Original Article

Prognosis after wedge resection in patients with 8th edition TNM stage IA1 and IA2 non-small cell lung cancer

Youngkyu Moon[1], Jae Kil Park[1], Kyo Young Lee[2], Eun Sung Kim[3]

[1]Department of Thoracic & Cardiovascular Surgery, [2]Department of Hospital Pathology, [3]Department of Anesthesiology and Pain Medicine, Seoul St. Mary's Hospital, College of Medicine, the Catholic University of Korea, Seoul, Republic of Korea

Contributions: (I) Conception and design: Y Moon, ES Kim; (II) Administrative support: ES Kim; (III) Provision of study materials or patients: Y Moon, JK Park; (IV) Collection and assembly of data: Y Moon, JK Park; (V) Data analysis and interpretation: Y Moon, KY Lee, ES Kim; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Eun Sung Kim, MD, PhD. Department of Anesthesiology and Pain Medicine, Seoul St. Mary's Hospital, College of medicine, The Catholic University of Korea. 222 Banpo-daero, Seocho-gu, Seoul 06591, Republic of Korea. Email: euns1503@catholic.ac.kr.

Background: According to the 8th edition TNM classification for non-small cell lung cancer (NSCLC), tumor stage (T) is determined by the maximum size of the invasive component, without the lepidic component, and the T category has been further subdivided. We investigated the indications for wedge resection using the 8th edition TNM staging system, which measures only the size of the invasive component in tumor size.

Methods: We compared 5-year disease-free survival (DFS) rates in 429 consecutive patients with 8th edition stage IA1 and IA2 NSCLC who underwent lobectomy or wedge resection from 2007 to 2017. We also analyzed the risk factors for recurrence after surgical resection.

Results: There were no significant differences in clinicopathological factors or 5-year DFS in patients with stage IA1 disease (5-year DFS 95.0%, lobectomy, *vs.* 91.6%, wedge resection; P=0.435). For patients with stage IA2 tumors, the 5-year DFS was 88.3% after lobectomy and 74.0% after wedge resection (P=0.118). There were significant differences in clinicopathological characteristics between lobectomy and wedge resection groups in stage IA2 NSCLC. On multivariate analysis, serum CEA level [hazard ratio (HR) =1.040, P=0.046] and lymphovascular invasion (HR =2.664, P=0.027), but not wedge resection, were significant risk factors for recurrence in stage IA2 NSCLC. On multivariate analysis for recurrence risk after wedge resection in stage IA1 and stage IA2 NSCLC, only the width of the resection margin was associated with recurrence.

Conclusions: Wedge resection may be an acceptable procedure in stage IA1 NSCLC. When performing wedge resection, it is necessary to ensure a sufficient resection margin distance.

Keywords: Wedge resection; 8th edition TNM classification; prognosis

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Introduction

The standard treatment of stage I non-small cell lung cancer (NSCLC) has been anatomical lobectomy with mediastinal lymph node dissection (1). However, for smaller (≤2 cm) tumors, the prognosis after sublobar resection (segmentectomy or wedge resection) may be comparable to that of lobectomy, although the results are not conclusive (2,3). At the time of this writing, two ongoing randomized trials (CALGB 140503 and JCOG 0802) were in progress to investigate the hypothesis that sublobar resection is comparable to lobectomy for small-sized (≤2 cm) NSCLC (4,5).

Among sublobar resections, wedge resection is a

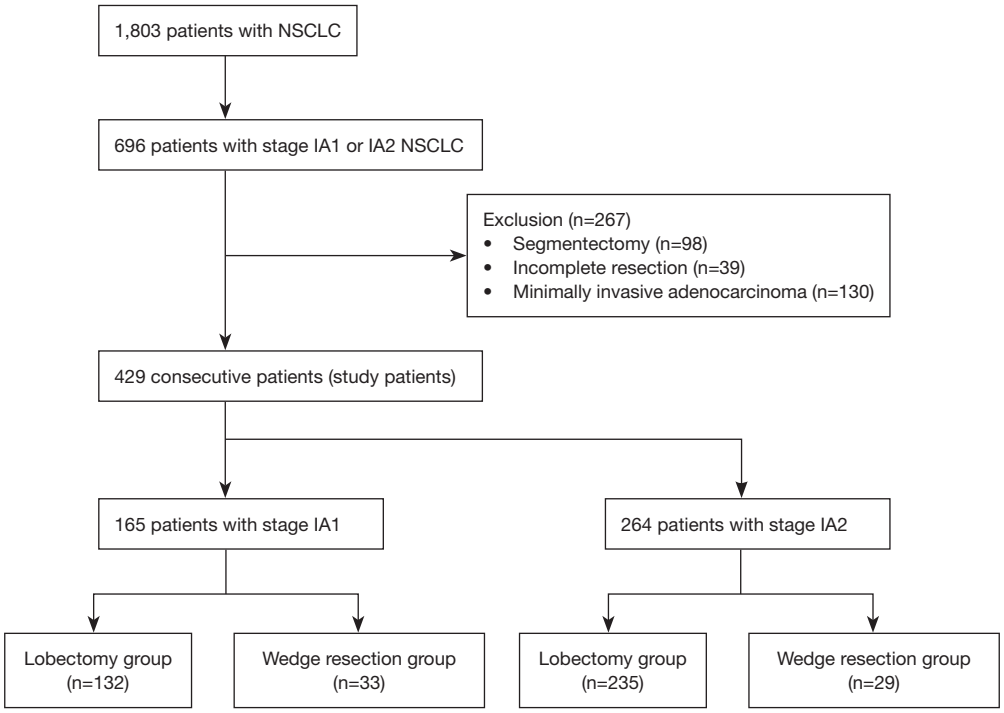


Figure 1 Study inclusion/exclusion algorithm.

less complex procedure than segmentectomy, with potential advantages including shorter operation time, less intraoperative blood loss, and better postoperative course. Segmentectomy, on the other hand, requires more sophisticated technique, and is not an easier procedure than lobectomy (6). As a result, the surgical burden after wedge resection should be much smaller. However, it is unclear when wedge resection is applicable for the treatment of small-sized (≤2 cm) lung cancer.

Most recent evaluations of the efficacy of sublobar resection have been based on the 7th edition of the TNM classification and have included tumors smaller than 2 cm. However, the criteria for tumor (T) stage have been updated in the 8th edition of the TNM staging system (7-9). In the 7th edition, the T stage was determined by the maximum size of the entire tumor, while in the 8th edition, the T stage is determined according to the maximum size of the invasive component, without the lepidic component, and the T category has been subdivided according to the size of the invasive component into stages T1a (≤1 cm), T1b (>1 to 2 cm), and T1c (>2 to 3 cm) (8). We wanted to know whether wedge resection is acceptable in a specific stage according to 8th edition of the TNM staging system.

The purpose of this study was to compare the prognoses after wedge resection or lobectomy in patients with stage IA1 and IA2 NSCLC according to the 8th edition of the TNM staging system and to investigate the indications for wedge resection using the 8th TNM staging system, which measures only the invasive component in tumor size.

Methods

Patients

From 2007 to 2017, 1,803 consecutive patients at a tertiary Hospital in Korea were diagnosed with non-small cell lung cancer (NSCLC) and underwent therapeutic surgical resection. Among these patients, 696 were diagnosed with stage IA1 or IA2 NSCLC. Patients with incomplete resection or who had preoperative chemo- or radiotherapy were excluded. We also excluded patients who underwent segmentectomy and those with minimally invasive adenocarcinomas [T1a(mi)N0M0], because it is already known that the prognosis after sublobar resection at this stage is superior to that of other stage I lung cancers. Finally, the study retrospectively enrolled 429 consecutive patients who, according to the 8th edition TNM classification, had TNM stage IA1 and IA2 NSCLC (*Figure 1*). We compared 5-year

disease-free survival (DFS) rates between lobectomy and wedge resection in stage IA1 and IA2 NSCLC and analyzed the risk factors for recurrence after curative resection. We also analyzed the risk factors for recurrence after wedge resection for stage IA1 and IA2 NSCLC in order to identify those cases for which wedge resection would be suboptimal. This study was approved by the Institutional Review Board of Seoul St. Mary's Hospital, the Catholic University of Korea (approval ID KC19RESI0064).

Surgical procedures

The first line of treatment for stage I NSCLC is anatomical lobectomy and mediastinal lymph node dissection. However, in patients with ground glass opacity (GGO) or small, solid peripheral nodules near the visceral pleura wedge resection is also considered. The surgical procedure was selected depending on the surgeon's preference or the patient's decision, and in the case of high-risk patients with decreased pulmonary function or comorbid disease, wedge resection was usually performed.

Anatomical lobectomy always included mediastinal lymph node dissection at more than 3 mediastinal lymph node stations. Lobectomy on the right side included dissection of paratracheal and subcarinal lymph nodes and lobectomy on the left side included dissection of subaortic and subcarinal lymph nodes. The technique used for lymph node dissection was *en bloc* resection of the lymph nodes, including adjacent fat tissue.

Wedge resection was performed using endostaplers. Most cases obtained a sufficient resection margin, in which the margin length was greater than the tumor diameter.

Histological evaluation and re-staging to the 8^{tb} edition staging system

Pathology reports were reviewed for tumor size, location, lymph node status, and lymphovascular invasion. Lymphovascular invasion was defined as tumor cells microscopically observed in the lymphatic or vascular lumen. Tumor specimens were remeasured by the pathologist to reclassify the T stage according to the 8th edition TNM classification (10), and the T stage was defined by the greatest dimension of the invasive component of the tumor (7). Finally, in the case of wedge resection, the gross cut-surface tumor margin width was measured, and the free resection margin distance was defined as the shortest distance between the tumor and the resection line.

Statistical analysis

Patients were grouped according to tumor stage and surgical procedure. Clinicopathological factors were compared with Student's t-test or the Wilcoxon rank-sum test for continuous variables and chi-squared or Fisher's exact test for categorical variables. The interval from surgery to the final follow-up visit was analyzed via the Kaplan-Meier method using confirmed recurrences to calculate 5-year DFS, and survival rates were compared by log-rank test. A Cox proportional hazards model was used in a multivariate analysis to identify risk factors for recurrence of stage IA1 and IA2 NSCLC. All variables with P<0.1 on univariate analysis were entered into the multivariate analysis. A P value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 24.0 software (IBM Corp, Armonk, NY, USA).

Results

Lobectomy versus wedge resection in stage IA1

Among patients with stage IA1 NSCLC, 132 underwent lobectomy and 33 underwent wedge resection. There were no significant differences in clinicopathological factors between these 2 groups (*Table 1*). The median follow-up time for patients with stage IA1 NSCLC was 1,358 days (range, 200–2,942 days), and 6 patients had recurrence (*Table 2*). The 5-year DFS rate after lobectomy was 95.0%, and 5-year DFS after wedge resection was 91.6% (P=0.435) (*Figure 2*).

Lobectomy versus wedge resection in stage IA2

Among patients with stage IA2 NSCLC, 235 underwent lobectomy and 29 had wedge resection. There were significant clinicopathological differences between the lobectomy group and the wedge resection group (*Table 3*). Older age, male sex, and smoking were more common in the wedge resection group, and pulmonary function was poorer in wedge resection group. Total tumor size, including the lepidic component, was also different between the lobectomy group and the wedge resection group, but the size of the invasive component was not different (1.5 *vs.* 1.4 cm, P=0.104). Squamous cell carcinoma and other histologic types were more prevalent in the wedge resection group, but the incidence of lymphovascular invasion was not different between the groups. The median follow-up time for patients with stage IA2 NSCLC was 1,224 days (range,

Table 1 Clinicopathological characteristics of patients undergoing lobectomy or wedge resection for stage IA1 non-small cell lung cancer

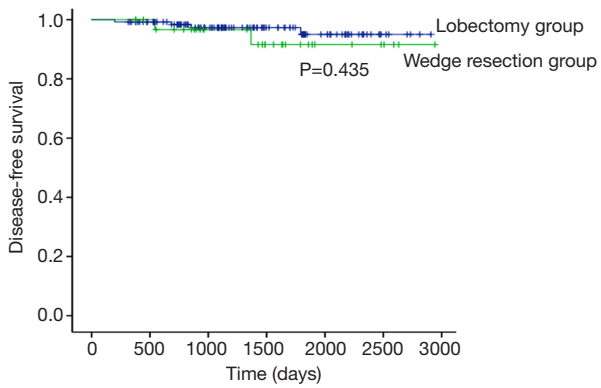
Variables	Lobectomy group (n=132)	Wedge resection group (n=33)	P value
Age (±SD)	61.9 (±8.9)	61.9 (±12.2)	0.997
Sex, n (%)			0.629
Male	50 (37.9)	11 (33.3)	
Female	82 (62.1)	22 (66.7)	
Current or former smoker, n (%)	33 (25.0)	6 (15.4)	0.410
Serum CEA level (ng/mL) (±SD)	1.8 (±1.5)	1.8 (±1.3)	0.778
SUVmax (±SD)	2.5 (±2.4)	1.7 (±1.1)	0.133
Involved lobe, n (%)			0.199
Right upper	49 (37.1)	9 (27.3)	
Right middle	13 (9.8)	4 (12.1)	
Right lower	27 (20.5)	4 (12.1)	
Left upper	22 (16.7)	5 (15.2)	
Left lower	21 (15.9)	11 (33.3))	
Pulmonary function			
FEV1 (%) (±SD)	98.7 (±14.8)	94.6 (±18.1)	0.191
DLCO (%) (±SD)	91.2 (±16.6)	84.8 (±14.4)	0.056
Surgical approach, n (%)			0.220
VATS	119 (90.2)	27 (81.8)	
Open thoracotomy	13 (9.8)	6 (18.2)	
Postoperative hospital stay (days) (±SD)	7.5 (±13.1)	5.5 (±3.4)	0.373
Postoperative complications, n (%)	14 (10.6)	3 (9.1)	1.000
Operative mortality	0	0	1.000
Total tumor size (±SD)	1.8 (±0.7)	1.2 (±0.5)	<0.001
Invasive component size (±SD)	0.7 (±0.2)	0.7 (±0.2)	0.826
Location, n (%)			0.359
Central	8 (6.1)	0	
Peripheral	124 (93.9)	33 (100)	
Histology, n (%)			0.746
Adenocarcinoma	129 (97.7)	32 (97.0)	
Squamous cell carcinoma	2 (1.5)	1 (3.0)	
Others	1 (0.8)	0	
Number of dissected lymph nodes (±SD)	13.5 (±6.8)	2.0 (±3.1)	<0.001
Lymphovascular invasion, n (%)	37 (28.0)	5 (15.2)	0.129

SD, standard deviation; CEA, carcinoembryonic antigen; SUVmax, maximum standardized uptake value; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

Table 2 Summary of recurrence in patients with stage IA1 non-small cell lung cancer after lobectomy and wedge resection

Variables	Lobectomy (n=132)	Wedge resection (n=33)	P value*
Sites of recurrence			0.182
Locoregional recurrence	3	2	
Local recurrence	1	2	
Regional recurrence	2	0	
Distant recurrence	0	0	
Both	1	0	

*, statistical method: chi-squared test for categorical variables. Locoregional, recurrence within ipsilateral hemithorax including pleura and mediastinal lymph nodes; Local, recurrence in stump or lung; Regional, recurrence in lymph nodes or pleura; Both, Locoregional recurrence + Distant recurrence.



Numbers at risk

	0	365 days	730 days	1,095 days	1,460 days	1,825 days	2,190 days
Lobectomy group	132	128	110	77	54	32	19
Wedge resection group	33	33	27	20	17	9	6

Figure 2 Disease-free survival after lobectomy versus wedge resection in stage IA1 non-small cell lung cancer.

20–3,751 days), and 29 patients had recurrence (*Table 4*). The 5-year DFS rate was 88.3% after lobectomy and 74.0% after wedge resection (*Figure 3*). This difference was not statistically significant (P=0.118), but because there were significant between-group differences in clinicopathological characteristics, it was difficult to conclude that lobectomy and wedge resection offered the same prognosis in stage IA2 NSCLC. Therefore, univariate and multivariate analyses using a Cox proportional hazard model were conducted (*Table 5*). Wedge resection was not a significant risk factor for recurrence on the univariate analysis. Specific variables identified as significant (P<0.1) by univariate analysis included sex, smoking status, serum carcinoembryonic antigen (CEA) level, maximum standardized uptake value (SUVmax), video-assisted thoracoscopic surgery (VATS), invasive component size, central location, number of dissected lymph nodes, and lymphovascular invasion. When these variables were entered into the multivariate model, only the CEA level [hazard ratio (HR) =1.040, P=0.046] and lymphovascular invasion (HR =2.664, P=0.027) were significant risk factors for recurrence of stage IA2 NSCLC.

Risk factors for recurrence after wedge resection

We next analyzed risk factors for recurrence in all patients who had wedge resection (n=62: 33 stage IA1 NSCLC and 29 stage IA2 NSCLC). The clinicopathological characteristics of these patients are shown in *Table 6*. The mean total tumor size was 1.4 cm and the size of the invasive component was 1.0 cm. The mean margin/invasive component ratio, defined as the resection margin distance (cm)/the greatest dimension of invasive component (cm), was 1.4. Forty patients (64.5%) underwent wedge resection intentionally [25 stage IA1 (75.8%) and 15 stage IA2 (51.7%); P=0.048], while the remaining patients underwent wedge resection because of underlying disease or old age.

The median follow-up time after wedge resection was 1,294 days (range, 146–2,969 days) and 7 patients had recurrence, 6 with locoregional recurrence and 1 with bone recurrence. Univariate and multivariate analyses using a Cox proportional hazard model were conducted to identify the risk factors for recurrence (*Table 7*) after wedge resection. Significant factors (P<0.1) on univariate analysis included CEA level, SUVmax, forced expiratory volume in 1 second (FEV1), diffusing capacity for carbon monoxide (DLCO), size of the invasive component, histologic type, lymphovascular invasion, and margin/invasive component ratio. When these variables were entered into the multivariate model, only the margin/invasive component ratio (HR =0.042, P=0.041) was a significant risk factor for recurrence. The mean margin/invasive component ratio in the recurrence group was 0.43 (range, 0.06–1.00), and there were no recurrences when the margin/invasive component ratio was >1.

Table 3 Comparison of clinicopathological characteristics between lobectomy and wedge resection groups in patients with stage IA2 non-small cell lung cancer

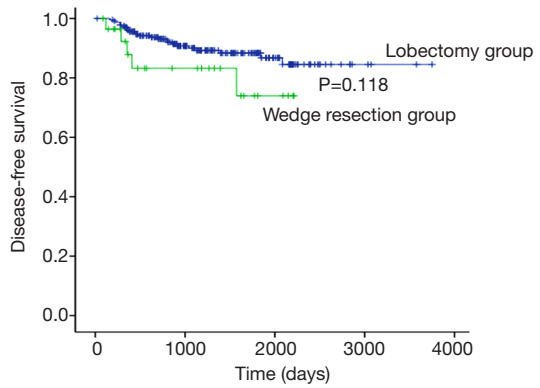
Variables	Lobectomy group (n=235)	Wedge resection group (n=29)	P value
Age (±SD)	63.6 (±10.5)	69.4 (±8.8)	0.005
Sex, n (%)			0.010
Male	103 (43.8)	20 (69.0)	
Female	132 (56.2)	9 (31.0)	
Current or former smoker, n (%)	83 (35.3)	16 (55.2)	0.037
Serum CEA level (ng/mL) (±SD)	2.6 (±3.7)	4.3 (±10.1)	0.380
SUVmax (±SD)	3.9 (±3.0)	4.9 (±3.7)	0.228
Involved lobe, n (%)			0.043
Right upper	89 (37.9)	7 (24.1)	
Right middle	17 (7.2)	1 (3.4)	
Right lower	52 (22.1)	3 (10.3)	
Left upper	45 (19.1)	10 (34.5)	
Left lower	32 (13.6)	8 (27.6))	
Pulmonary function			
FEV1 (%) (±SD)	96.3 (±17.6)	88.9 (±16.4)	0.034
DLCO (%) (±SD)	88.6 (±17.2)	74.5 (±16.3)	<0.001
Surgical approach, n (%)			0.589
VATS	197 (83.8)	26 (89.7)	
Open thoracotomy	38 (16.2)	3 (10.3)	
Postoperative hospital stay (days) (±SD)	6.6 (±4.0)	5.3 (±2.8)	0.099
Postoperative complications, n (%)	34 (14.5)	2 (6.9)	0.391
Operative mortality, n (%)	1 (0.4)	0	1.000
Total tumor size	2.0 (±0.6)	1.6 (±0.3)	<0.001
Invasive component size	1.5 (±0.3)	1.4 (±0.2)	0.104
Location, n (%)			0.142
Central	20 (8.5)	0	
Peripheral	215 (91.5)	29 (100.0)	
Histology, n (%)			0.024
Adenocarcinoma	206 (87.7)	20 (69.0)	
Squamous cell carcinoma	18 (7.7)	6 (20.7)	
Others	11 (4.7)	3 (10.3)	
Number of dissected lymph nodes (±SD)	13.6 (±7.2)	2.1 (±4.2)	<0.001
Lymphovascular invasion, n (%)	73 (31.1)	7 (24.1)	0.444

SD, standard deviation; CEA, carcinoembryonic antigen; SUVmax, maximum standardized uptake value; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

Table 4 Summary of recurrence in patients with stage IA2 non-small cell lung cancer after lobectomy and wedge resection

Variables	Lobectomy (n=235)	Wedge (n=29)	P value*
Sites of recurrence			0.297
Locoregional recurrence	11	4	
Local recurrence	5	2	
Regional recurrence	6	2	
Distant recurrence	7	0	
Both	6	1	

*, statistical method: chi-squared test for categorical variables. Locoregional, recurrence within ipsilateral hemithorax including pleura and mediastinal lymph nodes; Local, recurrence in stump or lung; Regional, recurrence in lymph nodes or pleura; Both, Locoregional recurrence + Distant recurrence.



Numbers at risk

	0	365 days	730 days	1095 days	1460 days	1825 days	2190 days
Lobectomy group	235	216	168	121	91	59	25
Wedge resection group	29	19	15	14	9	4	2

Figure 3 Disease-free survival after lobectomy versus wedge resection in stage IA2 non-small cell lung cancer.

Discussion

Wedge resection is a relatively simple and easy procedure in thoracic surgery that is usually associated with a better postoperative course than segmentectomy and lobectomy, along with well-preserved postoperative pulmonary function. Wedge resection is usually indicated for metastasectomy or lung biopsy, and the prognosis after wedge resection has also been good in some cases of lung cancer presenting as GGO nodules (11). Thus, patients with non-invasive or minimally invasive tumors can be candidates for wedge resection. However, it has not been established whether wedge resection is acceptable procedure in NSCLC. Therefore, we evaluated the prognosis of 8th edition TNM stage IA1 and IA2 NSCLC after wedge resection. The 8th edition TNM classification bases the T stage on the size of the invasive component of the tumor. The non-invasive (lepidic) component is not measured in the T category. As such, we thought that the 8th edition TNM staging system would be a better way to determine the indication for wedge resection because it allows for the exclusion of the non-invasive components, which have superior prognoses. Our results suggest that, especially in 8th edition stage IA1 NSCLC, the prognosis after wedge resection is not different from lobectomy. The 5-year DFS rate after wedge resection of 8th edition TNM stage IA1 NSCLC was 91.6%, and the 5-year disease-specific survival rate was 100%. The clinicopathological characteristics were well matched between the lobectomy group and the wedge resection group in stage IA1 NSCLC, and although patients with minimally invasive adenocarcinoma were excluded, the 91.6% 5-year DFS was comparable with other studies in this stage (12). Therefore, we concluded that wedge resection seems to be an acceptable procedure in 8th edition TNM stage IA1 NSCLC.

The 5-year DFS rate was also not statistically different between lobectomy and wedge resection in stage IA2 NSCLC. However, at this stage, the 5-year DFS after wedge resection was 74.0% and the 5-year disease-specific survival was 79.2%, which are not acceptable for stage IA2 NSCLC. Wedge resection itself was not a risk factor for recurrence in univariate analysis in stage IA2 NSCLC, but there were other risk factors related to surgical procedure. For instance, CEA level and lymphovascular invasion, which were both significant risk factors, reflect the aggressiveness of the tumor. In the presence of these risks, wedge resection may be insufficient. Furthermore, both CEA level and lymphovascular invasion have been associated with lymph node upstage after surgery (13-16). It is difficult to dissect N1 nodes when performing wedge resection. As such, the pathologic stage after wedge resection is not accurate. Our multivariate analysis suggested a strong (P=0.053), albeit not statistically significant, association between the number of dissected lymph nodes and recurrence. Since lymph node dissection is rarely performed with wedge resection, this could be interpreted as an increased risk for recurrence of stage IA2 tumors after wedge resection, and in the case of stage IA2 disease, segmentectomy may be a more suitable operation than wedge resection because more lymph nodes can be excised. This should be clarified

Table 5 Univariate and multivariate analysis for recurrence of stage IA2 non-small cell lung cancer after lobectomy (n=235) and wedge resection (n=29) (Cox-proportional hazard model)

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age	1.006	0.971–1.042	0.731			
Sex (male)	2.703	1.231–5.937	0.013	1.460	0.471–4.530	0.512
Smoker	2.215	1.065–4.606	0.033	1.220	0.409–3.635	0.721
CEA	1.066	1.035–1.098	<0.001	1.040	1.001–1.081	0.046
SUVmax	1.185	1.077–1.303	<0.001	1.100	0.966–1.252	0.151
Lobe			0.995			
Right upper (reference)	1					
Right middle	1.238	0.271–5.669	0.783			
Right lower	1.091	0.396–3.004	0.867			
Left upper	1.228	0.467–3.231	0.677			
Left lower	1.127	0.353–3.600	0.841			
FEV1 (%)	1.010	0.988–1.032	0.371			
DLCO (%)	1.002	0.979–1.024	0.892			
VATS	0.461	0.211–1.005	0.052	0.505	0.204–1.253	0.141
Total tumor size	0.630	0.296–1.339	0.229			
Invasive component size	3.749	1.018–13.809	0.047	2.318	0.539–9.974	0.259
Central location	2.611	0.995–6.853	0.051	2.301	0.731–7.249	0.154
Histology			0.497			
Adenocarcinoma (Reference)	1		0.256			
Squamous cell carcinoma	1.848	0.640–5.334	0.807			
others	0.779	0.105–5.766				
Number of dissected lymph nodes	0.954	0.905–1.005	0.079	0.941	0.884–1.001	0.053
Lymphovascular invasion	2.791	1.341–5.807	0.006	2.664	1.118–6.345	0.027
Wedge resection	2.120	0.808–5.560	0.127			

CEA, carcinoembryonic antigen; SUVmax, maximum standardized uptake value; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; VATS, video-assisted thoracoscopic surgery.

through further study in the future. On the other hand, our previous research has shown that lymph node upstaging did not occur in clinical N0 NSCLC <1 cm (14,17). Therefore, wedge resection in 8th edition TNM stage IA1 NSCLC with an invasive component size of ≤1 cm is also an acceptable procedure in terms of the possibility of lymph node metastasis.

When performing wedge resection, an adequate resection margin distance is important to achieve complete resection of the tumor (18). According to the National Comprehensive Cancer Network (NCCN) guidelines for NSCLC (Version 2, 2019), the parenchymal resection margins in wedge resection should measure at least 2 cm or be equal to the size of the tumor. In this study, the margin/invasive component ratio was a risk factor for recurrence after wedge resection. In our previous study, adenocarcinoma with a high lepidic component was less likely to recur even if the resection margin was short (19,20).

Table 6 Clinicopathological characteristics of patients undergoing wedge resection for stage IA1 and IA2 non-small cell lung cancer (n=62)

Variables	Mean (±SD) or N (%)
Age (±SD)	65.4 (±11.3)
Sex	
Male	31 (50.0)
Female	31 (50.0)
Current or former smoker	22 (35.5)
8th edition TNM stage	
Stage IA1	33 (53.2)
Stage IA2	29 (46.8)
Involved lobe	
Right upper	16 (25.8)
Right middle	5 (8.1)
Right lower	7 (11.3)
Left upper	15 (24.2)
Left lower	19 (30.6)
Surgical approach	
VATS	53 (85.5)
Open thoracotomy	9 (14.5)
Postoperative complications	5 (8.1)
Operative mortality	0
Tumor size (±SD)	1.4 (±0.5)
Invasive component size (±SD)	1.0 (±0.4)
Location	
Central	0
Peripheral	62 (100.0)
Histology	
Adenocarcinoma	52 (83.9)
Squamous cell carcinoma	7 (11.3)
Others	3 (4.8)
Lymphovascular invasion	12 (19.4)
Margin/Invasive component ratio (±SD)	1.4 (±1.3)
Reason for wedge resection	
Intentional wedge resection	40 (64.5)
Underlying cardiopulmonary disease	7 (11.3)
Underlying other malignant disease	3 (4.8)
Old age	1 (1.6)
Previous lung operation	11 (17.7)

SD, standard deviation; VATS, video-assisted thoracoscopic surgery; Margin/invasive component ratio, resection margin distance (cm)/greatest dimension of invasive component (cm).

In other words, it appears that the size of the invasive component is more important in determining the resection margin distance than the total tumor size including the lepidic component. Thus, wedge resection should be performed at a distance from the tumor of at least the size of the invasive component.

We evaluated 5-year DFS instead of overall survival because of the high rate of non-cancer related deaths during follow-up among patients with stage I NSCLC (21). DFS is a more accurate measurement for the survival analysis because it reflects the biological behavior of cancer rather than death due to unrelated factors.

This study has a few limitations. First, it was a retrospective review. Second, we obtained data from a single institution, and the sample size was relatively small to generalize our results. However, this study examined data from surgical patients treated by a mainly standardized protocol at our institution, a tertiary hospital in Korea. Furthermore, a very detailed analysis was possible because of the comprehensive information stored in the electronic medical record. We retrieved data that thoroughly described the surgical procedures with lymph node dissection along with exhaustive data from pathologic specimens and pathologic reports. We believe that our data will be useful as the basis for future investigations. A prospective randomized controlled study should be performed to validate our results. Finally, the follow-up period was relatively short. However, recurrence of NSCLC is most commonly reported within a

Table 7 Univariate and multivariate analysis for recurrence of stage IA1 and IA2 non-small cell lung cancer after wedge resection (n=62) (Cox-proportional hazard model)

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age	0.999	0.937–1.066	0.987			
Sex (male)	3.203	0.620–16.535	0.165			
Smoker	1.757	0.391–7.885	0.462			
CEA	1.054	1.009–1.100	0.017	0.593	0.158–2.225	0.439
SUVmax	1.218	1.028–1.444	0.023	0.944	0.577–1.544	0.819
Lobe			0.793			
Right upper (reference)	1					
Right middle	1.021	0.106–9.863	0.986			
Right lower	0.628	0.065–6.103	0.688			
Left upper	0.323	0.033–3.119	0.328			
Left lower	0.331	0.034–3.186	0.338			
FEV1 (%)	0.954	0.906–1.006	0.080	1.007	0.944–1.075	0.828
DLCO (%)	0.914	0.853–0.980	0.012	0.931	0.855–1.014	0.101
VATS	0.510	0.098–2.666	0.425			
Total tumor size	1.754	0.351–8.758	0.494			
Invasive component size	5.472	0.939–31.878	0.059	0.753	0.012–48.765	0.894
Histology			0.007			0.223
Adenocarcinoma (reference)	1			1		
Squamous cell carcinoma	6.935	1.252–38.422	0.027	18.883	0.640–557.504	0.089
Others	33.271	2.710–408.401	0.006	3.441	0.049–241.107	0.569
Number of dissected lymph nodes	0.896	0.648–1.237	0.503			
Lymphovascular invasion	3.585	0.801–16.054	0.095	1.894	0.048–74.171	0.733
Margin/invasive component ratio	0.022	0.001–0.425	0.012	0.042	0.002–0.875	0.041

HR, hazard ratio; CEA, carcinoembryonic antigen; SUVmax, maximum standardized uptake value; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity for carbon monoxide; VATS, video-assisted thoracoscopic surgery; Margin/invasive component ratio, resection margin distance (cm)/greatest dimension of invasive component (cm).

2-year postoperative period (22), and early recurrence seems to be an accurate reflection of the long-term outcome (23).

In conclusion, the prognosis after wedge resection or lobectomy in stage IA1 NSCLC was not different. Therefore, it seems that wedge resection may be an acceptable procedure for 8th edition TNM stage IA1 NSCLC. In stage IA2 NSCLC, the prognosis was not statistically different between lobectomy and wedge resection, but the 5-year DFS after wedge resection was not acceptable. Therefore, wedge resection can only be conducted in select cases of 8th edition TNM stage IA2 NSCLC, and accurate pathologic staging and tumor type must be considered. The resection margin was the main risk factor for recurrence in both stages for patients undergoing wedge resection. Therefore, when performing wedge resection, the surgeon must ensure that the resection margin distance is longer than the size of the invasive component of the tumor. Further studies that include data from larger cohorts and prospective randomized controlled trials may validate these conclusions and provide more

refined results.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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