Outcomes after lobar versus sublobar resection for clinical stage I non—small cell lung cancer in patients with interstitial lung disease

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ABSTRACT

Objective: Since the prognosis after standard lobectomy for non—small cell lung cancer (NSCLC) in patients with interstitial lung disease (ILD) is poor, we investigated the possibility of sublobar resection for the improvement of the surgical results in such patients.

Methods: Of 796 consecutive patients with clinical stage I NSCLC who underwent pulmonary resection, 107 were diagnosed with ILD using high-resolution computed tomography (HRCT). Overall survivals (OS) were compared between patients with non-ILD and those with ILD or between patients with ILD who underwent lobectomy and those who underwent sublobar resection. ILD patterns consisted of usual interstitial pneumonia (UIP), possible UIP, and inconsistent with UIP. The log-rank statistics and Cox proportional hazard models were used to test for survival differences.

Results: OS was significantly lower in patients with “ILD inconsistent with UIP” pattern (hazard ratio [HR], 2.66; 95% confidence interval [CI], 1.19-5.97; $P = .014$), or “ILD with possible UIP or UIP” patterns (HR, 2.38; 95% CI, 1.76-3.21; $P < .001$) compared with patients with non-ILD. No significant difference in OS was observed between patients with ILD who underwent either lobectomy or sublobar resection (HR, 1.82; 95% CI, 0.81-4.06; $P = .19$). Multivariable Cox analysis demonstrated diffusing capacity of the lung for carbon monoxide (HR, 0.95; 95% CI, 0.91-0.99; $P = .009$) and not surgical procedure (HR, 2.76; 95% CI, 0.83-9.16; $P = .099$), as an independent prognostic factor for OS.

Conclusions: Sublobar resection may be a potential alternative choice for clinical stage I NSCLC with ILD on HRCT. (J Thorac Cardiovasc Surg 2017;154:1089-96)

Overall survival in patients with clinical stage I non—small cell lung cancer with interstitial lung disease.

Central Message

Sublobar resection may be a potential alternative to lobectomy for clinical stage I non—small cell lung cancer with interstitial lung disease on high-resolution computed tomography.

Perspective

Sublobar resection may be a potential alternative choice for clinical stage I non—small cell lung cancer in patients with interstitial lung disease on high-resolution computed tomography, with overall survival comparable with that seen after lobectomy.

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Interstitial lung disease (ILD), including pulmonary fibrosis, has been reported to be associated with an increased risk of lung cancer.¹⁻³ It is reported that 4% to

6% of resected primary lung cancer specimens show evidence of ILD.^{4,5} Although the 30-day mortality rate of patients with lung cancer undergoing lobectomy is as low as 0.3% in Japan, interstitial pneumonia, which is one of the types of ILD, is the most frequent cause of death after lung cancer surgery.⁶ The incidence and mortality of

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Abbreviations and Acronyms

ALAT	= Latin American Thoracic Association
ATS	= American Thoracic Society
CI	= confidence interval
CSS	= cancer-specific survival
CT	= computed tomography
DLCO	= diffusing capacity of the lung for carbon monoxide
ERS	= European Respiratory Society
FDG-PET/CT	= F-18-fluorodeoxyglucose positron emission tomography/computed tomography
HR	= hazard ratio
HRCT	= high-resolution computed tomography
ILD	= interstitial lung disease
JRS	= Japanese Respiratory Society
NSCLC	= non–small cell lung cancer
OS	= overall survival
UIP	= usual interstitial pneumonia

postoperative acute exacerbations in patients with non–small cell lung cancer (NSCLC) with ILD has been reported to be 0% to 32% and 0% to 23%, respectively.^{7,8} The long-term survival rate of patients with NSCLC with ILD is also poor. In patients with pathologic IA NSCLC with ILD, the 5-year survival rates are reported to range between 54% and 59%,^{5,9} whereas the 5-year survival rate is reported to be 73% in patients with pathologic IA NSCLC with or without ILD.¹⁰ Thus, patients with NSCLC with ILD are considered to have worse short- and long-term outcomes after lung resection. Lung cancer is responsible for approximately 50% of deaths among patients with ILD with lung cancer, with the remaining deaths due to other causes, such as respiratory failure.^{5,7}

To improve the outcome of patients with NSCLC and ILD, techniques must simultaneously address the risks of diminished pulmonary function and the risks posted by the cancer. Several studies have demonstrated that the survival rate after sublobar resection is similar to that after standard lobectomy in certain patients with clinical stage IA NSCLC, and sublobar resection has functional advantages over lobectomy.^{11–15} In patients with NSCLC with ILD, sublobar resection may decrease the occurrence of acute exacerbations of ILD.^{8,16} We hypothesized that sublobar resection provides acceptable long-term outcomes and reduces the incidence of postoperative complications compared with lobectomy in patients with NSCLC with ILD. The purpose of the present exploratory study was to investigate the results of sublobar and lobar

resection in patients with clinical stage I NSCLC with ILD. Although ILD contains several subtypes such as idiopathic pulmonary fibrosis, nonspecific interstitial pneumonia, sarcoidosis, and others, the prognosis after surgery for NSCLC with each subtype of ILD is not well known. Therefore, we divided ILDs into 3 types based on radiographic findings in this study and compared the outcomes between the procedures stratified by radiographic ILD patterns to explore which patients would benefit from sublobar resection.

PATIENTS AND METHODS**Patients**

We included patients with clinical stage I NSCLC from Hiroshima University between April 1, 2007 and December 31, 2015. Patients with multiple tumors, or those who had previously undergone lung surgeries for lung tumors, were excluded from the present study. Patient data were analyzed retrospectively in the present study. High-resolution computed tomography (HRCT) and F-18-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) followed by surgical resection with curative intent were performed in all patients staged according to the *TNM Classification of Malignant Tumors, 7th Edition*.¹⁰ Neither mediastinoscopy nor endobronchial ultrasonography was performed routinely because all patients underwent preoperative HRCT and FDG-PET/CT. In all patients included in the present study, HRCT and FDG-PET/CT revealed an absence of an enlargement (<1 cm) in the mediastinal or hilar lymph nodes and an absence of >1.5 accumulation for maximum standardized uptake values in the lymph nodes, respectively. Sublobar resection (either wedge resection or segmentectomy) was allowed in patients with complete tumor removal as an optional procedure for peripheral tumors that were assessed intraoperatively as N0 by histologic examination of frozen sections of enlarged lymph nodes or by ensuring that there was no obvious lymph node enlargement in the thoracic cavity. Systematic lymph node dissection, ie, of the hilar or mediastinal nodes, was performed during segmentectomy but not during wedge resection (Video 1). Wedge resection was performed for predominantly ground-glass opacity lesions in patients

VIDEO 1. Right S9-10 segmentectomy for clinical stage IA non–small cell lung cancer with radiologic usual interstitial pneumonia pattern. UIP, Usual interstitial pneumonia. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)30635-9/addons](http://www.jtcvsonline.org/article/S0022-5223(17)30635-9/addons).

FIGURE 1. Representative interstitial lung disease patterns on computed tomography according to the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Association classifications. A, Findings inconsistent with UIP pattern; upper-lung predominant ground glass abnormality, which is one of the criteria for inconsistent UIP patterns. B, Possible UIP pattern; basal predominant, peripheral predominant reticular abnormality without honeycombing. C, UIP pattern; basal predominant, peripheral predominant reticular abnormality with honeycombing. *UIP*, Usual interstitial pneumonia.

who were considered unsuitable for lobectomy. We did not usually consider whether the tumor being resected was in an area of radiographic ILD for the choice of surgical procedure.

The inclusion criteria of the present study were as follows: preoperative staging determined using HRCT and FDG-PET/CT; potentially curative surgery without neoadjuvant chemotherapy or radiotherapy; and a definitive histopathologic diagnosis of NSCLC. The present study was approved by the institutional review boards of Hiroshima University. The requirement of obtaining informed consent from individual patients was waived because this study was a retrospective review of a patient database.

High-Resolution Computed Tomography

Sixteen-row multidetector computed tomography (CT) was used to obtain chest images independently of subsequent FDG-PET/CT examinations. The following parameters were used for high-resolution images of the lung: 120 kVp; 200 mA; 1- to 2-mm section thickness; 512×512 pixel resolution; 0.5- to 1.0-second scanning time; a high-spatial reconstruction algorithm with a 20-cm field of view; and mediastinal (level, 40 HU; width, 400 HU) and lung (level, -600 HU; width, 1600 HU) window settings. A radiologically determined ILD was defined according to the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Association (ATS/ERS/JRS/ALAT) classifications¹⁷ as follows:

1. Usual interstitial pneumonia (UIP) pattern (all 4 features): subpleural, basal predominance; reticular abnormality; honeycombing with or without traction bronchiectasis; absence of features listed as inconsistent with UIP pattern.
2. Possible UIP pattern (all 3 features): subpleural, basal predominance; reticular abnormality; absence of features listed as inconsistent with UIP pattern.
3. Inconsistent with UIP pattern (any of the 7 features): upper or mid-lung predominance; peribronchovascular predominance; extensive ground-glass abnormality (extent > reticular abnormality); profuse micronodules (bilateral predominantly upper lobes); discrete cysts (multiple, bilateral, away from areas of honeycombing); diffuse mosaic attenuation/air trapping (bilateral, in 3 or more lobes); or consolidation in bronchopulmonary segment(s)/lobe(s).

CT scans were reviewed, and tumor sizes and ILD patterns were determined preoperatively by the tumor board, which included surgical oncologists, medical oncologists, pulmonologists, radiologists, and pathologists.

Follow-up Evaluation

All patients who underwent lung resection were followed up from the day of surgery. Postoperative complications were defined according to

the Clavien-Dindo classification.¹⁸ The criteria for postoperative acute exacerbation of ILD included any unexplained worsening of dyspnea within 1 month, evidence of hypoxemia, as defined by worsened or severely impaired arterial blood gas exchange more than 10 mm Hg under similar conditions, new radiographic alveolar infiltrates, and an absence of an alternative complication, such as infection, pulmonary embolism, pneumothorax, or heart failure.¹⁹ Postoperative follow-up procedures, including a physical examination, chest roentgenogram every 3 months, and chest and abdominal CT examinations every 6 months, were performed for the first 2 years. Subsequently, a physical examination and chest roentgenogram were performed every 6 months, and a chest CT examination was performed every year.

Statistical Analysis

The results are presented as numbers (%) or medians, unless stated otherwise. The χ^2 test was used to compare categorical variable frequencies. The Fisher exact test was used for small sample sizes. The overall survival (OS) was defined as the time from the date of surgery until the time of death due to any cause or the last follow-up visit. The Kaplan-Meier method was used to assess OS durations, and these durations were compared with log-rank tests, which were truncated at the 36-month mark. To assess the potential independent effects of the surgical procedure on OS, we used a Cox proportional hazards model. To select variables for multivariable analysis, a backward stepwise method was used. The Statistical Package for the Social Sciences (SPSS; version 20; IBM Corp, Armonk, NY) was used for statistical analysis. The significance level was set at a *P* value of < .05.

RESULTS

Comparison of Outcomes Among Radiologic Non-ILD and ILD Patterns

Overall, 107 of 796 patients had clinical stage I NSCLC with ILD on HRCT. The median follow-up period postoperatively was 37.3 months (0.34-107.7 months). ILDs were divided into 3 groups (UIP, possible UIP, inconsistent with UIP) according to the ATS/ERS/JRS/ALAT classification (Figure 1). Patient characteristics based on ILD patterns are shown in Table 1. Pathologic findings of resected specimens are shown in Table E1. None of the 47 patients (0%) with “ILD inconsistent with UIP” on HRCT showed a pathologic UIP pattern. Seven of 33 (21.2%) with “ILD with possible UIP” on HRCT and 18 of 27 (66.7%) with “ILD with UIP” on HRCT showed pathologic UIP patterns in the resected lung tissue. OS was significantly lower in

TABLE 1. Clinicopathologic features of patients with clinical stage I non–small cell lung cancer with ILD according to the ATS/ERS/JRS/ALAT classification

Variables	Non-ILD (n = 689)	Inconsistent with UIP (n = 47)	Possible UIP (n = 33)	UIP (n = 27)
Age, y	67 (30-89)	74 (61-86)	72.5 (60-92)	72 (58-87)
Sex				
Male	385 (55.9%)	31 (66.0%)	29 (87.9%)	24 (88.9%)
Smoking history				
Yes	374 (54.3%)	28 (61.7%)	32 (97.0%)	26 (96.3%)
Clinical T				
T1	512 (74.3%)	35 (74.5%)	22 (66.7%)	17 (63.0%)
T2	177 (25.7%)	12 (25.5%)	11 (33.3%)	10 (37.0%)
%VC	99.4 (51.2-147.1)	91 (61.4-122.2)	93.7 (73.5-119.7)	84.6 (42.5-106.7)
FEV1, %	75.1 (36.4-100)	72.3 (31.6-93.5)	74.7 (53.8-90.0)	75.7 (62.1-86.1)
%DLCO	80.8 (16-135)	60.0 (16-99)	62.5 (34-103)	45 (21-60)
Serum KL-6	223 (72-1269)	282 (113-578)	404.5 (181-993)	710 (256-3115)
Histology				
Adenocarcinoma	569 (82.6%)	34 (72.3%)	15 (45.5%)	5 (18.5%)
Squamous cell carcinoma	67 (9.7%)	10 (21.3%)	13 (39.4%)	14 (51.9%)
Others	53 (7.7%)	3 (6.4%)	5 (15.6%)	8 (29.7%)
Procedure				
Lobectomy	400 (58.1%)	24 (51.1%)	19 (57.6%)	14 (51.9%)
Segmentectomy	198 (28.7%)	13 (27.7%)	9 (27.3%)	3 (11.1%)
Wedge resection	91 (13.2%)	10 (21.3%)	5 (15.6%)	10 (37.0%)

Values are n (%) or median (range). *ILD*, Interstitial lung disease; *UIP*, usual interstitial pneumonia; *VC*, vital capacity; *FEV1*, forced expiratory value in 1 second; *DLCO*, diffusion capacity of the lung for carbon monoxide; *KL-6*, Krebs von den Lungen-6.

patients with ILD than in those with non-ILD (hazard ratio [HR], 4.17; 95% confidence interval [CI], 2.46-7.06; $P < .001$). OS was significantly lower in patients with “ILD inconsistent with UIP” pattern (HR, 2.66; 95% CI,

1.19-5.97; $P = .014$) or in those with “ILD with possible UIP or UIP” patterns (HR, 2.38; 95% CI, 1.76-3.21; $P < .001$) than in those with non-ILD (Figure 2). Among those with ILD on HRCT evaluation, there was no

FIGURE 2. OS in patients with clinical stage I non–small cell lung cancer with or without ILD. In all patients, the 3-year OS rates of 93.3%, 82.1%, and 64.5% were observed among patients with non-ILD, inconsistent UIP patterns, and possible UIP or UIP patterns, respectively. *OS*, Overall survival; *ILD*, interstitial lung disease; *UIP*, usual interstitial pneumonia.

TABLE 2. Comparison of the clinical characteristics between patients who underwent lobectomy and those who underwent sublobar resection

Variables	Lobectomy (n = 57)	Sublobar resection (n = 50)	P value
Age, y	70.5 (58-85)	75 (62-92)	.14
Sex			
Male	46 (80.7%)	38 (76.0%)	.64
Smoking history			
Yes	48 (84.2%)	38 (76.0%)	.33
Clinical T			
T1	30 (52.6%)	44 (88.0%)	<.001
T2	27 (47.4%)	6 (12.0%)	
ILD pattern			
Inconsistent with UIP	24 (42.1%)	23 (46.0%)	.84
Possible UIP	19 (33.3%)	14 (28.0%)	
UIP	14 (24.7%)	13 (26.0%)	
%VC	90.6 (54.7-122.2)	92.1 (42.5-119.7)	.42
FEV1, %	73.8 (49.0-91.1)	76.2 (31.6-93.5)	.11
%DLCO	59.5 (25-99)	50 (16-103)	.88
Serum KL-6	421 (161-2639)	393 (113-3115)	.80
Histology			
Adenocarcinoma	28 (49.1%)	26 (52.0%)	.74
Squamous cell carcinoma	20 (35.1%)	17 (34.0%)	
Others	9 (15.8%)	7 (14.0%)	

Values are n (%) or median (range). *ILD*, Interstitial lung disease; *UIP*, usual interstitial pneumonia; *VC*, vital capacity; *FEV1*, forced expiratory value in 1 second; *DLCO*, diffusion capacity of the lung for carbon monoxide; *KL-6*, Krebs von den Lungen-6.

significant difference in OS between patients with “ILD inconsistent with UIP” pattern versus those with “ILD with possible UIP or UIP” patterns ($P = .069$).

Comparison of Outcomes Between Lobectomy and Sublobar Resection in Patients With ILD

Table 2 shows preoperative clinical factors between patients who underwent lobectomy and those who underwent sublobar resection. Eighteen (36%) sublobar resections were intended for patients who were not considered surgically fit to undergo lobectomy. Patient clinical characteristics were comparable between groups, except at the clinical stage. Pathologic stages are shown in Table E2. Operation

TABLE 3. Short-term outcomes after lobectomy or sublobar resection in patients with clinical stage I non–small cell lung cancer with interstitial lung disease

Variables	Lobectomy (n = 57)	Sublobar resection (n = 50)	P value
Operation time, min	164 (86-387)	126 (33-309)	.001
Postoperative acute exacerbation ($\leq$ POD 30)	3 (5.7%)	3 (6.0%)	1.0
Postoperative complication ($\geq$ grade 3)	5 (8.8%)	1 (2.0%)	.21
90-d mortality	3 (5.7%)	2 (4.0%)	1.0

POD, Postoperative day.

time was significantly longer for lobectomy than for sublobar resection (164 minutes vs 126 minutes, $P = .001$; Table 3). The short-term outcomes were comparable between lobectomy and sublobar resection. The incidences of postoperative acute exacerbation of ILD within 30-day and 90-day postoperative mortality were similar between lobectomy and sublobar resection (5.7% vs 6.0% exacerbation and 5.7% vs 4.0% 90-day mortality; $P = 1.0$ and $P = 1.0$, respectively; Table 3). The incidence of grade 3 or greater postoperative complications was greater after lobectomy than that after sublobar resection; however, this difference was not statistically significant (8.8% vs 2.0%, $P = .21$; Table 3).

Among patients with ILD, no significant difference in OS was observed between lobectomy and sublobar resection ($P = .19$; Figure 3, A). In patients with clinical stage IA NSCLC and ILD, no statistically significant difference in OS was observed between lobectomy and sublobar resection ($P = .87$; Figure 3, B). In patients with “ILD inconsistent with UIP” pattern, OS was similar between lobectomy and sublobar resection ($P = .91$; Figure 3, C). In patients with “ILD with possible UIP” or “ILD with UIP” patterns, OS was greater after sublobar resection than after lobectomy; however, this difference was not statistically significant ($P = .11$; Figure 3, D). Cox proportional hazard models including operative procedure, age, sex, clinical stage, ILD pattern, percent vital capacity, forced expiratory value in 1 second, and percent diffusing capacity of the lung for carbon monoxide (%DLCO) demonstrated that the %DLCO was an independent prognostic factor for OS (HR, 0.95; 95% CI, 0.91-0.99; $P = .009$; Table 4).

Cancer-specific survival was not significantly different between patients who underwent lobectomy and those who underwent sublobar resection ($P = .88$; Figure E1). Death occurred in 18 of 57 patients who underwent lobectomy (6 from lung cancer, 8 from respiratory failure, and 4 from other causes) and 9 of 50 patients who underwent sublobar resection (3 from lung cancer, 5 from respiratory failure, and 1 from other cause).

DISCUSSION

The present study aimed to explore the outcomes of sublobar resection and lobectomy for patients with early NSCLC with ILD. OS was not statistically different between lobectomy and sublobar resection in patients with clinical stage I NSCLC with ILD, even when stratified by radiographic ILD patterns. Radiologic ILD patterns defined according to the ATS/ERS/JRS/ALAT classification were consistent with the incidence of pathologically proven UIP patterns in the present study. However, 35.5% of patients with radiographic ILD did not have the evidence of ILD pathologically. One of the possible reasons for the discrepancy is that the resected specimens did not always include the radiographic ILD lesions.

FIGURE 3. OS between lobectomy and sublobar resection in patients with clinical stage I NSCLC and ILD. A, In all patients, the 3-year OS rates of 67.1% and 81.9% were observed between patients who underwent lobectomy and those who underwent sublobar resection, respectively ($P = .19$). B, In patients with clinical stage IA NSCLC with ILD, the 3-year OS rates of 76.9% and 80.2% were observed between patients who underwent lobectomy and those who underwent sublobar resection, respectively ($P = .87$). C, In patients with inconsistent UIP pattern, the 3-year OS rates of 81.1% and 83.6% were observed between patients who underwent lobectomy and those who underwent sublobar resection, respectively ($P = .91$). D, In patients with possible UIP or UIP pattern, the 3-year OS rates of 50.5% and 81.0% were observed between patients who underwent lobectomy and those who underwent sublobar resection, respectively ($P = .11$). *ILD*, Interstitial lung disease; *OS*, overall survival; *UIP*, usual interstitial pneumonia.

The surgical outcomes were compared between lobectomy and sublobar resection in the current study. Although the incidence of postoperative acute exacerbation and 90-day mortality was similar between the procedures, severe postoperative complications were less common in the sublobar resection group compared with those in the lobectomy group; however, this difference was not statistically significant but could be clinically important. Several studies have reported that sublobar resection reduces the incidence of postoperative acute exacerbation of ILD, postoperative complications, and short-term mortality in patients with lung cancer with or without ILD.^{4,6,8,16} Our results partially corroborate those of previous studies, indicating that sublobar resection may have an advantage in terms of short-term outcomes in patients with NSCLC with ILD.

Although no significant difference in OS was observed between lobectomy and sublobar resection in patients with clinical stage I NSCLC and ILD, 3-year OS was better

for sublobar resection (81.9%) than lobectomy (67.1%). A larger number of patients and longer follow-up will be needed for a more definitive prospective study. In the exploratory subgroup analyses, OS was similar between procedures in patients with “ILD inconsistent with UIP” patterns, whereas OS was better after sublobar resection without statistically significant difference in patients with “ILD with possible UIP or UIP” patterns. A previous multi-institutional retrospective study reported that wedge resection resulted in worse long-term survival than lobectomy in patients with stage IA NSCLC and ILD.⁵ However, the same study reported the prognosis by pathologic stage including wedge resection without lymph node dissection, which may result in stage migration and explain the apparent inconsistency in the results of our study. When comparing the outcomes between operative procedures in retrospective studies, preoperative factors should be used because the choice of the surgical procedure is not

TABLE 4. Uni- and multivariable Cox proportional hazard model for overall survival in patients with clinical stage I non–small cell lung cancer with ILD

Variables	Univariable		Multivariable	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Procedure				
Lobectomy (vs sublobar resection)	1.82 (0.81-4.06)	.15	2.76 (0.83-9.16)	.099
Age	1.05 (0.99-1.11)	.12		
Sex				
Female (vs male)	0.74 (0.28-1.94)	.54		
Clinical T				
T2 (vs T1)	2.12 (0.98-4.59)	.057		
ILD pattern				
UIP or possible UIP (vs inconsistent with UIP)	2.42 (1.07-5.44)	.033	3.79 (0.97-14.8)	.055
%VC*	0.97 (0.95-0.99)	.007		
FEV1, %*	1.01 (0.98-1.05)	.52		
%DLCO*	0.97 (0.94-1.00)	.035	0.95 (0.91-0.99)	.009

CI, Confidence interval; ILD, interstitial lung disease; UIP, usual interstitial pneumonia; VC, vital capacity; FEV1, forced expiratory value in 1 second; DLCO, diffusion capacity of the lung for carbon monoxide. *Continuous variables.

determined by postoperative factors. Although we compared the procedure in a preoperative setting, it was not possible to avoid selection bias because of the retrospective nature of the present study.

Because sublobar resections were performed predominantly for smaller tumors in the present study, we performed a subanalysis to compare the prognosis of clinical stage IA NSCLC between the procedures, which revealed that OS was similar between patients who underwent lobectomy and those who underwent sublobar resection. In addition, we used multivariable Cox analysis to adjust for potential bias and demonstrated that only %DLCO was an independent prognostic factor for OS and not the surgical procedure. Previous studies have reported that %DLCO is associated with long-term survival after lung resection for lung cancer.²⁰⁻²² Our result is consistent with these previous studies and indicates the preservation of DLCO may be important, particularly in patients with NSCLC with ILD, who generally have poor pulmonary function compared with patients without ILD. These patients may be potential candidates for sublobar resection despite being fit for lobectomy. When we focused on the oncologic effect of sublobar resection, cancer-specific survival was similar between the procedures.

The present study has some limitations. This was a single-institution retrospective study, and patients who underwent sublobar resection may be highly selected. The potential selection bias should be taken into account to evaluate the short-term or long-term results in this study. One half of the sublobar resections reported here were wedge resections without nodal dissection. The difference in outcomes between segmentectomy and wedge resection should be examined prospectively in the future. Relatively short follow-up period and small numbers of patients in this study may substantially impact the study power. Therefore, longer follow-up is needed to conclude the long-term results.

In conclusion, sublobar resection for clinical stage I NSCLC with ILD seems to be feasible with acceptable short- and long-term outcomes compared with lobectomy, suggesting that sublobar resection may be a potential alternative surgical procedure. The findings of the present study warrant further prospective studies that compare lobectomy and sublobar resection for clinical stage I NSCLC with ILD.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: interstitial lung disease, interstitial pneumonia, lobectomy, non-small cell lung cancer, segmentectomy, sublobar resection, wedge resection

FIGURE E1. Comparison of CSS between lobectomy and sublobar resection in patients with clinical stage I non–small cell lung cancer and interstitial lung disease. The 3-year CSS rates of 88.3% and 91.0% were observed between patients who underwent lobectomy and those who underwent sublobar resection, respectively ($P = .88$). OS, Overall survival.

TABLE E1. Pathologic findings of resected specimens

Variables	Total (n = 107)	Inconsistent with UIP		
		(n = 47)	Possible UIP (n = 33)	UIP (n = 27)
UIP	25 (23.4)	0 (0)	7 (21.2)	18 (66.7)
Subpleural fibrosis	14 (13.1)	4 (8.5)	8 (24.2)	2 (7.4)
Organizing pneumonia	6 (5.6)	4 (8.5)	2 (6.1)	0 (0)
Granulomatosis	4 (3.7)	1 (2.1)	1 (3.0)	2 (7.4)
Asbestosis	1 (0.9)	0 (0)	0 (0)	1 (3.7)
Eosinophilic pneumonia	1 (0.9)	0 (0)	0 (0)	1 (3.7)
Hemorrhage	1 (0.9)	1 (2.1)	0 (0)	0 (0)
Emphysema	16 (15.0)	7 (14.9)	8 (24.2)	1 (3.7)
Multifocal AAH	1 (0.9)	1 (2.1)	0 (0)	0 (0)
No evidence of disease	38 (35.5)	29 (61.7)	7 (21.2)	2 (7.4)

Values are n (%). UIP, Usual interstitial pneumonia; AAH, atypical adenomatous hyperplasia.

TABLE E2. Pathologic stages between lobectomy and sublobar resection

Pathologic stage	Lobectomy (n = 57)	Sublobar resection (n = 50)
IA	20 (35.1)	18 (36.0)
IB	22 (38.6)	6 (12.0)
IIA	5 (8.8)	0 (0)
IIB	4 (7.0)	0 (0)
IIIA	5 (8.8)	1 (2.0)
IIIB	1 (1.8)	0 (0)
X*	0 (0)	25 (50.0)

Values are n (%). *Cases of wedge resection; due to no lymph node dissection/sampling.