>Tumour size ≤ 1 cm</i>				
OS	1.535(1.146, 2.056)	0.004	1.394(0.990, 1.963)	0.057
LCSS	1.787(1.087, 2.938)	0.022	1.619(0.904, 2.901)	0.105
<i>Grade I</i>				
OS	1.203(0.913, 1.585)	0.189	0.943(0.683, 1.302)	0.723
LCSS	1.729(1.094, 2.733)	0.019	1.565(0.877, 2.793)	0.129

Table 3. Adjusted hazard ratios for OS and LCSS in patients with tumour size ≤ 1 cm and Grade I.

node dissection can reduce the risk of death in patients with clinical N0 disease³⁵. Studies have shown that sublobar resection increases the risk of undetected lymph node disease in patients with 1.5–2.0 cm NSCLC³⁶, and increasing the number of lymph nodes sampled reduces the survival difference between lobectomy and wedge resection^{7,37}. These may explain why our results suggest that wedge resection is not an alternative to lobectomy in the total population, but early-stage NSCLC patients with a tumour size ≤ 1 cm or with a tumour

size ≤ 2 cm and with Grade I. It may be due to lower positive N disease in early-stage NSCLC patients with a tumour size ≤ 1 cm or with a tumour size ≤ 2 cm and with Grade I.

Histologic grade is also an important factor in prognosis, with more poorly differentiated tumours possessing a worse prognosis and a more pronounced tendency to metastasize^{38,39}. It has been reported that the efficacy of wedge resection in the treatment of early-stage NSCLC is largely attributable to the histological grade of the tumour⁴⁰. In addition, one study found that both the potential for elevated tumour stage and elevated risk of recurrence in early-stage lung cancer were strongly associated with poorer tumour differentiation⁴¹. In patients with clinical Stage I NSCLC who underwent anatomical pneumonectomy, grade was identified as an independent predictor of recurrence, and high grade was closely related to a high risk of recurrence⁴². Moreover, Grade I was shown to be associated with better OS and LCSS than other high grades in NSCLC ≤ 1 cm^{43,44}. In this study, we compared the survival benefits of lobectomy and wedge resection in early-stage NSCLC patients with a tumour size ≤ 2 cm and with Grade I. To our knowledge, we have reported for the first time that wedge resection might be the first choice for early-stage Grade I NSCLC patients with a tumour size ≤ 2 cm.

We must acknowledge and accept the limitations of our study. First, potential selection bias cannot be excluded due to its retrospective nature, but we used propensity score matching to balance the differences between groups and minimize the impact of bias. Second, the SEER database does not have a clear definition of the location of the primary tumour, and we could not determine whether the tumour was peripheral or hilar, but even the mixed data suggested that wedge resection was feasible for patients with NSCLC lesions that are less than 1 cm in diameter. It can be speculated that for peripheral lung cancer, this result will be more credible, and the choice of wedge resection will be more certain. Third, the seer database did not have important information on comorbidities, pulmonary function or surgical indications, and we were unable to perform further analyses. However, our study endpoints included OS and LCSS, which potentially evaluated these indicators to some extent. We do not have intuitive data to reflect the patient's own pulmonary function, comorbidities or other factors on the choice of surgical methods. And we know patients who choose wedge resection tend to be elderly patients with worse cardiopulmonary function or patients in clinic practice. However, wedge resection can still result in approximately the same prognosis as lobectomy in our study. Therefore, we concluded that wedge resection can be used as an alternative to lobectomy in patients with T1aN0M0 or well-differentiated T1bN0M0 NSCLC. Finally, there is no information on adjuvant therapy other than radiotherapy and chemotherapy in the SEER database. Although we tried to avoid the impact of radiotherapy and chemotherapy on patient survival, it is unclear whether targeted therapy or immunotherapy should be administered before and after surgery, which may affect the results, but our study included only early-stage NSCLC patients with a tumour size ≤ 2.0 cm. Patients at this stage rarely receive these therapies, so this limitation had little effect on our results.

For early-stage NSCLC patients with tumour size ≤ 1 cm or tumour size ≤ 2 cm with Grade I, there was no significant difference in survival between wedge resection and lobectomy. Therefore, wedge resection may be considered as an alternative to lobectomy in NSCLC patients with T1aN0M0 or well-differentiated T1bN0M0.

Method

Selection the study population

SEER*Stat 8.4.2 software was used to extract patient information from the SEER database (17 Regs, 2022nov sub). The SEER database has an open access policy, and patient information is processed by deidentification without formal ethical approval. The workflow for inclusion and exclusion of study subjects is shown in Fig. 4. The inclusion criteria were as follows: (1) T1a/b N0M0 NSCLC patients diagnosed between 2010 and 2015 and (2) only a single primary tumour. The exclusion criteria included: (1) nonpathologically confirmed diagnosis; (2) case source of autopsy or death certificate; (3) histological type of neuroendocrine carcinoma; (4) uncertain or unknown information such as tissue differentiation and primary tumour site; (5) surgical method other than lobectomy or wedge resection; (6) tumour size more than 2 cm; (7) received radiotherapy or chemotherapy. The following variables were extracted from the database for the study: patient ID, year of diagnosis, age, marital status, sex, primary site, laterality, histological type, grade, T-N-M stage, tumour size, surgical method, radiotherapy and chemotherapy use, survival time, survival status, and cause of death. According to the international classification of disease for oncology third edition (ICD-O3), the tumours were classified as adenocarcinoma (SEER code 8140, 8250–8255, 8260, 8310, 8323, 8333, 8480, 8481, 8550, 8551, 8570, 8574), squamous cell carcinoma (SEER code 8070–8074, 8083, 8084) and others (SEER codes 8010, 8012, 8013, 8020, 8022, 8033, 8046, 8050, 8082, 8200, 8201, 8230, 8240, 8430, 8441, 8490, 8507, 8560).

Statistical analysis

Categorical variables were expressed as frequencies and percentages, and the Pearson χ^2 test was used to determine the balance between groups. To balance the baseline characteristics of the lobectomy and wedge resection groups, the nearest method and 0.02 caliper were used to perform 1:1 propensity score matching between the two groups. The variables used for matching were as follows: age, sex, marital status, primary site, laterality, histologic type, grade, and tumour size. The primary outcomes of this study were overall survival (OS) and lung cancer-specific survival (LCSS). The Kaplan-Meier method was used to draw survival curves, and the log-rank test was used to compare the differences between survival curves. Univariate and multivariate Cox proportional hazards models were used to determine the independent prognostic factors of NSCLC patients. All analyses and plots were performed with the use of R software (4.2.1) and associated R packages, and a two-sided $P < 0.05$ was considered a statistically significant difference in this study.

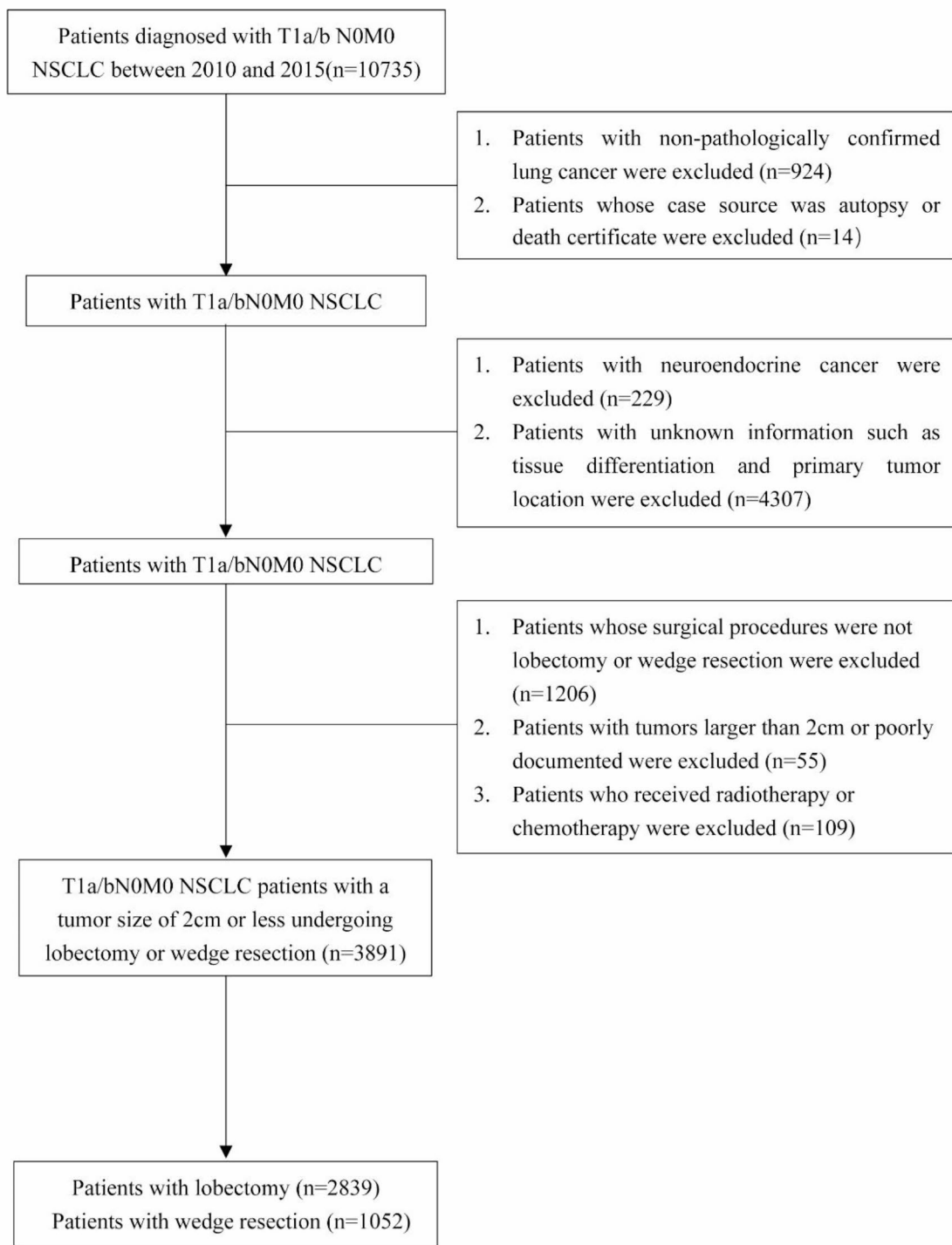


Fig. 4. Flowchart of patients There were 3891 patients who met the inclusion and exclusion criteria. There were 2839 patients who had lobectomy, whereas 1052 patients had wedge resection.

Declarations

Data availability

The data presented in this study can be obtained in online repositories: <https://seer.cancer.gov>. SEER data is publicly available and de-identified.

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References

- Sung, H. et al. Global Cancer statistics 2020: GLOBOCAN estimates of incidence and Mortality Worldwide for 36 cancers in 185 countries. *CA Cancer J. Clin.* **71** (3), 209–249. <https://doi.org/10.3322/caac.21660> (2021).
- Duma, N., Santana-Davila, R. & Molina, J. R. Non-small Cell Lung Cancer: Epidemiology, Screening, diagnosis, and treatment. *Mayo Clin. Proc.* **94**(8), 1623–1640. <https://doi.org/10.1016/j.mayocp.2019.01.013> (2019).
- Ettinger, D. S. et al. Non-small Cell Lung Cancer, Version 3.2022, NCCN Clinical Practice guidelines in Oncology. *J. Natl. Compr. Canc Netw.* **20** (5), 497–530. <https://doi.org/10.6004/jnccn.2022.0025> (2022).
- Herbst, R. S., Morgensztern, D. & Boshoff, C. The biology and management of non-small cell lung cancer. *Nature.* **553** (7689), 446–454. <https://doi.org/10.1038/nature25183> (2018).
- Tandberg, D. J., Tong, B. C., Ackerson, B. G. & Kelsey, C. R. Surgery versus stereotactic body radiation therapy for stage I non-small cell lung cancer: a comprehensive review. *Cancer.* **124** (4), 667–678. <https://doi.org/10.1002/cncr.31196> (2018).
- Rami-Porta, R. & Tsuboi, M. Sublobar resection for lung cancer. *Eur. Respir J.* **33** (2), 426–435. <https://doi.org/10.1183/09031936.00099808> (2009).
- Ding, H., Song, N., Zhang, P., Jiang, G. & Wang, H. Wedge resection plus adequate lymph nodes resection is comparable to lobectomy for small-sized non-small cell lung cancer. *Front. Oncol.* **12**, 1022904. <https://doi.org/10.3389/fonc.2022.1022904> (2022).
- Ginsberg, R. J. & Rubinstein, L. V. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. *Ann. Thorac. Surg.* **60**(3), 615–623. [https://doi.org/10.1016/0003-4975\(95\)00537-u](https://doi.org/10.1016/0003-4975(95)00537-u) (1995).
- Chen, P., Liu, Y., Wen, Y. & Zhou, C. Non-small cell lung cancer in China. *Cancer Commun. (Lond).* **42** (10), 937–970. <https://doi.org/10.1002/cac2.12359> (2022).
- Aokage, K. et al. A non-randomized confirmatory trial of segmentectomy for clinical T1N0 lung cancer with dominant ground glass opacity based on thin-section computed tomography (JCOG1211). *Gen. Thorac. Cardiovasc. Surg.* **65** (5), 267–272. <https://doi.org/10.1007/s11748-016-0741-1> (2017).
- Chiang, X. H. et al. Propensity-matched analysis comparing Survival after Sublobar Resection and Lobectomy for cT1N0 Lung Adenocarcinoma. *Ann. Surg. Oncol. Mar.* **27** (3), 703–715. <https://doi.org/10.1245/s10434-019-07974-9> (2020).
- Altorki, N. et al. Lobar or Sublobar Resection for Peripheral Stage IA Non-small-cell Lung Cancer. *N Engl. J. Med.* **388** (6), 489–498. <https://doi.org/10.1056/NEJMoa2212083> (2023).
- Suzuki, K. et al. A single-arm study of sublobar resection for ground-glass opacity dominant peripheral lung cancer. *J. Thorac. Cardiovasc. Surg.* <https://doi.org/10.1016/j.jtcvs.2020.09.146> (2022).
- Saji, H. et al. Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial. *Lancet.* **399** (10335), 1607–1617. [https://doi.org/10.1016/S0140-6736\(21\)02333-3](https://doi.org/10.1016/S0140-6736(21)02333-3) (2022).
- Jacobson, M. J., Zand, L., Fox, R. T. & Lees, W. A comparison of wedge and segmental resection of the lung. *Thorax.* **31** (4), 365–368 (1976).
- Inderbitzi, R. et al. Thoracoscopic wedge resection. *Surg. Endosc.* **6** (4), 189–192 (1992).
- Bertolaccini, L. et al. Real-world survival outcomes of wedge resection versus lobectomy for cT1a/b cN0 cM0 non-small cell lung cancer: a single center retrospective analysis. *Front. Oncol.* **13**, 1226429. <https://doi.org/10.3389/fonc.2023.1226429> (2023).
- Song, W., Hou, Y., Zhang, J. & Zhou, Q. Comparison of outcomes following lobectomy, segmentectomy, and wedge resection based on pathological subtyping in patients with pN0 invasive lung adenocarcinoma ≤ 1 cm. *Cancer Med.* **11** (24), 4784–4795. <https://doi.org/10.1002/cam4.4807> (2022).
- Zhang, Y. et al. Surgery for pre- and minimally invasive lung adenocarcinoma. *J. Thorac. Cardiovasc. Surg.* **163** (2), 456–464. <https://doi.org/10.1016/j.jtcvs.2020.11.151> (2022).
- Cao, J. et al. Survival Rates after Lobectomy, Segmentectomy, and Wedge Resection for Non-small Cell Lung Cancer. *Ann. Thorac. Surg.* **105** (5), 1483–1491. <https://doi.org/10.1016/j.athoracsur.2018.01.032> (2018).
- Dai, C. et al. Choice of Surgical Procedure for patients with non-small-cell Lung Cancer ≤ 1 cm or > 1 to 2 cm among Lobectomy, Segmentectomy, and Wedge Resection: a Population-based study. *J. Clin. Oncol.* **34** (26), 3175–3182. <https://doi.org/10.1200/JCO.2015.64.6729> (2016).
- Khullar, O. V. et al. Survival after Sublobar Resection versus Lobectomy for Clinical Stage IA Lung Cancer: an analysis from the National Cancer Data Base. *J. Thorac. Oncol.* **10** (11), 1625–1633. <https://doi.org/10.1097/JTO.0000000000000664> (2015).
- Veluswamy, R. R. et al. Limited resection Versus Lobectomy for older patients with early-stage Lung Cancer: impact of histology. *J. Clin. Oncol.* **33** (30), 3447–3453. <https://doi.org/10.1200/JCO.2014.60.6624> (2015).
- Wolf, A. S. et al. Lobectomy versus sublobar resection for small (2 cm or less) non-small cell lung cancers. *Ann. Thorac. Surg.* <https://doi.org/10.1016/j.athoracsur.2011.06.099> (2011).
- Rami-Porta, R. et al. The IASLC Lung Cancer Staging Project: Proposals for the Revisions of the T Descriptors in the Forthcoming Eighth Edition of the TNM Classification for Lung Cancer. *J. Thorac. Oncol.* <https://doi.org/10.1097/JTO.0000000000000559> (2015).
- Hattori, A. et al. Distinct clinicopathologic characteristics and prognosis based on the Presence of Ground Glass Opacity Component in Clinical Stage IA Lung Adenocarcinoma. *J. Thorac. Oncol.* **14** (2), 265–275. <https://doi.org/10.1016/j.jtho.2018.09.026> (2019).
- Koike, T., Koike, T., Yamato, Y., Yoshiya, K. & Toyabe, S-I. Predictive risk factors for mediastinal lymph node metastasis in clinical stage IA non-small-cell lung cancer patients. *J. Thorac. Oncol.* **7** (8), 1246–1251. <https://doi.org/10.1097/JTO.0b013e31825871de> (2012).
- Zhang, Y., Sun, Y. & Chen, H. Effect of tumor size on prognosis of node-negative lung cancer with sufficient lymph node examination and no disease extension. *Onco Targets Ther.* **9**, 649–653. <https://doi.org/10.2147/OTT.S98509> (2016).
- Zhang, J. et al. Relationship between tumor size and survival in non-small-cell lung cancer (NSCLC): an analysis of the surveillance, epidemiology, and end results (SEER) registry. *J. Thorac. Oncol.* **10** (4), 682–690. <https://doi.org/10.1097/JTO.0000000000000456> (2015).
- Yoon, D. W. et al. Reappraising the clinical usability of consolidation-to-tumor ratio on CT in clinical stage IA lung cancer. *Insights Imaging.* **13** (1), 103. <https://doi.org/10.1186/s13244-022-01235-2> (2022).
- Asamura, H., Aokage, K. & Yotsukura, M. Wedge Resection Versus Anatomic Resection: extent of Surgical Resection for Stage I and II lung Cancer. *Am. Soc. Clin. Oncol. Educ. Book.* **37**, 426–433 (2017).
- Kent, M. et al. Segmentectomy versus wedge resection for non-small cell lung cancer in high-risk operable patients. *Ann. Thorac. Surg.* <https://doi.org/10.1016/j.athoracsur.2013.05.104> (2013).
- Khullar, O. V. et al. Socioeconomic risk factors for long-term mortality after pulmonary resection for lung cancer: an analysis of more than 90,000 patients from the National Cancer Data Base. *J. Am. Coll. Surg.* <https://doi.org/10.1016/j.jamcollsurg.2014.10.009> (2015).
- Thomas, P-A. Lymph node dissection during sublobar resection: why, when and how? *J. Thorac. Dis.* **10** (Suppl 10), S1145–S1150. <https://doi.org/10.21037/jtd.2018.01.30> (2018).

35. Mokhles, S. et al. Systematic lymphadenectomy versus sampling of ipsilateral mediastinal lymph-nodes during lobectomy for non-small-cell lung cancer: a systematic review of randomized trials and a meta-analysis. *Eur. J. Cardiothorac. Surg.* **51** (6), 1149–1156. <https://doi.org/10.1093/ejcts/ezw439> (2017).
36. Rodriguez-Quintero, J. H. et al. Sublobar resection is associated with less lymph nodes examined and lower delivery of adjuvant therapy in patients with 1.5- to 2.0-cm clinical IA2 non-small-cell lung cancer: a retrospective cohort study. *Eur. J. Cardiothorac. Surg.* <https://doi.org/10.1093/ejcts/ezad431> (2024).
37. Ding, H., Wang, H., Xu, L., Song, N. & Jiang, G. Survival and Resected Lymph Node Number during Sublobar Resection for N0 Non-small Cell Lung Cancer 2 cm or less. *Ann. Thorac. Surg.* **107** (6), 1647–1655. <https://doi.org/10.1016/j.athoracsur.2018.12.024> (2019).
38. Chung, C. K., Zaino, R., Stryker, J. A., O'Neill, M. & DeMuth, W. E. Carcinoma of the lung: evaluation of histological grade and factors influencing prognosis. *Ann. Thorac. Surg.* **33** (6), 599–604 (1982).
39. Fujikawa, R. et al. Clinicopathologic and genotypic features of Lung Adenocarcinoma characterized by the International Association for the study of Lung Cancer Grading System. *J. Thorac. Oncol.* **17** (5), 700–707. <https://doi.org/10.1016/j.jtho.2022.02.005> (2022).
40. Aokage, K. et al. Limited resection for early-stage non-small cell lung cancer as function-preserving radical surgery: a review. *Jpn J. Clin. Oncol.* <https://doi.org/10.1093/jjco/hyw148> (2017).
41. Heiden, B. T. et al. Analysis of delayed Surgical Treatment and oncologic outcomes in clinical stage I non-small cell Lung Cancer. *JAMA Netw. Open.* **4** (5), e2111613. <https://doi.org/10.1001/jamanetworkopen.2021.11613> (2021).
42. Schuchert, M. J. et al. Factors influencing recurrence following anatomic lung resection for clinical stage I non-small cell lung cancer. *Lung Cancer.* **128**, 145–151. <https://doi.org/10.1016/j.lungcan.2018.12.026> (2019).
43. Huang, W. et al. Surgical resection versus radiotherapy for clinical stage IA lung cancer ≤ 1 cm in size: a population-based study. *Asian J. Surg.* **46** (1), 385–393. <https://doi.org/10.1016/j.asjsur.2022.04.078> (2023).
44. Shen, J. et al. Surgery or non-surgical treatment of ≤ 8 mm non-small cell lung Cancer: a Population-based study. *Front. Surg.* **8**, 632561. <https://doi.org/10.3389/fsurg.2021.632561> (2021).

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Not applicable.

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